

# Screening Case Study

## History

1968: Wilson and Junger of the World Health Organisation develop 10 principles that should govern a national screening programme. The condition should be an important health problem; its natural history should be well understood; it should be recognisable at an early stage, with treatment better at an early stage; a suitable and acceptable test should exist; there should be adequate facilities to cope with abnormalities detected; screening should be repeated at intervals; the chance of harm should be less than the chance of benefit, and the cost should be balanced against benefit.

1986: Forrest Report recommends the introduction of an NHS Breast Screening Programme. NHS Breast Screening Programme introduced in 1988 in response to the report.

1988: The NHS Cervical Screening Programme is set up. Cervical screening began in Britain in the mid-1960s but by the mid-1980s there was concern that those at greatest risk were not being tested.

1996: The NHS is instructed not to introduce any new screening programmes until the UK National Screening Committee (NSC) has reviewed their effectiveness and advised on policy.

1997: Two HTA reports (Vol 1.2 & 1.3) into strategies of screening for prostate cancer stimulate debate which later leads to the creation of the Prostate Cancer Risk Management Programme, set up to ensure testing was only undertaken in appropriate and informed circumstances.

1997: HTA programme funds a critical review of the role of neonatal hearing screening (Vol 1.10). Following the report the NSC recommends the introduction of universal screening using auto-acoustic technology to replace the existing distraction test.

1998: HTA evidence synthesis suggests there may be a role for HPV testing as part of the NHS Cervical Screening Programme (Vol 3.14) and a major clinical trial is subsequently funded (2001).

1999: HTA report (Vol 3.11) finds that there is a case for developing screening programmes for haemoglobinopathies (thalassaemias and sickle cell disease).

2000: HTA research (Vol 4.18) makes the case for liquid-based cytology in cervical screening and the technique is subsequently integrated into the Cervical Screening Programme.

2000: The Chlamydia Screening Studies project (Vol 11.8), one of the largest trials of its kind, is commissioned by the HTA programme to investigate the most effective way to screen for chlamydia, informing the development of a national screening programme.

2001: The NSC recommends that all pregnant women, irrespective of age, should be offered second trimester serum screening for Down's syndrome. Informed by evidence from HTA reports published in 1998 and 2000 (Vol 2.1 & Vol 4.16).

2002: The roll out of a National Screening Programme for Chlamydia starts. Full screening begins across England in 2006.

2002: The UK Newborn Screening Programme Centre is established. The Cystic Fibrosis Screening Programme and the NHS Sickle Cell & Thalassaemia Screening Programme come under its umbrella.

2003: The English Diabetic Screening Project Advisory Group is set up to steer the development of a National Screening Programme for Sight-Threatening Diabetic Retinopathy.

2003: The Diabetes, Heart Disease and Stroke Prevention Project is set up by the NSC. The project adopts the recommendations of an HTA study (Vol 7.31) into a new preventative strategy for lowering blood pressure to prevent heart disease and stroke in high-risk groups.

2005: HTA programme funds a clinical trial to investigate the use of automated image analysis for cervical screening samples (project ref. 03/04/02).

2006: NHS Newborn Hearing Screening Programme is rolled out to every newborn in England.

2007: As a result of the Diabetes, Heart Disease and Stroke Prevention Project, the NSC recommends the introduction of a Vascular Risk Management Programme.

## **Background**

Detecting serious conditions early gives the opportunity to start effective treatment or intervention before the disease or condition progresses. The NHS currently has a number of national screening programmes in place that are proving successful for the early identification of diseases and conditions. The NHS Breast Screening Programme, one of the first national screening programmes introduced in the UK, now screens around one-and-a-half million women each year, saving up to 1,400 lives. The NHS Cervical Screening Programme, also one of the first systems to be put in place, screens over four million women annually, and experts estimate that the programme prevents up to 3,900 cases of cervical cancer each year.

The success of early screening programmes and the expansion of the evidence base around their effectiveness has led to the creation of programmes in other important health areas in recent years. Bowel cancer is the third most common cancer in the UK, responsible for over 16,000 deaths each year. The NHS Bowel Cancer Screening Programme is now being rolled out across England and it is thought that this will reduce the risk of dying from the disease by 16 per cent. A National Chlamydia Screening Programme is also being rolled out, aiming to tackle the UK's commonest sexually transmitted infection, and as a result of the Diabetes, Heart Disease and Stroke (DHDS) Prevention Project, a population-based Vascular Risk Management Programme is being established to offer individual assessment of cardiovascular disease risk.

Antenatal and newborn screening programmes form the UK's largest series of programmes, covering 600,000 pregnancies and babies each year. They include the Down's Syndrome Screening Programme and the NHS Newborn Hearing Screening Programme, launched in 2006 in place of the existing 'hearing distraction' test. Under the Newborn Bloodspot Screening Programme babies are screened for phenylketonuria and congenital hypothyroidism. Together with newer screening programmes for sickle cell and thalassaemia and cystic fibrosis, the programme is managed by the UK Newborn Screening Programme Centre.

## **Policy**

In 1996 the National Screening Committee (NSC) was created to assess proposed new screening programmes against a criteria based on the internationally recognised Wilson and Junger principles covering the condition, the test, the treatment options, and effectiveness and acceptability of the screening programme. The NSC advises government health ministers on all aspects of screening policy. The NHS was instructed not to introduce any new screening programmes until the NSC had reviewed their effectiveness.

Since its introduction, the NSC has frequently based its advice to ministers on reports produced by the HTA programme, part of the National Institute for Health Research (NIHR). The evidence to support or refute particular screening programmes is often limited because of the complex issues involved and sometimes by the rarity of the conditions being screened for. The NSC relies heavily upon providers of independent scientific research, particularly the HTA programme, to inform much of its advice. Indeed, the NSC website states that the work of the HTA programme provides the single most important and largest influence on its work.

[www.nsc.nhs.uk/uk\\_nsc/uk\\_nsc\\_ind.htm](http://www.nsc.nhs.uk/uk_nsc/uk_nsc_ind.htm)

## **Adding to the evidence base**

By 2007, the HTA programme has invested more than £13 million in 64 screening-related research projects, 44 of which have been published in its monograph series (12% of the 360 titles it has published to date), and 20 of which are ongoing. HTA research into screening covers four broad categories: antenatal and neonatal screening, screening young children, screening for cancers, and screening in other priority disease areas such as sexually transmitted infections (STIs), diabetes and heart disease. Several of the HTA programme's screening projects have been commissioned directly in support of the National Screening Committee.

## **Antenatal and neonatal screening**

Half of the HTA programme's portfolio of research into screening focuses on antenatal and neonatal screening and screening young children, reflecting the importance of these areas in national screening arrangements. The programme has commissioned 31 research projects in this area, including seven clinical trials.

Twenty-three HTA-funded projects have concentrated on antenatal and neonatal screening. This includes investigations of the effectiveness of screening for a number of genetic and chromosomal disorders such as Down's syndrome, Fragile X syndrome and the haemoglobinopathies, as well as hearing impairments, congenital heart disease and metabolic disorders. Research has also investigated the role of screening to prevent pre-term birth and antenatal screening for group B streptococcus infection.

### **Down's syndrome**

HTA reports played an important role informing the discussions of the NSC that led to the launch of the NHS Down's Syndrome Screening Programme in 2001. A 1998 (Vol 2.1) review of the evidence around antenatal screening for Down's syndrome and a report from 2000 (Vol 4.16) into ultrasound screening in pregnancy helped inform both the decision to recommend the introduction of the programme, as well as the establishment of explicit quality criteria for the programme to meet.

The NSC formulated its current policy to screen all women for Down's syndrome based on the 2003 HTA-funded Serum, Urine and Ultrasound Screening Study (SURUSS) (Vol 7.11). The study aimed to identify the most effective, safe and cost-effective method of antenatal screening for Down's syndrome. The researchers evaluated nuchal translucency (NT), maternal serum and urine markers in the first and second trimesters of pregnancy, and maternal age in various combinations. They found that screening performance in the first trimester of pregnancy was virtually the same as that in the second trimester, and in either it was much less effective than integrating screening measurements from both trimesters into a single test.

### **Sickle cell/thalassaemia**

The development of an NHS Sickle Cell & Thalassaemia Screening Programme has also been informed by HTA research. Reports in 1999 (Vol 3.11) into antenatal and neonatal haemoglobinopathy screening found that there was a case for developing appropriate population-based screening programmes for haemoglobinopathies

(thalassaemias and sickle cell disease), and the national programme of screening for the diseases was introduced on the basis of the reports. A clinical trial (project ref. 03/02/03) has also been funded by the HTA programme because, although it is now UK policy to offer antenatal screening to all women in areas where they are at high risk of these conditions, there is little evidence about the most cost-effective way of delivering the service to ensure all women receive timely screening. This research is due to be published in 2008.

## **Hearing**

A critical review of the evidence base around neonatal hearing screening was funded by the HTA programme in 1997 (Vol 1.10) because of increasing doubt about the ability of the existing screening programme (a health visitor distraction test) to identify children with hearing impairment, along with technological advances that had made neonatal hearing screening an alternative option. Researchers found that universal neonatal screening was a more clinically and cost-effective method than the existing system, and following the report the NSC recommended the introduction of universal screening, using auto-acoustic technology to replace the distraction test. Further HTA research (project ref. 98/39/02) is now under way in this area to assess the most cost-effective criteria for the national screening programme, as well as investigating interventions for mild to moderate hearing impairments identified during screening. This research is due to be published in 2008.

## **Heart disease**

Although screening for congenital heart defects has been part of the routine physical examination of newborns, HTA research in 2005 (Vol 9.44) found that the current system performs poorly and lacks monitoring of quality assurance, performance management and longer term outcomes. The research found that pulse oximetry is a promising alternative newborn screening strategy and requires further evaluation. A clinical trial is now being considered under the new HTA Clinical Trials funding stream.

## **Screening for cancer**

The HTA research portfolio includes 13 projects commissioned to investigate screening for cancers, including three major clinical trials. In particular, the HTA programme has funded five research projects related to screening for cervical cancer, and these are playing an important role informing the development of the national screening programme.

## **Cervical cancer**

Human Papilloma Virus (HPV) is a sexually transmitted disease and there is an association between certain types of HPV and the development of cervical cancer. Nearly 100% of all cervical cancers are HPV-positive. In 1998 (Vol 3.14) the HTA programme funded a review of the available evidence around HPV testing as part of the cervical screening programme. The important link between HPV and cervical cancer had been clearly demonstrated and there was interest in HPV testing to improve both the effectiveness and cost-effectiveness of cervical screening. The researchers found that HPV testing could not currently be recommended, but there was evidence to suggest a role for it in cervical screening. They concluded that a large clinical trial should be considered, and the NSC also recommended a pilot study on the basis of the report.

Following this the HTA programme commissioned the 'ARTISTIC' trial, which involves 25,000 women undergoing routine cervical screening (project ref. 98/04/64). The women have been randomised into two groups, either a smear plus HPV test where HPV results are revealed or a smear plus HPV test where HPV results are concealed. Women with a negative smear test result and a positive HPV test result revealed will be later retested and, if still HPV positive, offered treatment. All of the women in the trial will be retested after three years to establish whether there is a reduction in pre-cancers due to earlier detection and treatment. The findings of the ARTISTIC trial will be published in mid-2008, informing ongoing NSC policy discussions.

Further HTA-funded research into cervical cancer screening includes a systematic review published in 2000 (Vol 4.18) which assessed the evidence for the role of liquid-based cytology in cervical screening. The researchers found that it is likely that the new technique (in which samples are put into liquid rather than smeared on a slide) would reduce the number of inadequate smears and false-negative test results, as well as decreasing the time needed for examination of specimens by cytologists. On the basis of this report and following pilots the cervical screening programme in England has started to convert to liquid-based cytology.

Research in 2005 (Vol 9.13) also investigated the evidence for the cost-effectiveness of introducing automated image analysis for screening samples. Researchers concluded that there was insufficient evidence for the use of automated image analysis systems, but they were able to specify in which areas further research was needed. Building on

the findings of this study, a clinical trial funded by the HTA programme is comparing automated technology with manual cervical screening. The MAVARIC trial (project ref. 03/04/02) is aiming to find out what benefits could come from the use of automated technology, where cytoscreeners are aided by computerised software, to make it easier and quicker to identify abnormal cells. This research is due to be published in 2010.

### **Prostate cancer**

HTA research into screening for cancers has also included two early projects (1997, Vol 1.2 & 1.3) investigating strategies of screening for prostate cancer. Debate around these reports led to the creation of the Prostate Cancer Risk Management Programme, set up to improve testing for the disease.

Problems with recruiting patients to clinical trials in the area of prostate cancer means that the evidence base around treatments for the disease is limited. In 1999 the HTA programme funded a feasibility study (Vol 7.14) to investigate different ways of approaching and recruiting patients to trials in the area. Researchers found that there is reticence among patients about being randomised into the non-radical intervention arms of such trials, where the intervention is 'watchful waiting.' GPs and surgeons were given training on how to talk to patients and the term 'watchful waiting' was changed to 'active surveillance' as this made patients feel like the intervention they may be randomised to receive was more proactive.

Following this research the HTA programme commissioned a major clinical trial to investigate different methods of treating early prostate cancer. The £20 million ProtecT trial (project ref. 96/20/99), which is due to publish its interim findings in 2009, has recruited over 1,200 patients, more than any other trial in the area.

### **Other cancers**

- **Ovarian cancer:** a 1998 HTA review of the evidence about screening for ovarian cancer (Vol 2.2) generated NSC support for a clinical trial which was subsequently funded by the MRC.
- **Lung cancer:** a 2006 review of computed tomography screening for lung cancer (Vol 10.3) reinforced NSC policy not to screen and led the MRC to commission a review of the evidence relating to breath test screening.
- **Oral cancer:** an HTA review of screening for oral cancer in 2006 (Vol 10.14) also reinforced NSC policy not to screen.

- **Anal cancer:** there is ongoing research into screening high risk populations for anal cancer (project ref. 05/11/02)
- **Colorectal cancer:** a large clinical trial is investigating different methods for diagnosing colorectal cancer in older patients (project ref. 02/02/01)

## **Other priority areas**

### **STIs**

Research commissioned by the HTA programme has helped to expand the evidence base and inform policy in a number of other priority health areas including sexually transmitted infections. The HTA-funded Chlamydia Screening Studies project, one of the largest of its kind, has helped answer some of the biggest questions about screening for Chlamydia infection in the UK, informing the development of the NHS National Chlamydia Screening Programme. Comprising six linked studies, the research, published in 2007 (Vol 11.7), reports that using trained practice nurses to notify partners is as effective as referral to a specialist health advisor and costs the same, and that chlamydia affects as many men as women, so they should be targeted as intensively as women.

### **Cardiovascular disease**

The findings of a 2003 HTA study (Vol 7.31) into a new preventative strategy for lowering blood pressure to prevent myocardial infarction and stroke were adopted by the Diabetes, Heart Disease and Stroke Prevention Project, set up by the NSC in October 2003. The researchers identified a range of policy options in relation to treatment of high blood pressure, concluding that a combination of identifying all people with established cardiovascular disease and offering treatment to all persons above a specified age is likely to have the greatest public health impact (reducing stroke by about two-thirds and ischaemic heart disease by half.) A Vascular Risk Management Programme is now being set up. People at high risk of type 2 diabetes will also be systematically screened within this programme after an HTA review (project ref. 05/02/01) of the research evidence in this area informed a meeting of the NSC in November 2005 (this research is due to be published in full in the HTA monograph series in early May 2007).

### **Reducing uncertainty**

The HTA programme's research portfolio has played an integral role in the development of UK screening services over the past decade. HTA reports have informed crucial policy decisions in health areas such as haemoglobinopathies, cystic

fibrosis, chlamydia, Down's syndrome and vascular risk, where national screening programmes are now in place or being introduced.

HTA research has been important in helping the NSC to decide when screening should and should not be offered, as well as informing wider decisions about the best tests and procedures that screening systems should use. HTA studies have also helped to establish what areas need further investigation, as well as clarifying how research should be carried out to best meet the information needs of the Committee.

## Ends

## Appendix:

### Cancer

Project Title. (Click on the project title of your choice to view further details)	Research Type	HTA Ref
<a href="#">Systematic review of detection, management and screening for prostatic carcinoma <i>Published</i></a>	SR	93/21/02
<a href="#">A review of evidence on the cost-effectiveness of different strategies for detecting and managing prostatic carcinoma <i>Published</i></a>	SR	93/21/04
<a href="#">Screening for ovarian cancer <i>Published</i></a>	SR	94/26/01
<a href="#">Systematic review of the role of human papilloma virus testing in the cervical screening programme <i>Published</i></a>	SR	98/04/01
<a href="#">Liquid-based cytology in cervical screening <i>Published</i></a>	TarNice	99/18/01
<a href="#">The determinants of screening uptake and effective interventions for increasing uptake <i>Published</i></a>	SR	95/14/01
<a href="#">Systematic review and modelling of the cost-effectiveness of screening for helicobacter pylori to reduce mortality and morbidity from gastric cancer and peptic ulcer disease <i>Published</i></a>	SR	96/01/03
<a href="#">Cervical screening programmes: can automation help? Evidence from a systematic review and economic modelling, applied to the UK. <i>Published</i></a>	SR	98/38/01
<a href="#">The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews <i>Published</i></a>	TarHta	04/41/01
<a href="#">The cost-effectiveness of screening for oral cancer in primary care <i>Published</i></a>	SR	99/46/02
<a href="#">What are the pros and cons of screening high risk populations for anal cancer?</a>	SR	05/11/02
<a href="#">CT colonography, colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients (SIGGAR1)</a>	PR	02/02/01
<a href="#">A comparison of automated technology and manual cervical</a>	PR	03/04/02

screening (MAVARIC)		
A randomised trial of human papilloma virus testing in primary cervical screening (ARTISTIC)	PR	98/04/64

### Neonatal and children

Information needed for health planners: screening for fragile X syndrome <i>Published</i>	SR	93/34/03
Neonatal metabolic screening: cost, yield and effects on outcome <i>Published</i>	SR	93/36/01
Preschool vision screening <i>Published</i>	SR	94/05/01
Critical review of the role of neonatal screening in the detection of congenital hearing impairments <i>Published</i>	SR	93/27/01
Systematic review of neonatal screening for inborn errors of metabolism <i>Published</i>	SR	93/36/03
Establishing appropriate screening practice for Down's syndrome <i>Published</i>	SR	93/25/24
Antenatal screening for group B streptococcus colonisation - protocol development	Other	05/05/01
Child health surveillance: an evaluation of screening for language delay <i>Published</i>	SR	94/05/02
Information needs for health planners: screening for cystic fibrosis <i>Published</i>	SR	93/32/03
Accuracy and cost effectiveness of rapid diagnosis of Group-B streptococcus during labour	PR	02/38/04
Interventions for mild to moderate permanent childhood hearing impairments identified by neonatal hearing screening	PR	98/39/02
Antenatal screening for haemoglobinopathies in primary care: a cluster randomised trial to inform a simulation model (SHIFT)	PR	03/02/03
Current practice, accuracy, effectiveness and cost effectiveness of the School Entry hearing Screen (SES)	SR	03/05/01
Accuracy of screening procedures for non-accidental injury in children: systematic review and modelling of clinical effectiveness	SR	03/37/06
Screening to prevent pre-term birth - systematic reviews of accuracy and effectiveness literature with economic modelling	SR	05/03/01
Methods of prediction and prevention of pre-eclampsia - Systematic reviews of accuracy and effectiveness literature with economic modelling	SR	01/64/04
Systematic review of ultrasound screening during pregnancy <i>Published</i>	SR	93/30/03
An assessment of screening for the fragile X syndrome <i>Published</i>	SR	93/34/04
Cost analysis of child health surveillance <i>Published</i>	PR	94/05/03
SURUSS (serum, urine and ultrasound screening study) <i>Published</i>	PR	93/25/05
Evaluation of molecular prenatal diagnosis for Down syndrome <i>Published</i>	PR	94/43/04

Screening for fragile X syndrome: a literature review and modelling study <i>Published</i>	TarHta	01/32/01
Clinical effectiveness and cost-effectiveness of neonatal screening for inborn errors of metabolism using tandem mass spectrometry: a systematic review <i>Published</i>	TarHta	01/31/01
Autoantibody testing in children with newly diagnosed type 1 diabetes mellitus <i>Published</i>	TarHta	01/33/01
Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review <i>Published</i>	SR	93/56/99
Screening in the first year of life for congenital heart disease: review and cost-effectiveness analysis <i>Published</i>	SR	99/45/01
Amniocentesis results: investigation of anxiety (ARIA) <i>Published</i>	PR	99/48/04
Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost effectiveness and expected value of information analyses	SR	04/51/01
What is the clinical and cost effectiveness of screening programmes for amblyopia and squint in children up to the ages of 4-5 years?	SR	04/32/05

#### Other priority areas

A randomised controlled trial of different approaches to universal antenatal HIV testing: acceptability, costs and benefits <i>Published</i>	PR	93/24/11
Screening for haemoglobinopathies in the UK: review and economic analysis <i>Published</i>	SR	93/33/01
Haemoglobinopathy - a systematic review <i>Published</i>	SR	93/33/03
Cost-effectiveness of screening for hypercholesterolaemia versus case finding for familial hypercholesterolaemia <i>Published</i>	SR	95/29/04
Screening for hepatitis c among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice <i>Published</i>	TarHta	01/29/01
Screening for thrombophilia: benefits, risks and cost-effectiveness <i>Published</i>	SR	01/04/03
The cost-effectiveness of testing for hepatitis c in former injecting drug users <i>Published</i>	TarHta	04/40/01
The effectiveness and cost-effectiveness of computed tomography screening for coronary artery disease: systematic review <i>Published</i>	TarHta	04/45/01
How far does screening women for partner violence in different health care settings meet the UK National Screening Committee criteria for a screening programme in terms of condition, screening method and intervention?	SR	05/09/07
Cross-cutting issues: the implications of false negatives <i>Published</i>	SR	95/40/01
The clinical and cost-effectiveness of screening for open angle glaucoma	SR	04/08/02

Is a screening programme for early age-related macular degeneration likely to be cost-effective? What are the major areas of uncertainty?	SR	03/06/01
Screening for gestational diabetes: a systematic review and economic evaluation <b>Published</b>	TarHta	99/09/50
The impact of screening programmes on health related beliefs and health promoting behaviour <b>Published</b>	SR	96/23/56
Randomised controlled trial and cost effectiveness study of targeted screening versus systematic population screening for atrial fibrillation in the over 65s: the SAFE study <b>Published</b>	PR	96/22/11
Surveillance of Barrett's oesophagus: exploring the uncertainty through systematic review, expert workshop and economic modelling <b>Published</b>	TarHta	03/49/01
A study to evaluate the most cost effective way to screen for chlamydia trachomatis genital tract infection and reduce its prevalence and associated burden of disease (ClaSS)	PR	97/32/31
Screening for Type 2 Diabetes: literature review	Other	05/02/01
Acceptability, benefit and costs of early screening for hearing disability	PR	94/46/01
Screening for stroke <b>Published</b>	SR	93/05/02