B-CAST

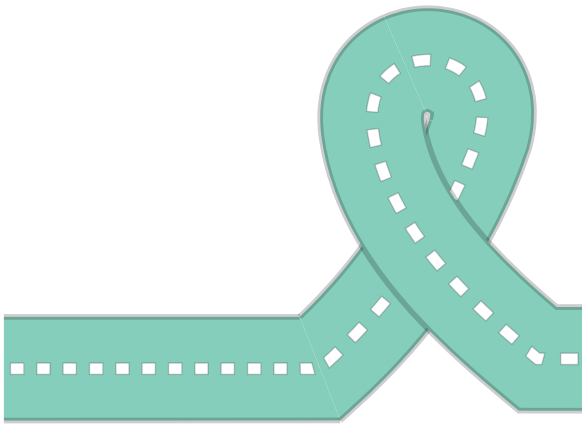
phg foundation
making science work for health

Personalising prevention for breast cancer

Workshop programme

Lucy Cavendish College, Cambridge

19 - 21 September 2018



UNIVERSITY OF CAMBRIDGE

About our work for B-CAST

B-CAST is a European Commision funded research project with an overall aim of gaining a better understanding of the environmental and biological factors that influence breast cancer development and prognosis. Building a better understanding of the influence of different risk factors on specific subtypes of cancer can, ultimately, help clinicians target prevention and treatment strategies to deliver improved health outcomes for patients.

As part of this project, PHG Foundation is leading work to examine the potential for developing personalised prevention for breast cancer within national health systems.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 633784

Agenda

The objective for this workshop is to develop a vision for a more personalised prevention pathway for breast cancer. For the first part of the workshop we consider the next 5 years, for the second part we take the longer view and consider how the pathways could look in 20 years.

Day 1 19 September 2018

12:00	**Registration and lunch, Warburton Hall terrace**
13:30	**Welcome and introductions** *Dr Hilary Burton* PHG Foundation
14:00	**Current landscape of personalised prevention** *Dr Sowmiya Moorthie* PHG Foundation
14:30	**Health promotion in the context of breast cancer prevention** *Professor Anthony Howell* University of Manchester
15:00	**What do we know about changing health related behaviour? The (limited) role of personalised risk information, and more promising intervention approaches** *Professor David French* University of Manchester
15:30	**Break**
15:45	**Clinical utility of preventive interventions aimed at moderate and high risk individuals** *Professor Rita Schmutzler* University Hospital Cologne

Agenda

16:15	**Risk categorisation in breast cancer** *Professor Montserrat Garcia-Closas* National Cancer Institute, USA
16:45	**Discussants**
17:30	**Round-up and instructions for next day**
17:45	**Room check-in and free time**
19:00	**Pre-dinner drinks**
19:30	**Dinner**

Day 2 20 September 2018

09:00	**Recap and aims for the day** *Dr Sowmiya Moorthie* PHG Foundation
09:30	**Break-out sessions (working coffee)**
11:00	**Feedback from breakout sessions**
12:15	**Group discussion**
13:00	**Lunch**

Agenda

14:00	**Introduction to session** *Dr Sowmiya Moorthie* PHG Foundation
14:30	**The future outlook - epidemiology of breast cancer** *Professor Paul Pharoah* University of Cambridge
15:00	**Break**
15.30	**Biomarkers in personalised breast cancer prevention** *Dr Esther Lips* Netherlands Cancer Institute
16:00	**Biosensors for cancer diagnosis and patient stratification: electrochemical protein and DNA sensors** *Dr Pedro Estrela* University of Bath
16:30	**Summary and close** *Dr Hilary Burton* PHG Foundation
17:00	**Free time**
19:00	**BBQ** Optional walk into town for post dinner drink

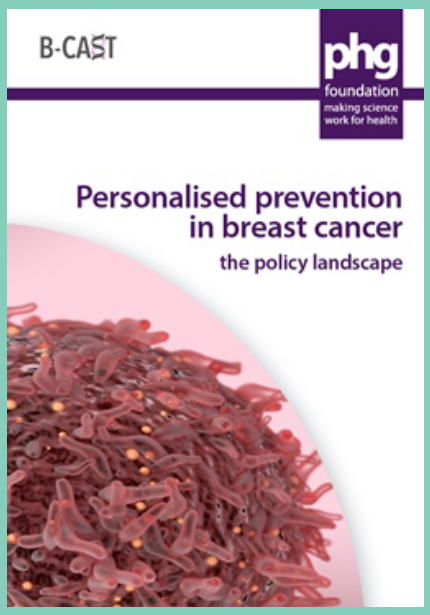
Agenda

Day 3 21 September 2018

09:00	**Recap and aims for the day** *Dr Hilary Burton* PHG Foundation
09:15	**The role of wearables and apps in prevention** *Louise Brennan* Beacon Hospital Dublin, University College Dublin
09:35	**How digital disintermediation (apps) and cloud computing change the precision prevention landscape** *Professor Jonas Almeida* National Cancer Institute, USA
09:55	**Issues arising from the introduction of new technologies** *Dr Hilary Burton* PHG Foundation
10:15	**Break**
10:45	**Breakout session**
12.00	**Next steps**
13:00	**Lunch and departure**

The policy landscape

A vision for the future starts with an understanding of the present. We have undertaken an analysis of current approaches to breast cancer prevention and the discourse around personalised breast cancer prevention, with focus on primary and secondary prevention programmes.



Key finding

Personalised prevention as a concept has gained traction in many government policy documents as evidenced by the commitment to develop methods to enable it. However, our review of the literature finds little discussion on specific mechanisms to deliver personalised prevention or a vision in this area especially in relation to breast cancer.

Personalised prevention in breast cancer - the policy landscape

In our report we set out our analysis of current approaches to breast cancer prevention and the discourse around personalised breast cancer prevention. The analysis focuses on primary and secondary prevention programmes i.e. prevention of disease development (through health promotion) and early detection (screening). We examined policy and prevention activities at an international level wherever possible, with specific emphasis on three key countries (United Kingdom, Netherlands and Australia) to act as case studies. Although the focus is on breast cancer, it was viewed within the wider context of prevention activities for other chronic diseases.

The policy landscape

Preventative strategies

The goal of most breast cancer control programmes is to reduce the incidence and mortality from the disease. Due to the paucity of specific interventions proven to reduce incidence of disease, most breast cancer control programmes focus on early detection and screening. As part of these programmes, health education activities aim to raise awareness about risk factors, breast health and screening in order to ensure effective early detection and diagnosis. These activities also allow for identification and management of women at high risk due to family history or genetic predisposition. Provision of interventions and the management of such individuals is guided by risk assessment, which can be undertaken using a variety of tools.

The prevention pathway

Examination of the global and national policy landscape indicates that there is recognition that breast cancer is an important cause of mortality and morbidity, and improving primary prevention is a goal of many policy makers.

The main approach to prevention is through health promotion that informs and empowers individuals to reduce their own risk. However, these messages are not targeted at specific at-risk groups or modulated in any way. Policy documents aimed at general health often do not identify breast cancer as a disease for which risk could be reduced. Whilst preventative strategies are available for those at high or moderate risk as a result of genetic factors or family history, identification of these women is not systematic. In most countries pathways of care are most well established for those who are considered high risk due to possessing *BRCA1/2* mutations.

Policy discourse

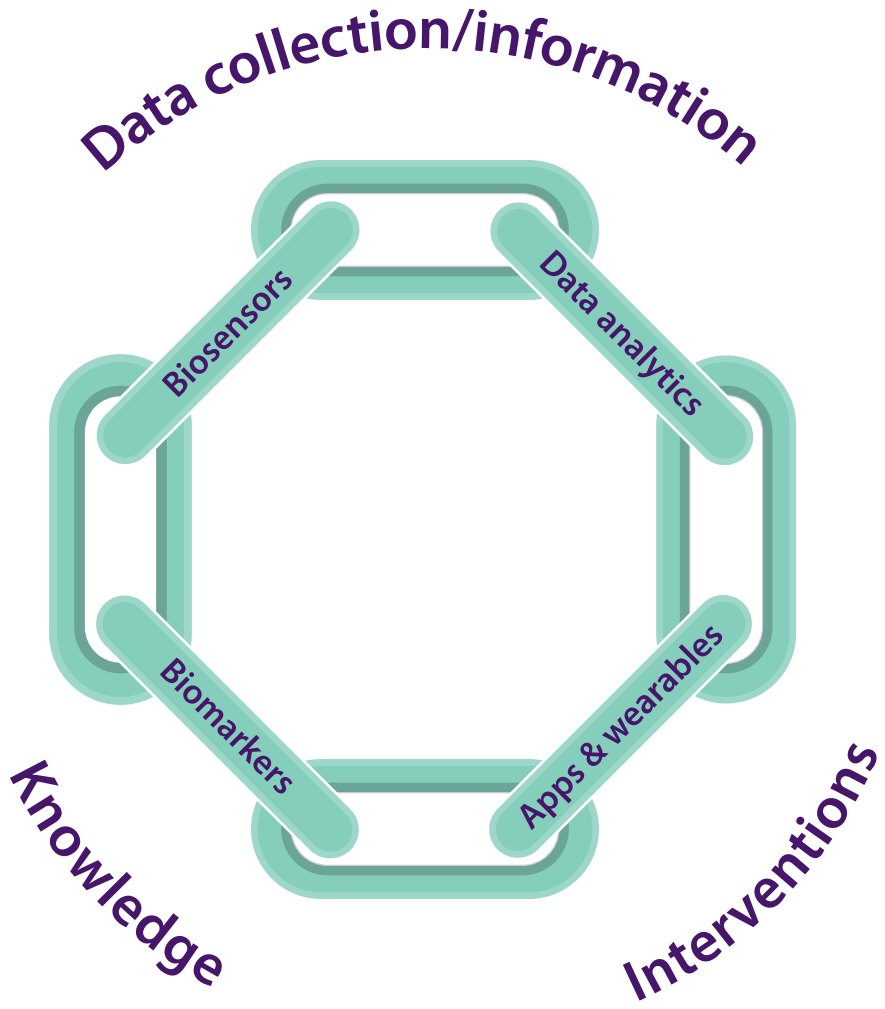
As can be seen in many policy documents, personalised prevention which aims to place individual citizens at the centre of care is often conflated with person-centred care. To some extent technologies that enable personalised prevention – especially those that are more patient facing – also enable person-centred care. A distinction we make in our report is that personalised prevention is based on biological stratification of individuals as well as consideration of their individual wishes and values.

Personalised prevention as a concept has gained traction in many government policy documents as evidenced by the commitment to develop methods to enable it. However, there is little discussion on specific mechanisms to deliver personalised prevention and a lack of vision, especially in relation to breast cancer. Personalised prevention in relation to breast cancer is only discussed in the context of risk stratified screening.

The full report can be downloaded at:

www.phgfoundation.org/report/personalised-prevention-in-breast-cancer-policy

Perspectives on the future



Developing a vision of what personalised prevention might look like 20 years into the future can help us to identify the issues it raises for individuals, health systems and society. This workshop aims to contribute to that process, with discussion of how these interrelated technologies are likely to change our approach to breast cancer prevention.

Novel technologies for breast cancer prevention pathways

A wide range of emerging technologies are showing considerable potential for improving healthcare through enabling personalised approaches at different stages of care and disease prevention pathways.

Currently, health promotion and screening are the predominant vehicles for breast cancer prevention and, in the main, are targeted at large sub-sets of the population. This means they do not take into account detailed biological characterisation of individuals or provide tailored prevention pathways.

We know that the development of breast cancer is influenced by many different factors, which are likely to vary between individuals, and that breast cancer is not one disease but has many sub-types with different outcomes. Can we create prevention pathways that take these factors into consideration?

In this section we provide some perspectives on particular technology areas to stimulate discussion on the vision for the future. These perspectives have been developed together with experts in these fields with the aim of stimulating discussion about the 20 year horizon. The broad areas considered are:

- Biomarkers
- Biosensors
- Apps and wearables
- Data analytics

There is some way to go in gathering the scientific knowledge and technical capabilities sufficient to optimising the impact of these technologies. Nevertheless, it is important to reflect on their potential in order to visualise how prevention pathways could differ in the future and how health systems will need to adapt to move towards more personalised prevention pathways.

We'd like to thank Dr. Esther Lips, Dr. Pedro Estrela, Professor Brian Caulfield, and Professor Jonas Almeida for their work on these think pieces.

Biomarkers in breast cancer prevention pathways

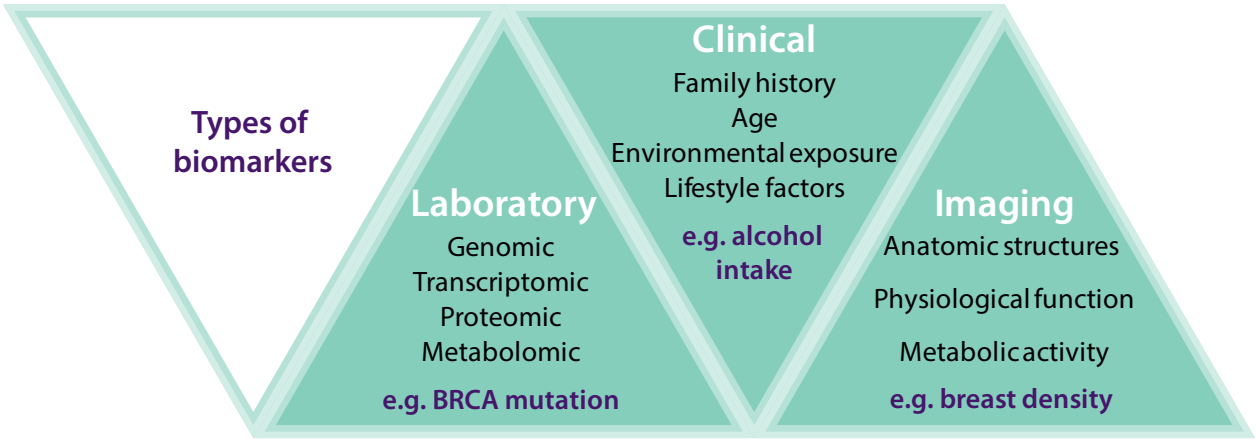
What is a biomarker?

A biomarker is anything that can be measured in an individual to predict incidence or outcome of a disease. They can consist of simple measures such as clinical features (e.g. age) to more complex factors such as biochemical or imaging markers.

What are they useful for?

Biomarkers have many uses in healthcare including identifying those at increased risk of disease, screening, diagnosis and guiding management and treatment of patients. To be useful in a clinical context, biomarkers need to be measurable with a high degree of accuracy and reproducibility, and must be clinically meaningful. Different biomarkers or combinations of biomarkers are relevant in different contexts.

Biomarkers are an important mechanism through which to stratify individuals to offer particular preventative options. They are already in use within current breast cancer prevention pathways. For example, age is one marker considered when offering routine mammography screening while genes such as *BRCA1/2* are used as markers to identify high risk individuals and inform decisions on more specific prevention pathways such as enhanced screening, chemoprophylaxis and mastectomy.



Perspectives on the future

Emerging developments

Knowledge of biomarkers in relation to breast cancer is increasing, with research endeavours such as B-CAST examining various markers that may be used in assessing an individual's risk of developing the disease. These could be important in identifying the specific sub-type of breast cancer they may develop.

Other efforts include the PRECISION project, in which researchers are defining which ductal carcinoma *in situ* (DCIS); a lesion that sometimes develops into breast cancer will need treatment and those that will not, based on a deep characterization of various molecular and imaging markers.

Parallel developments are being made in the characterisation of novel and existing biomarkers. For example, there are currently attempts to identify blood-borne tumour markers which could be used for early disease detection. This includes techniques to isolate and analyse circulating tumour DNA, proteomic or metabolic signatures and volatile organic compounds in the breath that may be indicative of disease development.

Meanwhile, improving progress in the range, utility and accuracy of biosensors and their incorporation into wearable and digital tools, could be used for precise collection of data on biomarkers which are more difficult to measure, such as lifestyle and environmental factors. Better knowledge of these factors could improve risk assessment processes and contribute to more refined preventative pathways.

Points for reflection

The future of personalised prevention for breast cancer will be very different in the light of further development and knowledge on biomarkers. How will this knowledge be used in prevention?

- Do we see a future in which women undergo yearly blood tests to identify and examine circulating tumour DNA rather than participating in mammographic screening?
- What are likely to be the different preventative pathways developed for different sub-types of breast cancer?
- Which biomarkers are likely to be incorporated into preventative pathways over the next 20 years?

Biosensors in breast cancer prevention pathways

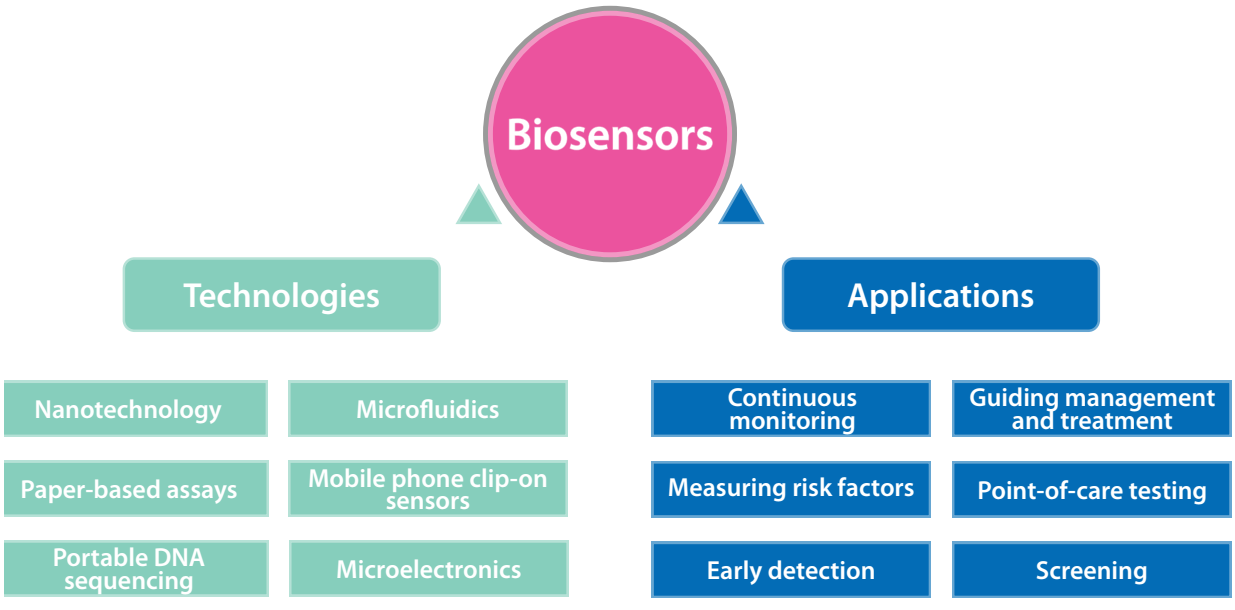
What are biosensors?

Biosensors are integrated devices that detect and/or quantify biomolecules. They typically contain a biochemical recognition element coupled with a transmission method (transducer) that generates signals that are interpreted and conveyed to the individual through a user-friendly biosensor reader device. The biochemical receptors may use enzymatic, immune, DNA or whole-cell detection methods, and may be transmitted by electrical, optical or thermal signals.

What are they useful for?

Biosensors enable identification and monitoring of biological, chemical or physical biomarkers. As such, they play an important role in aiding the identification of those at increased risk of disease, screening, diagnosis and guiding management and treatment of patients.

There are many different types of sensors already in use by individuals and healthcare systems. Thermometers, pregnancy tests, blood-oxygen saturation monitors and glucose sensors are examples of biosensors that have been used for many years by health systems and individuals.



Perspectives on the future

The future for biosensors

Progress in nanomaterials and wireless technology in particular are enabling advances in the miniaturisation and connectivity of implantable biosensors. This has led to a proliferation in the development of devices for near patient testing and monitoring. Several techniques, such as electrochemical sensors, can be used for the development of portable, low cost, easy to use devices.

Early diagnosis

Current screening and early detection techniques have limitations. New advanced biosensors could provide solutions through their capability to analyse a wider range of biomarkers or by provision of new modalities for detection. The correlation between different biomarkers is still in its infancy and considerably more work needs to be done in this field. Nonetheless there is clear evidence that blood tests (and possible urine tests) that measure a panel of biomarkers, either proteins, microRNAs, or circulating tumour DNA can provide accurate early detection of breast cancer and be good tools for routine monitoring of those at increased risk or in treatment.

Continuous monitoring

In principle, the continuous monitoring capabilities offered by biosensors could be used to detect biomarkers for pre-clinical disease in presumptively healthy individuals. However, until gaps in our knowledge and understanding of disease-specific biomarker patterns are addressed, this remains a more distant prospect for biosensor technology.

One of the main limitations of non-implantable sensors for continuous monitoring is the availability of biomarkers in fluids such as sweat or dermal interstitial fluid. Many chronic diseases biomarkers are not present or present only in very low concentrations in fluids than can be extracted through the skin.

Beyond disease-specific applications, biosensors could be used to continuously measure biological risk factors, such as those which are common to a number of preventable and non-communicable diseases such as cardiovascular disease and cancer. Communicating quantifiable biological risk factors to individuals via apps and wearable devices (mHealth) has the potential to empower individuals to engage with their health and modulate their disease risk to enable a more personalised approach to disease prevention.

Points of reflection

How can biosensors help personalise prevention pathways? Can we see a future in which they provide a rapid, simple and cost-effective route for early diagnosis or monitoring? How will our ability to monitor a range of biomarkers more easily impact on prevention of breast cancer?

- In which settings (i.e. primary care, screening etc.) are emerging biosensors likely to have the most impact over the next 20 years?
- Are we going to see a future where continuous monitoring becomes part of the prevention pathway for breast cancer?
- What type of biomarker information is likely to be most relevant in different settings?

Apps and wearables in breast cancer prevention pathways

What are apps and wearables?

Apps and wearables can both be categorised as mHealth technologies, with the broad purpose of tracking behaviours, providing information, capturing data and providing personalised feedback. Wearables generally comprise miniature biomedical sensing technologies to capture a range of biometric markers of behaviour and performance over time. This information can be stored and fed back to the wearer via software such as apps and online platforms. Apps are programmes created for smart devices such as phones and tablets, that offer a range of health related services. Although apps and wearables are often employed together, they can be used as standalone technologies.

What are apps and wearables useful for?

Apps and wearables are already a popular means of health and lifestyle monitoring and are commonly used as physical activity trackers or diet aids. However, many currently lack the accuracy and regulatory oversight neccessary for use within the healthcare system and are generally aimed at consumers. Apps and wearables targeting breast cancer are available and range from those that focus solely on providing information to ones that provide tools for prevention or early detection.

One sphere where there is already widespread use of mhealth is patient-facing healthcare administration, such as in automated appointment reminders and booking applications (e.g. automated reminders). However, the use of such applications in delivering patient care is increasing. For example through devices such as glucose monitors and the ActiPatch – an NHS approved device for chronic pain management.

The future for wearables and apps

Apps and wearables offer an effective means of capturing and visualising biomedical data for individual or health system use. However, merely capturing the data and presenting it back to the user is not enough. In addition to making the information available to users in an accessible fashion is the need for tools that enable individuals and clinicians to act on this information.

Perspectives on the future

We are now entering an interesting phase of development where researchers and industry are coming together to develop the data analytics, visualisation and feedback concepts to provide this functionality to users. Future applications will be enhanced through more precise biomarker information generated by smarter sensors embedded in less obtrusive wearables e.g. second skin sensors, ingestibles and implantables. Techniques such as integration of advanced machine learning models for personalisation and context aware explainable recommendations for users are being developed in order to maximise functionality and thereby the value to users.

In anticipation of the potential clinical benefits of apps and wearables, healthcare systems are already investigating the inclusion of data generated from such devices into health records. Consequently, in the future it is likely that such information will play an important role in diagnosis, and monitoring responses to therapeutic interventions.

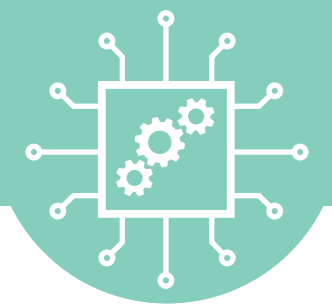
For breast cancer prevention, it is envisaged that this data could be leveraged to provide tailored information or specific interventions - for example through individualised behaviour change programmes. Monitoring individual biomedical data may also provide an alternate means of early disease detection or identification of those at higher risk.

The field of apps and wearables is relatively new and their full potential across the healthcare spectrum is yet to be realised. Enabled by the creation of devices that not only provide data on health status but also leverage this information to encourage behaviour change to improve health status, this is likely to change.

Points for reflection

The future of personalised prevention for breast cancer will be very different in the light of further development and increasing use of apps and wearables. How will this knowledge be used in prevention? For example:

- What types of wearables and apps do we see having the greatest impact on breast cancer prevention pathways?
- Could risk assessment via apps be an integral part of the prevention pathway?
- Could monitoring of information from wearables and apps be part of early detection programmes for breast cancer?



Data analytics in breast cancer prevention pathways

What is data analytics?

In broad terms data analytics can be thought of as the processes used to examine and derive conclusions from data. Analysis may be confined to single small datasets or to large volumes of diverse data (big data). Processes for data analysis are dependent on the type, volume and source of material.

What is data analytics useful for?

Data analysis is essential to understanding health and disease and has always played an important role in healthcare delivery at the individual and population level. For example, analysis of information from single or multiple biomarkers can contribute to clinical decision making by providing a diagnosis or identifying individuals at increased risk of disease through predictive analytics. Population disease surveillance relies on data analysis to identify and respond to healthcare emergencies.

Data analytics is already used in prevention of breast cancer. One application is in the development of models that predict risk of disease in individuals by bringing together diverse sets of information (e.g. age, family history etc.). It is also an important part of genomic analysis, which enables identification of individuals at high risk of disease.

The future for data analytics

Many factors are impacting on the prospective use of data analytics in healthcare. The volume, variety and velocity at which we are accumulating health related data is increasing. This is being enabled by the digitisation of healthcare as systems move towards the use of electronic healthcare records, increasing knowledge of biomarkers and development of tools to monitor these through biosensors, wearables and apps.

There is a concomitant rise in interaction of individual citizens with data and information through their access to and use of consumer health devices. This, together with improvements in interoperability and use of electronic health records and the internet-of-things is likely to lead to more interactive or connected repositories of data.

Perspectives on the future

The increased use of data requires infrastructure and automated processes for collection, storage, sharing and analysis. Mechanisms to process data can take the form of simple or sophisticated algorithms or machine learning techniques that are less reliant on explicit human programming. The latter is a means of building artificial intelligence (AI) systems based on analysis of large data sets that can perform tasks which would normally require human intelligence (e.g. visual recognition).

Algorithms or machine learning techniques can increase the efficiency with which particular tasks are carried out. This can improve prevention pathways by enabling the inclusion of a wider range of biomarkers. For example, breast density is a key risk factor for breast cancer but current analytical techniques can be onerous - a trained machine learning algorithm could dramatically improve turnaround times. An example of more sophisticated use would be the incorporation of machine learning techniques to develop more accurate predictive AI models for estimating risk.

Sophisticated integrative analysis, together with developments in apps, may enable tailored messages to be delivered to individuals, after taking into account a diverse array of information. In addition, researchers are envisaging the development of individualised coaching programmes created by AI systems based on analysis of behavioural and predictive models.

Points for reflection

Two overarching trends are changing the way data is analysed. One is the increasing use of artificial intelligence, where the ability to model risk is achieved by methods that are more powerful but also not immediately amenable to interpretation (black box models). The other trend is the availability of these models in mobile devices, enabling an unprecedented level of personalised risk assessment.

- Consumer-facing tests, including genomics, continue to become more affordable. Will this change the way participant data is acquired for risk assessment?
- The ability to deliver advanced machine learning models onto mobile devices is disintermediating the health care system. Who will be the new stakeholders for precision prevention?
- We do envisage patients taking a much more active role in devising their own prevention pathways. How will clinicians configure access to information from a variety of sources in order to promote effective responses to real-time analytical results?

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PHG Foundation is a health policy think tank with a special focus on how genomics and other emerging health technologies can provide more effective, personalised healthcare

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