Horizon 2020

Tailored screening as a research challenge

Mireille Broeders
30 January 2014, Bologna

Dept for Health Evidence, Radboudumc & National Expert and Training Centre for Breast Cancer Screening, Nijmegen, The Netherlands

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Finding the right balance

ANALYSIS

Maximising benefit and minimising harm of screening

Gordon Brown has pledged to increase screening services in the NHS. **Muir Gray, Julietta Patnick,** and **Roger Blanks** show how experience with the UK breast screening programme can help ensure that they are effective

All screening programmes do harm; some do good as well, and, of these, some do more good than harm at reasonable cost. The first task of any public health service is to identify beneficial programmes by appraising the evidence. However, evidence of a favourable balance of benefit to harm in a research setting does not guarantee that a similar balance will be reproduced in practice, so screening programmes need to be introduced in a way that allows their quality to be measured and continuously improved.

J A Muir Gray director, National Knowledge Service, Oxford OX3 7LG
J Patnick director, NHS Cancer Screening Programmes, Sheffield
R G Blanks epidemiologist, Institute of Cancer Research, Sutton, Surrey
Correspondence to: J A Muir Gray muir.gray@medknox.net
Accepted: 13 September 2007

The policy decision

the professions and the women to be offered screening, to deliver the programme within a specific time and budget and to set out performance standards. To achieve its objectives the implementation team was given a discrete budget sufficient to fund the programme; authority to centralise certain aspects of screening, notably the multidisciplinary assessment of women with abnormal mammography results; and separate funds to set up four training centres, procure an information system, and prepare clear information for the women offered screening.

Each of the 14 regional authorities then in Eng-

British Medical Journal 2008

Finding the right balance

		Potential Benefits (vs. no screening)			Potential Harms	
Strategy	**Average Screens/ 1000**	**% Mortality Reduction**	**Deaths Averted/ 1000**	**Life Years Gained per 1000**	**# False positives/ 1000**	**# extra biopsies/ 1000**
Biennial						
B 40-69	**13865**	**16%**	**6.1**	**120**	**1250**	**88**
B 45-69	**11771**	**17%**	**6.2**	**116**	**1050**	**74**
B 50-69	**8944**	**15%**	**5.4**	**99**	**780**	**55**
B 55-69	**6941**	**13%**	**4.9**	**80**	**590**	**41**
B 60-69	**4246**	**9%**	**3.4**	**52**	**340**	**24**
Annual						
A 40-69	**27583**	**22%**	**8.3**	**164**	**2250**	**158**
A 45-69	**22623**	**22%**	**8.0**	**152**	**1800**	**126**
A 50-69	**17759**	**20%**	**7.3**	**132**	**1350**	**95**
A 55-69	**13003**	**16%**	**6.1**	**102**	**950**	**67**
A 60-69	**8406**	**12%**	**4.6**	**69**	**600**	**42**

Mandelblatt et al, Ann Intern Med 2009

Tailored screening?

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Tailored screening

Personalizing Mammography by Breast Density and Other Risk Factors for Breast Cancer: Analysis of Health Benefits and Cost-Effectiveness

John T. Schousboe, MD, PhD; Karla Kerlikowske, MD, MS; Andrew Loh, BA; and Steven R. Cummings, MD

Ann Intern Med 2011;155:10-20.

Stratifying women according to their risk of breast cancer – will **tailored screening** become the new screening paradigm?

Bevolkingsonderzoek naar borstkanker: verwachtingen en ontwikkelingen

Developments with potential promise in the medium-term

Population screening currently offers the same screening programme to all women in the target group. One appealing way of improving the risk-benefit ratio of screening would be to adapt this process to the individual risk of breast cancer involved. Using existing risk models, however, it is not possible to draw sharp distinctions on the basis of risk. Better risk assessment will probably be possible when more comprehensive models become available. Risk factors such as mammographic breast-tissue density and blood tests for genetic variants and sex hormones, in particular, may have added value. A great deal of research is currently focusing on candidate markers and the validity of new risk models. There are also questions regarding the logistics of risk stratification in the context of service screening, and the effects of providing intensive screening (younger starting age, additional screening method) to the high-risk group and less intensive screening to the low-risk group.

Breast cancer risk prediction model

- Several models are available, but all are missing one or more risk factors
- These models have not been used for targeting screening efforts in the context of population-based programmes
- Discriminatory power - the ability to differentiate between high- and low-risk groups – is still moderate

Breast cancer risk prediction model

Table 1. Known risk factors and their incorporation into existing risk models*

Variable	Relative risk at extremes†	Gail	Claus	BRCAPRO	IBIS	BOADICEA	Jonker
Personal information							
Age	30	Yes	Yes	Yes	Yes	Yes	Yes
Body mass index	2	No	No	No	Yes	No	No
Alcohol intake	1.24	No	No	No	No	No	No
Hormonal and reproductive factors							
Age at menarche	2	Yes	No	No	Yes	No	No
Age at first live birth	3	Yes	No	No	Yes	No	No
Age at menopause	4	No	No	No	Yes	No	No
Hormone replacement therapy use	2	No	No	No	Yes	No	No
Oral contraceptive pill use	1.24	No	No	No	No	No	No
Breast feeding	0.8	No	No	No	No	No	No
Plasma estrogen level	5	No	No	No	No	No	No
Personal history of breast disease							
Breast biopsies	2	Yes	No	No	Yes	No	No
Atypical ductal hyperplasia	3	Yes	No	No	Yes	No	No
Lobular carcinoma in situ	4	No	No	No	Yes	No	No
Breast density	6	No	No	No	No	No	No
Family history of breast and/or ovarian cancer							
First-degree relatives with breast cancer	3	Yes	Yes	Yes	Yes	Yes	Yes
Second-degree relatives with breast cancer	1.5	No	Yes	Yes	Yes	Yes	Yes
Third-degree relatives with breast cancer	1.3	No	No	No	No	Yes	No
Age of onset of breast cancer in a relative	3	No	Yes	Yes	Yes	Yes	Yes
Bilateral breast cancer in a relative	3	No	No	Yes	Yes	Yes	Yes
Ovarian cancer in a relative	1.5	No	No	Yes	Yes	Yes	Yes
Male breast cancer	3–5	No	No	Yes	No	Yes	Yes

* BOADICEA = Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm; IBIS = International Breast Cancer Intervention Study.

† Data from Evans and Howell (79).

Amir et al. JNCI 2010;102:680-91

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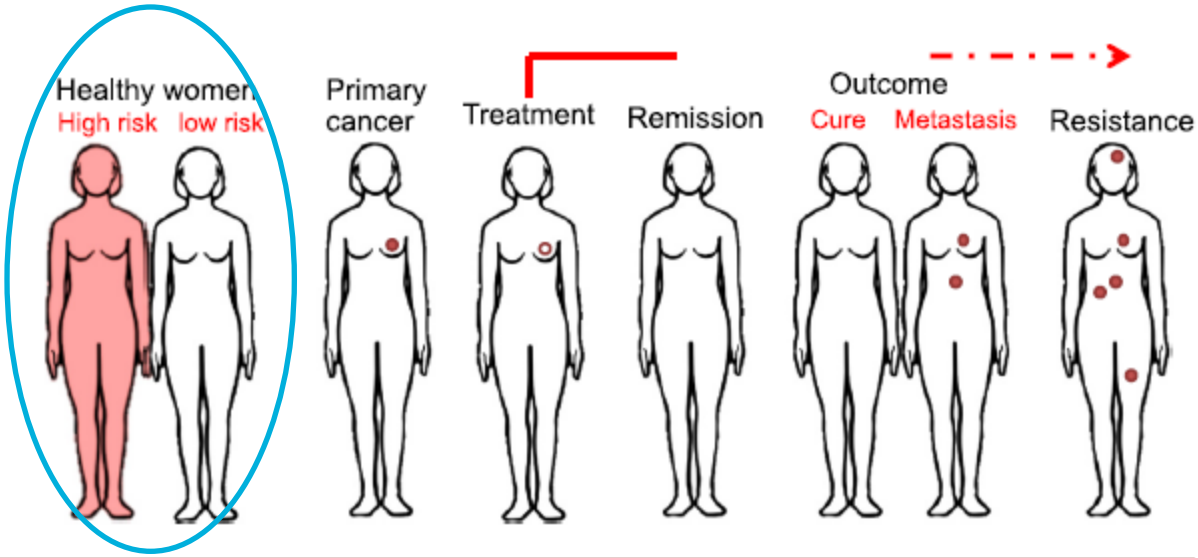
Breast cancer risk prediction model



SAMPLES	Blood /genomic DNA Normal breast tissue	Tumour -FNA/TMA Blood - ctDNA, CTC, metabolomics Marrow biopsy - DTC Multimodality imaging	Male/female Ethnically diverse Pre/post menopausal
		Metastases Blood - ctDNA, CTC, Metabolomics Multimodality imaging	

OUTPUT	• Biomarkers of risk • Effects of lifestyle changes/interventions • Early detection	• Molecular subtypes/staging • Known biomarkers (ER, HER2 etc) • Diagnostic biomarkers • Prognostic biomarkers • Response biomarkers • Treatment toxicity biomarkers • New cell lines and PDX	• Progression biomarkers • Changes in ER/HER2 etc • Metastasis genes • 'Organotropism' genes • Resistance biomarkers • New therapeutic targets • New cell lines and PDX

Eccles et al. Breast Cancer Res 2013;15:R92

Examples in Europe

- PROCAS

PROCAS study

The PROCAS study aims to predict breast cancer risk for women who attend routine NHS breast screening in Greater Manchester. A woman's risk will be assessed by collecting extra information on each of the most important breast cancer risk factors – family history, lifestyle factors, breast density and genetics.

Professor Gareth Evans is heading up a major new research study, which is being carried out throughout Greater Manchester. 60,000 women will be invited to join the study, and you can be part of it!

- KARMA

Research Article

Prevention Research

Assessing Individual Breast Cancer Risk within the U.K. National Health Service Breast Screening Program: A New Paradigm for Cancer Prevention

D. Gareth R. Evans[1,2], Jane Warwick[6], Susan M. Astley[3], Paula Stavrinos[1], Sarah Sahin[1], Sarah Ingham[4], Helen McBurney[2], Barbara Eckersley[1], Michelle Harvie[1], Mary Wilson[1], Ursula Beetles[1], Ruth Warren[7], Alan Hufton[3], Jamie C. Sergean

BJC

LETTER TO THE EDITOR

British Journal of Cancer (2014), 1–2 | doi: 10.1038/bjc.2013.747

Darabi et al. Breast Cancer Research 2012, 14:R25
http://breast-cancer-research.com/content/14/1/R25

Distribution of breast cancer risk from SNPs and classical risk factors in women of routine screening age in the UK

A R Brentnall*[,1], D G Evans[2] and J Cuzick[1]

[1]Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, Barts and The London, Charterhouse Square, London EC1M 6BQ, UK and [2]Genesis Breast Cancer Prevention Centre, University Hospital of South Manchester NHS Trust, Wythenshawe, Manchester M23 9LT, UK

RESEARCH ARTICLE

Breast cancer risk prediction and individualised screening based on common genetic variation and breast density measurement

Hatef Darabi[1*], Kamila Czene[1], Wanting Zhao[2], Jianjun Liu[2], Per Hall[1] and Keith Humphreys[1]

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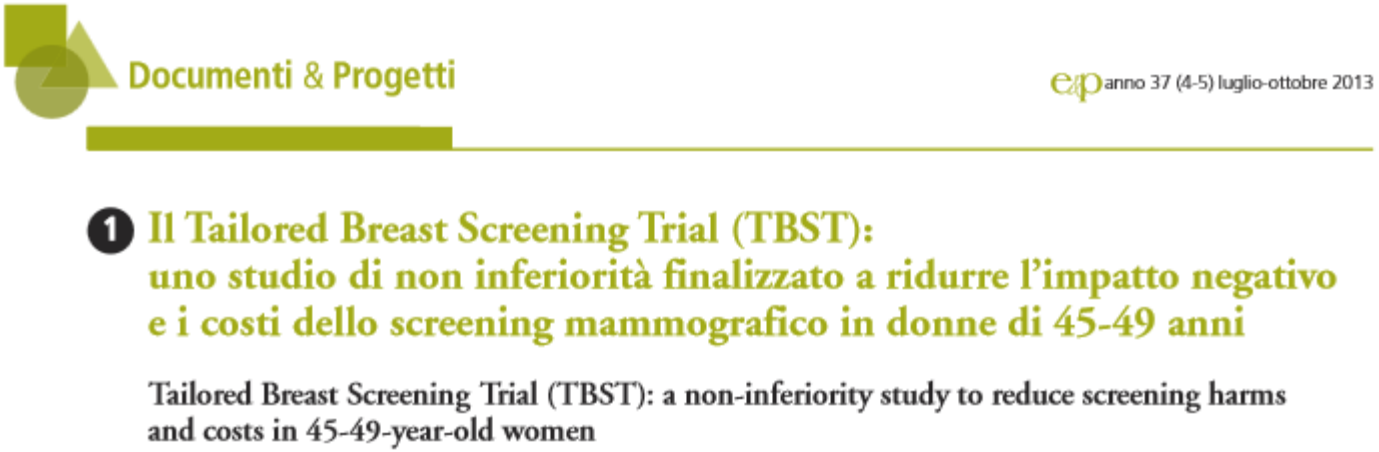
Examples in Europe



Documenti & Progetti

e&p anno 37 (4-5) luglio-ottobre 2013

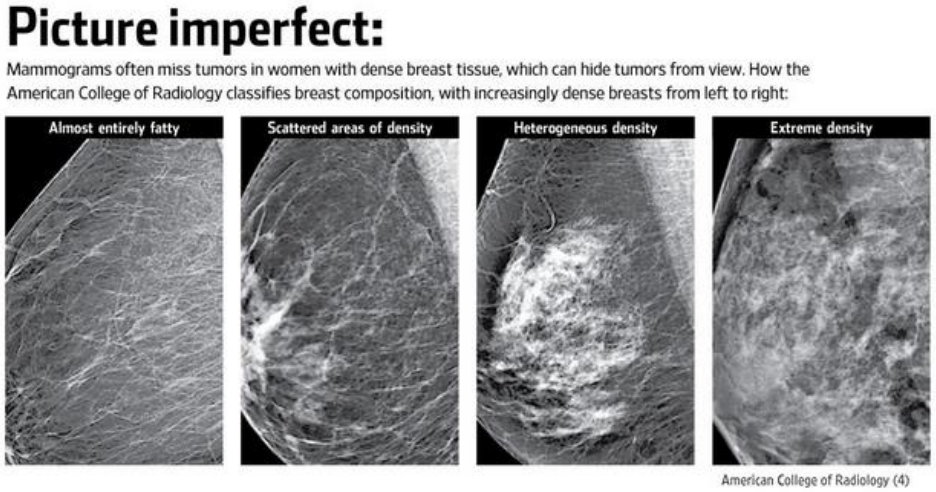
1 **Il Tailored Breast Screening Trial (TBST): uno studio di non inferiorità finalizzato a ridurre l'impatto negativo e i costi dello screening mammografico in donne di 45-49 anni**

Tailored Breast Screening Trial (TBST): a non-inferiority study to reduce screening harms and costs in 45-49-year-old women

Tailored ~ RCT using a breast density classification to allocate women 45-50 to a screening interval of 1 or 2 years

(coordinator: Eugenio Paci)

Examples in Europe



Tailored ~ RCT offering MRI to women with ACR 4 and a negative screening mammogram

(coordinator: Carla van Gils)

Tailored Supplemental Screening for Breast Cancer: What Now

The Breast 23 (2014) 76–80

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Incremental effect from integrating 3D-mammography (tomosynthesis) with 2D-mammography: Increased breast cancer detection evident for screening centres in a population-based trial

Francesca Caumo [a], Daniela Bernardi [b], Stefano Ciatto [a,b,1], Petra Macaskill [c], Marco Pellegrini [b], Silvia Brunelli [a], Paola Tuttobene [b], Paola Bricolo [a], Carmine Fantò [b], Marvi Valentini [b], Stefania Montemezzi [a], Nehmat Houssami [c,*]

[a] Centro di Prevenzione Senologica, Marzana, Verona, Italy
[b] U.O. Senologia Clinica e Screening Mammografico, Department of Diagnostics, Azienda Provinciale Servizi Sanitari (APSS), Trento, Italy
[c] Screening and Test Evaluation Program (STEP), School of Public Health, Sydney Medical School, University of Sydney, Sydney, Australia

[2] Diagnostic Radiology, Department of Clinical Sciences in Malmö, Lund University, Skåne University Hospital Malmö, 20502 Malmö, Sweden

Reprints

Permissions

Tailored screening

- Logistics in the context of service screening?
- Other issues?

Implementing risk-stratified screening for common cancers: a review of potential ethical, legal and social issues

A.E. Hall[1], S. Chowdhury[1], N. Hallowell[1], N. Pashayan[2], T. Dent[1], P. Pharoah[3,4], H. Burton[1]

[1]PHG Foundation (Foundation for Genomics and Population Health), 2 Worts Causeway, Cambridge CB1 8RN, UK
[2]UCL Department of Applied Health Research, University College London, 1-19 Torrington Place, London WC1E 6BT, UK
[3]Department of Public Health and Primary Care, Institute of Public Health, University of Cambridge, University Forvie Site, Robinson Way, Cambridge CB2 OSR, UK
[4]Department of Oncology, University of Cambridge, Cambridge CB2 2QQ, UK
Address correspondence to A.E. Hall, E-mail: alison.hall@phgfoundation.org

J Public Health 2013, Aug 28 [Epub ahead of print]

FP 7 projects

The aim is to identify individuals at an increased risk of breast, prostate and ovarian cancer thereby having the possibility to reduce the number of individuals that will be diagnosed with these disorders. These interventions could be anything from **increased screening procedures, altered lifestyle factors or even profylactic therapy**.

A project funded by the European Commission and 7th Framework Programme (coordinator: Per Hall)

assure
PERSONALISED BREAST CANCER SCREENING

HOME | BREAST DENSITY | NEWS | ABOUT | OVERVIEW | PARTNERS | PRESS |

home

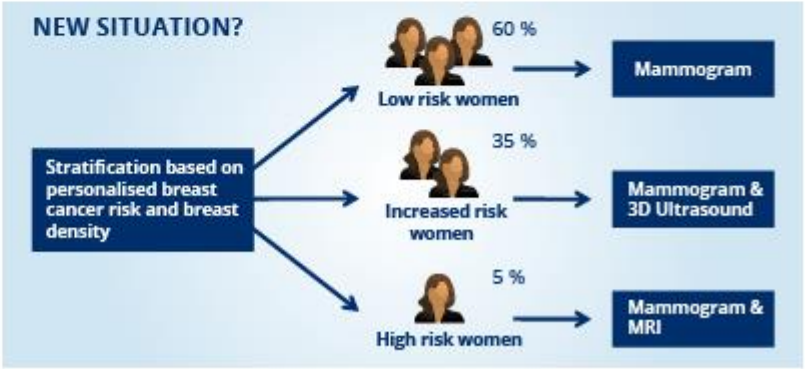
Personalised Breast Cancer Screening

Welcome to the website of the ASSURE project for personalised breast cancer screening. The ASSURE project is supported by the European Union under the 7th Framework Programme for Health Research, and started in December 2012. The project is coordinated by the Radboud University Nijmegen Medical Centre.

SEVENTH FRAMEWORK PROGRAMME

ASSURE is partially funded by the European Commission's FP7 Cooperation programme

Currently, breast screening is almost exclusively performed with mammography. However, for women with dense breasts the sensitivity of mammography for detecting breast cancer is low. The aim of ASSURE is to develop methods to personalise breast cancer screening, based on risk and breast density markers.



New screening methods using MRI and automated breast ultrasound imaging will be developed. Personalised screening will minimize the risk of a particular patient to have a cancer missed at an early stage, resulting in decreased mortality and increased quality of life due to less radical treatment options.

Coordinator: Nico Karssemeijer, Nijmegen

Horizon2020?

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Horizon 2020 is the biggest EU Research and Innovation programme ever with nearly €80 billion of funding available over 7 years (2014 to 2020) – in addition to the private investment that this money will attract. It promises more breakthroughs, discoveries and world-firsts by taking great ideas from the lab to the market.

Horizon2020

- Pillar 1: Excellent Science
- Pillar 2: Industrial Leadership
- Pillar 3: Societal Challenges

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1. Excellent science

- European Research Council
- Future and Emerging Technologies
- Marie Skłodowska Curie Actions
- Research Infrastructures

2. Industrial Leadership

- Enabling and industrial technologies
  ICT, nanotechnologies, materials, biotechnology, manufacturing, space
- Access to risk finance
- Innovations in SMEs

3. Societal Challenges

- Health, demographic change and well being
- Food security, sustainable agriculture, marine and maritime research & bioeconomy
- Secure, clean and efficient energy
- Smart, green and integrated transport
- Climate action, resource efficiency and raw materials
- Inclusive, innovative and secure societies

mainly bottom-up

mainly top-down

mainly top-down

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Societal Challenge 1 – Health, Demographic Change and Wellbeing

- Translating science to benefit citizens
- Improve health outcomes
- Support a competitive health & care sector
- Test and demonstrate new health & care models, approaches and tools
- Promote healthy and active ageing

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Horizon 2020

2014	2015	2016	2017	2018	2019	2020
Strategic Programme 1						
Work Programme 1 (+ tentative info for 2016)		Strategic Programme 2				
		WP 2 (+ tentative info for 2018)		Strategic Programme 3		
				WP (+ tentative info for 2020)		
						WP 4

Strategic Programme 1: Personalised Health and Care

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Tailored screening

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Health, Demographic Change and Wellbeing

Responding to this challenge, research and innovation (R&I) under Horizon 2020 is an investment in better health for all. It aims to keep older people active and independent for longer and supports the development of new, safer and more effective interventions. R&I under Horizon 2020 also contributes to the sustainability of health and care systems.

During the first two years of Horizon 2020 (Work Programme for 2014/15), the EU will invest some €1 200 million in this Challenge.

Personalising health and care

Research & Innovation supported by this call will:

- improve our understanding of the causes and mechanisms underlying health, healthy ageing and disease;
- improve our ability to monitor health and to prevent, detect, treat and manage disease;
- support older persons to remain active and healthy;
- and test and demonstrate new models and tools for health and care delivery.

Horizon 2020

Calls

Search Topics

Call Updates

FP7 & CIP Programmes

Calls

Call Updates

COSME

Other Funding Opportunities

The following services of Participant Portal may be be unavailable on Thursday 23rd January from 17:30 (CET) while system maintenance is performed.

- Unique Registration Facility
- Role Management
- Reporting Tools
- Negotiation Facility
- Proposal list and Proposal Submission System

We apologise for any inconvenience this may cause.

Funding Opportunities

H2020 ONLINE MANUAL

Find the European Union funding opportunities and search for new or closed calls, grouped by the following programmes:

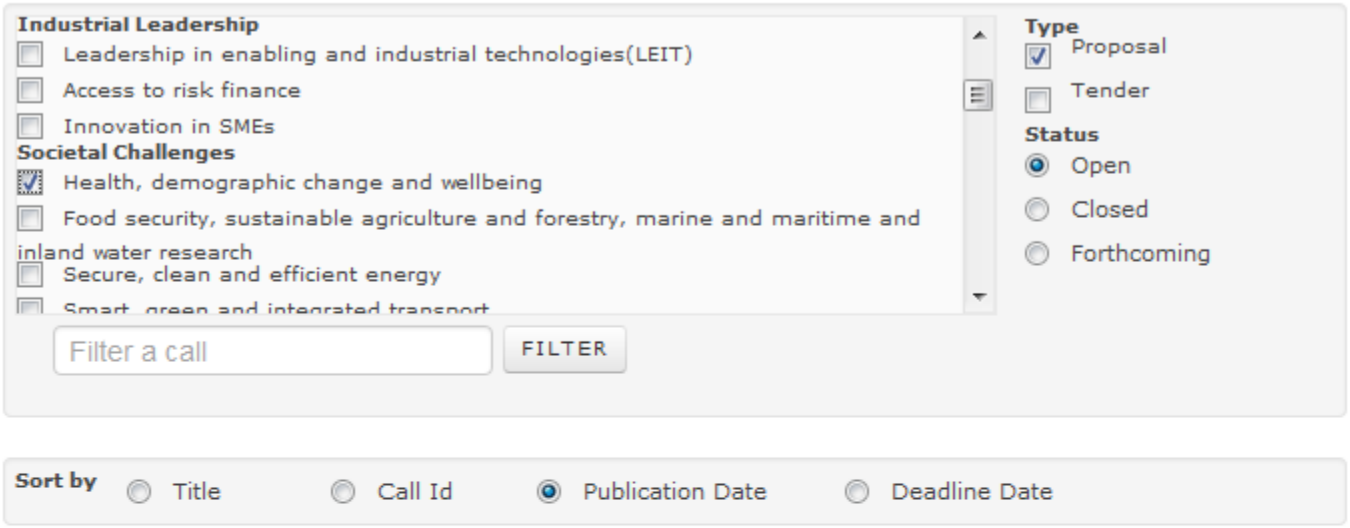
- **Horizon 2020 - EU research funding from 2014**
- **Seventh Framework Programme (FP7)**
- **Competitiveness and Innovation Framework Programme (CIP)**
- **other research and innovation programmes**

Horizon 2020

FP7 and CIP - previous programmes

FP7 and CIP are previous instruments to fund research

Horizon 2020



In addition to the search facilities, the full list of H2020 Calls can be found **here.**

dumc

PERSONALISING HEALTH AND CARE

H2020-PHC-2014-two-stage — Sub call of: H2020-PHC-2014-2015

Publication date	2013-12-11	**Deadline Date**	2014-03-11 +17:00:00 (Brussels local time)
		Stage 2	2014-08-19 +17:00:00 (Brussels local time)
Budget	€303,000,000	**Main Pillar**	Societal Challenges
Status	Open	**OJ reference**	OJ C 361 of 11 December 2013

Call description | Call documents | Get support | Subscribe to Notifications

Call updates

- ## 2013-12-20 16:39:13

The submission session is now available for: PHC-01-2014(RIA), PHC-05-2014(RIA), PHC-06-2014(RIA), PHC-10-2014(RIA), PHC-13-2014(RIA), PHC-17-2014(RIA), PHC-23-2014(RIA), PHC-32-2014(RIA)

Topics and submission service

- PHC-05-2014: Health promotion and disease prevention: translating 'omics' into stratified approaches
- PHC-06-2014: Evaluating existing screening and prevention programmes
- PHC-10-2014: Development of new diagnostic tools and technologies: in vitro devices, assays and platforms
- PHC-17-2014: Comparing the effectiveness of existing healthcare interventions in the elderly
- PHC-23-2014: Developing and comparing new models for safe and efficient, prevention oriented health and care systems
- PHC-01-2014: Understanding health, ageing and disease: determinants, risk factors and pathways
- PHC-13-2014: New therapies for chronic non-communicable diseases
- PHC-32-2014: Advancing bioinformatics to meet biomedical and clinical needs

Personalising health and care

H2020-PHC-2014-two-stage — Sub call of: H2020-PHC-2014-2015

Publication date	2013-12-11	**Deadline Date**	2014-03-11 17:00:00 (Brussels local time)
		Stage 2	2014-08-19 +17:00:00 (Brussels local time)
Total Call Budget	€303,000,000	**Main Pillar**	Societal Challenges
Status	Open	**OJ reference**	OJ C 361 of 11 December 2013

Topic: Understanding health, ageing and disease: determinants, risk factors and pathways **PHC-01-2014**

Topic Description | Topic Conditions & Documents | Submission Service

Specific challenge: The development and preservation of good health, and the occurrence and evolution of common diseases and disabilities result from varying degrees of interaction between the genetic make-up of individual human beings and behavioural, environmental (including endocrine disruptors), occupational, nutritional and other modifiable lifestyle factors. This applies from the earliest stages of development throughout life.

Understanding these factors, their interactions and the extent to which they contribute to health preservation and/or to disease development is important for the development of preventive and therapeutic measures supporting good health, prolonged active independence and a productive working life, not least in the context of changing demographic patterns and the ageing of the European population. In particular, proposals should contribute to improving risk identification and validation, and will allow better diagnosis, risk-based prevention strategies and policies.

Personalising health and care

H2020-PHC-2014-two-stage — Sub call of: H2020-PHC-2014-2015

Publication date	2013-12-11	**Deadline Date**	2014-03-11 17:00:00 (Brussels local time)
		Stage 2	2014-08-19 +17:00:00 (Brussels local time)
Total Call Budget	€303,000,000	**Main Pillar**	Societal Challenges
Status	Open	**OJ reference**	OJ C 361 of 11 December 2013

Topic: Health promotion and disease prevention: translating 'omics' into stratified approaches — **PHC-05-2014**

Topic Description | Topic Conditions & Documents | Submission Service

Specific challenge: 'Omics' research (including but not limited to genomics, epi-genomics, meta-genomics and proteomics) is moving at a breath-taking pace. A major challenge for the next decade is to determine when and how this wealth of 'omics' information can be usefully applied by both the public and private sectors for the development of personalised /stratified approaches in health promotion and disease prevention.

Personalising health and care

H2020-PHC-2014-two-stage — Sub call of: H2020-PHC-2014-2015

Publication date	2013-12-11	**Deadline Date**	2014-03-11 17:00:00 (Brussels local time)
		Stage 2	2014-08-19 +17:00:00 (Brussels local time)
Total Call Budget	€303,000,000	**Main Pillar**	Societal Challenges
Status	Open	**OJ reference**	OJ C 361 of 11 December 2013

Topic: Evaluating existing screening and prevention programmes **PHC-06-2014**

Topic Description | Topic Conditions & Documents | Submission Service

Specific challenge: Some existing population based screening and disease prevention programmes have not been assessed for their effectiveness, or vary in terms of their application within and across countries throughout Europe. This may result in inappropriate interventions, delayed provision of the correct treatment, increased disease burden, health inequities and increased costs for health and care systems.

Such programmes therefore need systematic evaluation for their impact on health outcomes, cost effectiveness and health equity.

Deadlines and timelines

deadline stage 1 of 2	11 March 2014
deadline single stage	15 April 2014
evaluation stage 1 of 2	April–May 2014?
evaluation single stage	June 2014?
deadline stage 2 of 2	19 August 2014
evaluation stage 2 of 2	September 2014?

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