# First NAEDI Research Conference

## February 2011

The first NAEDI Research Conference took place on 17th and 18th February 2011. It saw presentations from leading researchers in the cancer awareness, screening and early diagnosis fields and spanned research from epidemiology to primary care to behaviour change. On this page you can find information about presentations given at the conference and the agenda for the day can be found as an appendix to this document.

## On this page



## Welcome and Overview

**Sara Hiom, Director of Health Information & Cancer Data, Cancer Research UK**

The aim of this conference is to encourage participation, dialogue, constructive challenge, and collaboration between researchers in the field of cancer early diagnosis, and to strengthen the research base in this area.

The early diagnosis of cancer is an incredibly complex issue. There are many points along the pathway where delays can occur, from an individual recognising the first signs or changes, to presenting to primary care, to being referred secondary care, and so on.

What we have known for some years:

- From EUROCARE, the UK has poorer cancer survival than other comparable countries, with one year survival being particularly poor.
- The idea that delays lead to poorer outcomes makes intuitive sense, but getting evidence to support such a link is tricky. As such, the evidence is currently only strong and clear for breast cancer.
- A variety of factors contribute to patient delay.
- From Willie Hamilton's CAPER studies, we know that risk of cancer can be quantitatively assessed in primary care based on age, symptoms and combinations thereof.
- Our work on oral cancer awareness pilots in Tower Hamlets showed that targeted activities to raise awareness of signs and symptoms can be effective in detecting the disease early.

More recently, NAEDI has filled in several gaps in our knowledge:

- The UK's survival rates for a variety of cancers trails behind those of several other developed nations, and we learned recently through the International Cancer Benchmarking Partnership that we are not narrowing this gap as much as we'd like.
- From surveys using the Cancer Awareness Measure, we know that there's poor awareness of signs and symptoms.

- From the National Cancer Intelligence Network, we know that all English PCTs have poor one-year-survival rates in comparison with international best practice, and there are wide variations in resection and referral rates in primary care.
- The Routes to Diagnosis work indicated that 23% of all cancers are diagnosed via an emergency route.
- From our qualitative research, we know that there are lots of barriers to consulting GPs, from getting appointments, to feeling that we're wasting the doctor's time, to embarrassment and fear.
- From modelling studies, we know that early diagnosis is likely to be very cost-effective, with QALY costs of £2,000-5,000, compared to over £30,000 for cancer drugs.

This is a good start, but there are also many gaps in our knowledge including:

- The contribution of different factors to poor one-year-survival rates – patient awareness, primary care, post-operative mortality?
- How our problems of awareness, referrals and so on compare with other countries – the ICBP should give us some answers here
- Effective interventions for changing behaviour
  Research in this area is challenging. Definitions, tools and methods are inconsistent, which makes it difficult to draw comparisons between studies and areas. This is why we're encouraging the use of validated measures like the CAM, and of agreed definitions of key intervals and time points. It's why we're investing so much into research in this vital area, and why we've arranged this conference.

# Keynote

**Prof Peter Vedsted - Vice Director, Research Unit for General Practice, Danish Research Centre for Cancer Diagnosis in Primary Care.**

- A complex but rewarding challenge: changing the time to diagnosis

According to GLOBOCAN, Denmark is the world's cancer capital – the country with the highest incidence and mortality rates. Thirty per cent of people will develop and die of cancer before the age of 85. The International Cancer Benchmarking Project has shown that relative cancer survival is improving, but Denmark is still lagging behind many other countries. And while lifestyle and screening clearly play a major role in cancer outcomes, early detection is vitally important too. We're looking at a potential reward of 2,000 avoided deaths per year in Denmark.

The problem is that studying the benefits of early detection is difficult. There are lots of different definitions and intervals that can cloud the results of studies, making people question the value of speeding up the diagnostic process.

For example, people often cite the "waiting time paradox", where patients with shorter delays to diagnosis have worse outcomes. But these "counter-intuitive associations" come from simplistic analyses. There's a triage effect, where patients with the worst symptoms (and thus the poorest outcomes) are rushed through the system more quickly and treated with shorter delays. Look at the data carefully, and you see that the quartile of patients with the longest diagnostic intervals have higher mortality than those with median intervals.

We need to stop the debate about whether time to diagnosis matters or not. We need to stop doing inappropriate analysis of mortality and intervals. And we should insist on better diagnosis. After all, the time from first symptom to treatment has a median of 98 days – that's a problem that we need to deal with!

Detecting cancer symptoms in primary care is like looking for a needle in a haystack. Even with alarm symptoms, the average GP sees around 8-10 cancers a year and they must refer 20 people without cancer to find one who has it. There's not a lot of good evidence on the prevalence of alarm symptoms in the general population. In Denmark, GPs say that around half of people present to them with alarm symptoms but there's a mismatch between this and the proportion of cancer patients who actually have official, evidence-based, guideline alarm symptoms.

If a GP refers someone with alarm symptoms, the median time to diagnosis is just 15 days. That's important for patients, since longer diagnostic delays track with higher mortality. Fast-track referrals are mandatory for good outcomes.

However, we may never get a good evidence-based cancer symptom guideline and GPs may not follow them anyway. To get around that, we need three separate diagnostic strategies:

- Alarm symptom - Fast track investigations for a specific cancer
- General serious symptom (i.e. "I think the patient is sick and it might be cancer") - Referrals to a diagnostic centre for a multidisciplinary, parallel, staged approach
- Vague symptoms - Quick and direct access to specialised investigations (e.g. CT scan) At the moment, we're asking GPs to act as gatekeepers, to act as the first point of contact with patients. There are many advantages to this model but there are drawbacks too. GPs can be seen as "hostages", caught between the need to ration care and keep waiting lists short. And countries with gatekeeper systems have 5-7% lower one-year cancer survival rates than countries without them. The message from this is not that gatekeeper systems don't work, but that they need support.

# NCRI/NAEDI Research Call Session

**Jane Cope - Introduction and Chair:**

The NAEDI research stream falls under the auspices of the National Cancer Research Initiative (NCRI) and is funded by a consortium of 6 partners – Cancer Research UK, The Departments of Health (England, Scotland, Wales and Northern Ireland) and the Economic and Social Research Council. This is a new portfolio of high quality research on awareness and early diagnosis of cancer, with the ultimate aim of improving survival.

**Dr Ekaterini Blaveri, Senior Research Funding Manager, Cancer Research UK**

- Response to Call 1 and introduction to Call 2

Research grants are/were invited in the following areas:

- High-risk populations
- Public awareness of cancer symptoms and reasons for late presentation
- Health services
- Methodology for, and evaluation of, early detection and awareness research
- Development and evaluation of:
    - Computer-based decision support systems
    - Models, tools and approaches to improve cervical and bowel cancer screening uptake

      The topics covered by the NAEDI Call 1 funded projects broke down as follows:
        - 43% Health service
        - 35% Public awareness
        - 16% High-risk populations

- 6% Methodology

Three subsequent speakers discussed examples of funded projects.

Brief presentations/outlines of funded NAEDI/NCRI Call 1 projects:

**Dr Alice Simon, Research Associate, Health Behaviour Research Centre, University College London**

- Evaluating the acceptability and feasibility of a gynaecological cancer information leaflet.

Dr Simon is developing a leaflet to raise awareness of, and reduce barriers to, early diagnosis of gynaecological cancers – ovarian, cervical, vulval, vaginal and womb cancers.

Evidence from Thomson et al (BJC v101 supp2: S102) suggests that earlier diagnosis of uterine and ovarian cancer could reduce the survival gap between the UK and the best of Europe. Another paper from Austoker et al (BJC v101 supp2: S31) noted that there are few intervention studies in this area, and those that exist tend to focus on awareness and knowledge, rather than on behaviour change and earlier presentation.

To address this gap, Simon will develop a leaflet which includes a symptom checklist, text designed to overcome emotional barriers, and an accompanying letter. A pilot study will recruit volunteers through Cancer Research UK's Cancer Awareness Roadshow and measure the leaflet's impact on their awareness, attitudes and intention to present, as well as their levels of fear and embarrassment.

In the next phase, the leaflet will be piloted in one GP surgery to test its acceptability. Following this, there will be a full trial where every woman over 21 on a GP list will receive the leaflet. The same impact measures will be used as before, and outcomes such as appointments and referrals will be monitored.

These phases have all been funded by NAEDI, and additional research (funded through other means) might include a survey of the prevalence of gynaecological cancer symptoms, and an analysis of data from the ovarian and cervical Cancer Awareness Measures.

During the questions, there were concerns about the phrase "gynaecological cancer" in the title, as it might be alienating and difficult to understand. The term "women's cancer" was mooted instead.

**Ms Patsy Whelehan, Senior Research Radiographer (Breast Imaging), Centre for Oncology and Molecular Medicine, Ninewells Hospital & Medical School, Dundee**

- The effects of pain in mammography on reattendance for breast cancer screening: a systematic review

The public perceives that mammography is painful. The prevalence of pain and discomfort varies from 1.2% to 92.3%. (Bennett et al; Reghan et al). This is important in terms of quality of care and re-attendance.

This project will look into the range, nature and quality of the current evidence on how pain affects breast screening attendance. How commonly do people say they won't attend, how often do they actually not attend, and which sub-groups are more likely to not re-attend? The project will run for 10 months and look at both organised and ad hoc screening programmes, and observational studies as well as RCTs.

The audience asked if the researchers will look at whether having a bad or painful experience with mammography can affect your friends' chance of re-attending? Perhaps a

prospective study could look into this. The project could also look at the effect of self-efficacy on the experience and tolerance of pain.

**Dr Tom Marshall, Senior Lecturer in Public Health, University of Birmingham**

- ColoRectal Early Diagnosis: Information Based Local Evaluation (CREDIBLE)

Most cases of bowel cancer are diagnosed clinically. Screening has a 50% uptake and 70% sensitivity. Even among people aged 60 to 69, only 35% of bowel cancers are detected through screening. The rests are diagnosed symptomatically, but diagnostic delays are common and at least 15% of cases present as emergencies.

Almost everyone's registered with a GP so almost everyone has an electronic primary care record that includes information about symptoms, diagnoses, prescriptions and lab results. There is potential to use this data for early diagnosis research.

Marshall plans to analyse electronic primary care records, create weekly lists of eligible patients who meet NICE referral criteria, and review those cases with the patients' GPs. He will track their final diagnoses, be they bowel cancer, polyps or inflammatory bowel disease.

In 20 GP practices and a 120,000-strong population, he would expect to see records from 20,000 people aged 60 to 79. Of these, 1000 will meet NICE referral criteria in the space of 18 months and 24 will have bowel cancer. Marshall will look at outcomes, as well as the views of GPs and patients.

When asked about the difference between NICE referral criteria, CAPER criteria and the new system of electronic records, Marshall answered that the CAPER and electronic criteria are similar, but both are better indicators of early disease than NICE referral criteria.

When asked how he'll know if he's made a difference to these patients, he said that he hopes there will be an educational impact to this study, as evidenced by a potential reduction in the number of referrals afterwards. "In a later study, we hope to down-stage bowel cancer or improve survival. But this is just the start," he added.

## Epidemiology and Cancer Outcomes

**Prof Jean Faivre, Professor of Oncology, Dept of Hepatogastroenterology, Dijon University Hospital Director of the Burgundy Colorectal Cancer Registry, Dijon**

- Keynote - Colorectal cancer: why has survival improved, and what more can be done?

A number of different elements in the diagnosis and management of colorectal cancer have contributed to improvements in survival over the years.

The first driver was the dramatic fall in post-operative mortality over the past 30 years, as revealed by data collected in Burgundy, France. Between 2004 and 2006, post-operative mortality in England, was two-fold higher than in Burgundy (Eva Morris et al).

The second driver was a rising proportion of patients, particularly over the age of 75, who were resected with curative intent. This was accompanied by technical improvements in surgery. In Burgundy, there was a trend towards earlier stage disease between 1976-1980 and 2001-2005. This, combined with a more aggressive attitude of surgeons towards resection, probably drove the increase in curative resection rates.

| | 1976-1980 | 2001-2005 |
|---|---|---|
| Stage 1 | 13.5 | 25.6 |
| Stage 2 | 26.7 | 26.3 |
| Stage 3 | 18.8 | 19.7 |
| Advanced disease | 28.0 | 40.3 |

Adjuvant treatments, particularly the use of pre-operative radiotherapy (R/T), might also have contributed to improvements in colorectal cancer survival.

When it comes to treatment, there are discrepancies between what is recommended and what is performed, e.g. in terms of whether R/T is delivered pre-operatively or post-operatively, and in terms of the number of lymph nodes that are resected. Some studies have found no relation between co-morbidity score and the treatment that is performed.

On top of that, treatments with proven clinical effectiveness are often slow to roll out, and elderly patients do not receive potentially beneficial treatments as often as other people. This should sound an alarm bell to policymakers and health services.

Further improvements in colorectal cancer survival can be expected over the coming years, driven by increases in public awareness, further progress in treatment, and organised mass screening.

**Catherine Foot, Cancer Research UK ICBP Programme Director/Senior Fellow, Kings Fund**

- International Cancer Benchmarking Partnership (ICBP) - Overview

Catherine Foot gave an overview of the ICBP. Its aim is to understand not only how, but why cancer survival rates differ between countries or jurisdictions.

Twelve jurisdictions in six countries across three continents are involved in the Partnership:

- Australia (New South Wales and Victoria)
- Cancer (Alberta, British Columbia, Manitoba and Ontario)
- Denmark
- Norway
- Sweden
- United Kingdom (England, Wales and Northern Ireland)

All of the jurisdictions involved in the ICBP have comparable wealth, universal access to health care and high-quality, population-based cancer registration. The ICBP is looking specifically at four cancers (breast, bowel, lung and ovarian), and is organised into 5 modules:

- Module 1 – Epidemiology
- Module 2 – Population awareness and beliefs
- Module 3 – Beliefs, behaviours and systems in primary care
- Module 4 – Root cause of diagnosis and treatment delays

- Module 5 – Treatment, co-morbidities and other factors

The first peer-reviewed publication from the Partnership reported results from Module 1 and has been published in The Lancet. In December 2010, IPSOS Mori was appointed to carry out the surveys for Module 2. Planning for the remaining modules continues, and outputs are expected throughout 2011 and 2012.

**Dr John Butler, ICBP & Clinical Advisor to Professor Sir Bruce Keogh, Department of Health**

- International Cancer Benchmarking Partnership (ICBP) - Focus on survival and ovarian cancer

The first report from the ICBP, published in The Lancet, compared cancer survival in breast, bowel, ovarian and lung cancer in Australia, Canada, Denmark, Norway, Sweden, and the UK. Ovarian cancer was chosen as an example of a less common cancer with large variations in survival across countries.

The analyses included 121,000 cases of ovarian cancer registered between 1995 and 2007. Relative survival increased across this period (from 33%-36%) but the gap between countries remains and the UK and Denmark show the lowest one and five-year survival rates. In the UK, those who survive for one year do relatively well, indicating that poorer one-year survival rates are down to late diagnosis rather than quality of care or treatment.

The data also suggest that late diagnosis is more of problem in older women (over 65 years of age) who showed lower relative survival compared with younger women. Deaths within 1 month of diagnosis are also more common in the UK (12%) compared with other countries (6% in Norway and 8% in British Columbia).

Future work will explore international variations in staging, treatment (by stage and age) and survival (by stage and treatment). Further information about the ICBP is available at www.icbp.org.uk

# Policy Research Unit

**Dr Russel Hamilton, Director of Research and Development, Department of Health**

- Introduction to the new Policy Research Unit (PRU) on cancer awareness, screening and early diagnosis

The Department of Health's new Policy Research Unit (PRU) will carry out research on cancer awareness, screening and early diagnosis.

The Department of Health is committed to evidence-based policy-making and, as such, has protected and increased funding for health research through the National Institute for Health Research and the Policy Research Programme. The Policy Research Programme has been allocated £4.7m over five years to fund the new Policy Research Unit.

The PRU meets the need for medium- to long-term research and specialist expertise in key policy areas. It will help build an evidence base to support the Outcomes Framework and to inform NAEDI. The PRU will report to the Director General of the Research and Development Department at the Department of Health and will be responsive to policy research calls from the Department of Health.

**Prof Stephen Duffy, Director of the PRU & Professor of Cancer Screening, Wolfson Institute of Preventive Medicine, Barts & the London School of Medicine & Dentistry**

- Director's Overview

The Policy Research Unit's work will cover the areas of cancer awareness, screening and early diagnosis. Its ultimate aim is to accelerate the reduction of cancer mortality.

The PRU will do several studies on awareness and inequalities. They will evaluate policies, develop and support the use of the Cancer Awareness Measure, link in with the ICBP, and study compliance with referral guidelines.

The UK can be proud of the quality assurance in its screening programmes, which do well as a result. PRU will evaluate the clinical benefits of the three screening programmes. It will also look at harms, including overdiagnosis and anxiety from false positives, and investigate the impact of changes to screening policy. It will evaluate new technologies and interventions on the accessibility of screening, and use this and other research to inform policy.

PRU will focus on health professionals' response to symptoms (by patients' age, sex and socio-economic status) and the predictive values of symptoms in primary care. They will do qualitative research on GP attitudes and ways of dealing with barriers to early diagnosis. They will define what we mean by early diagnosis (for example, whether it is ideal to define early-stage lung cancer as stages I and II).

PRU will also have PhD studentships and take part in methodological development activities.

**Prof Amanda Ramirez, Professor of Liaison Psychiatry & Director of Promoting Early Presentation Group, King's College London**

- Cancer awareness

The Cancer Awareness Measure (CAM) has been developed and used in a nationally representative survey of 2,000 adults. The results indicated low levels of cancer awareness overall, especially among men, ethnic minority groups and younger adults. The conclusion: we have a public health problem.

There are now also site-specific CAMs. These have been used, for example, to measure breast cancer awareness in north-east London with respect to age-related risk, symptom awareness and checking behaviour. Significant differences were found between ethnic minorities. For example, Asian women were less aware of non-lump symptoms and less likely to check their breasts, although they were more aware that breast cancer is more common in older women. Such results can be used to find out who is most at risk of late presentation and poor survival.

Module 2 of the ICBP aims to find out whether observed survival differences between participating countries can be explained in terms of variation in awareness and beliefs. The CAM has been incorporated into the ABC measure (awareness and beliefs about cancer), which measures opinions about such statements as "most cancer treatment is worse than the cancer itself", and "I would not want to know if I had cancer".

The PRU will support evaluation of the local NAEDI projects to oversee and interpret data across all 59 projects. It will also examine:

- associations between awareness and survival at a local level
- inequalities in awareness (using the CAM data repository)
- awareness and survival on a tumour-by-tumour basis

- interventions to promote awareness and early presentation (their recent systematic review identified little good evidence, although they gained some good evidence through an RCT of a new health professional delivered intervention to promote breast cancer awareness in older women)

**Prof Michel Coleman**

Cancer survival: from small-area to international comparisons

Survival figures can help to evaluate the impact of the Cancer Plan. Coleman has developed an all-cancers survival index for PCTs, with the aim of giving PCT managers data on their year-on-year progress. The index uses one-year survival in 11 consecutive single years. It's both a local measure of outcomes, and a national tool for surveillance and strategy.

The index showed a stark north-south divide in survival, one that failed to close over time even though survival rates improved in all areas.

To evaluate the Cancer Plan, Coleman used one-year survival trends to see if the rise in survival rates was accelerating in England (where the Cancer Plan had been implemented) and Wales (where it had not). The trends indicated accelerating improvement in colon cancer, but not breast cancer. Overall, there was some evidence of accelerating improvement in England compared to Wales, although it was not especially convincing.

**Prof Peter Sasieni, Professor of Biostatistics & Cancer Epidemiology, Wolfson Institute of Preventive Medicine, Barts & the London School of Medicine & Dentistry**

- Screening efficacy

The PRU will look at the efficacy of existing screening, and how to improve it. It is important to use screening technologies in a controlled, managed and evaluated way. Otherwise, we will not see any falls in mortality rates. As well as a good screening test, it is important to have good coverage, high-quality failsafe procedures, and good treatment.

Screening a population is like mass-producing goods in a factory – you need good quality assurance and you need to investigate the failures. Why did someone die of cancer even though a screening programme exists? Was it because they weren't screened, or because of failures in the test, follow-up or treatment?

You need to look at screen-detected cancers. It is necessary for them to have a better prognosis and survival, but not sufficient (because of lead time and length biases). It is important to study interval cancers too, looking at the effect after the last routine screen and in those who miss a screen.

The PRU plans to use a nested case-control approach to investigate questions about screening efficacy.

For breast cancer, they will look at:

- node positive cancers by time since last screen
- DCIS and cumulative incidence by screening interval
- interval cancers by density.

For bowel cancer, they will look at:

- the effect of screening at preventing advanced cancers
- the duration of protection of FOBt
- age and sex differences in these two aspects
- and the need for FOBt after colonoscopy.

**Prof Jane Wardle, Deputy Director of the PRU & Director, Cancer Research UK Health Behaviour Research Centre, University College London**

- Screening accessibility and coverage

We have a good programme of research but we need more psychosocial work on screening accessibility and coverage. Areas of interest include quantifying and explaining demographic variation in screening participation, looking at individual determinants of screening participation, and understanding how people make the decision to attend screening or not.

Gender, age, ethnicity and education inequalities are associated with screening uptake. The PRU will explore explanations for these inequalities to understand which mediators have the biggest effects on socio-economic differences in screening uptake.

The PRU will use the psychology of decision-making to look at screening and develop interventions, including:

- using discrete choice experiments
- giving a 'drip feed' of information about screening to find out the effects of each piece of information
- understanding the effect of framing, ordering and complexity of information.

**Prof Una Macleod, Professor of Primary Care, University of Hull**

- Early diagnosis and primary care

A significant event audit (SEA) in upper GI cancers is being conducted to understand what happened during "significant events", why, and how to learn for the future. Seventy-eight SEAs have been received. A report will be available soon.

**Prof Rosalind Raine, Professor of Health Care Evaluation, UCL Dept of Epidemiology & Public Health**

- Inequalities and early diagnosis

Inequalities will be a common theme for research in the PRU. The Unit is looking at ways of reducing inequalities in screening uptake (e.g. FOBt). Much has been achieved since the cancer plan, but inequalities persist in late presentation and undertreatment. Older people and those from poorer backgrounds are more likely to have emergency presentations for colorectal and lung cancers.

# Grantsmanship session

**Prof Peter Sasieni**

- Applicant's and committee member's perspective

**Prof Clare Wilkinson, Professor of General Practice CU & Director of Research in the North Wales Clinical School, Cardiff University**

- Community's perspective

**Dr Ekaterini Blaveri**

- Funder's perspective

# Keynote

**Prof Sir Mike Richards, National Clinical Director for Cancer, Department of Health**

- Research to policy and practice Q&A

# Cancer in Primary Care research session

**Prof David Weller, Head of General Practice, Division of Community Health Sciences, University of Edinburgh**

- Methods in early diagnosis research: Raising the standard

There are a number of challenges involved in early diagnosis research, ranging from consistency of definitions to methodology.

Diagnosis and patient journeys are complex and non-linear with little common understanding of time points and intervals. The research in this area has focused little attention on definitions of intervals and time points, and it often uses a minimalist approach with little theoretical basis. In addition, the methods and instruments are often poorly described or non-existent.

This makes research difficult to reproduce and interpret, which hinders international comparisons. It also means there is a limited pool of validated instruments or approaches that researchers can use.

These issues prompted the development of the Ca-PRI Consensus Working Group (CWG) on early diagnosis. Its aim is to promote greater international consistency in definitions and methods and produce guidance for early diagnosis researchers.

Its methods include the ‘consensus conference’ approach, nominal group techniques, and systematic reviews. The group have drafted a final report to go to the Expert Reference Group before going for wider consultation.

As an example of the process, the “date of first symptom” is a vital time point for basic research but has been difficult to define. Which symptoms are necessarily associated with an eventual diagnosis of cancer? What about chronic symptoms, or multiple symptoms? The

CWG suggested a definition of: “time point when the first bodily change and/or symptom are noticed”.

Likewise, “date of first presentation to primary care” is difficult to pin down, particularly with chronic or multiple symptoms. The CWG suggested a definition of: “the point at which, given the presenting signs, symptoms, history and other risk factors, it would be at least possible for the primary care clinician to have started investigation or referral for possible important pathology, including cancer”.

The definitions all need clarity and transparency. In studies where they will be used, the following methods should be employed in order of importance in order to obtain them: in-depth qualitative interviews; patient-completed questionnaires; practice-based case notes; and primary and secondary care database analysis.

This work will help to produce greater consistency in the use of time points. This will allow for better descriptions of intervals, which will, in turn, help determine the differences in survival.

**Dr Richard Neal, Clinical Senior Lecturer in General Practice, Department of Primary Care & Public Health, School of Medicine, Cardiff University North Wales Clinical School**

- Time to diagnosis in symptomatic cancer: Does it have an effect on clinical outcomes? Systematic review

We know around 90% of cancers present with symptoms and NAEDI consequently focuses on symptomatic presentation. There is potential to change clinical outcomes by intervening to hasten diagnosis with the assumption that it will mean earlier stage disease.

Mike Richards’ 1999 paper in the British Journal of Cancer demonstrated survival benefits for earlier diagnosis for breast cancer but as reported in Neal et al’s 2009 paper in the same journal, evidence for other cancers is mixed. This is difficult to understand because it is inconceivable to think that a quicker diagnosis cannot help.

There are two possible explanations for this observation. Firstly, at least for some cancers, there simply isn’t a benefit for early diagnosis once symptoms are present. Or secondly, there are some fundamental problems with the literature, partly due to methodological difficulties.

Neal conducted a systematic review, looking solely at primary cancers and incorporating a method of study quality assessment. The results confirmed the poor state of the evidence base, with poor reporting of methods, context of health system, samples, definitions etc. There were also issues with lead time correcting, confounding by indication, failure to adjust for outliers, and very few attempts to minimise bias in patient selection and sampling.

Neal found 310 studies that reported on impact of time delays on stage at diagnosis and/or survival. Their results show that the picture is still not clear.

Of the studies looking at time delay and its effect on stage at diagnosis, more than half found no association. Cancer types showing a tendency for positive associations include pharynx/larynx/oral, testicular, lung, melanoma and sarcoma. There were no studies showing a positive association for gastric cancer, and none with a negative association for oesophageal, ocular or sarcoma.

More than half of the studies looking at time delay and survival found no association too, but there were more negative associations overall. Studies on lung cancer showed about half positive and half negative associations. Pharyngeal, laryngeal and oral cancers studies all

either show no association or were positive. Half of the gastric cancer studies were negative, the other half showed no association. Other cancer types generally showed about one third of each type.

So we are still seeing mixed evidence and differences in stage and survival outcomes, which is likely due to methodological issues. Neal will continue with the work to see if more positive associations can be found, especially after adjusting for study quality. Stage is a proxy for survival, so he will concentrate on survival.

Why do results for cancer types vary? It could be that where a tumour's precise location is more predictable and accessible (e.g. breast, skin, pharynx and larynx), and when its growth rate is fairly predictable, then time is more likely to be linked to symptoms. This could make associations easier to detect.

**Prof Greg Rubin, Professor of General Practice & Primary Care, Durham University**

- DISCOVERY - a programme of research to optimise diagnosis of symptomatic cancer

The aims of DISCOVERY are to optimise diagnosis of symptomatic cancer using the three examples of lung, colorectal and pancreatic cancer at 3 levels:

- Patient level – identify symptoms associated with later stage at diagnosis and explore factors involved in later presentation.
- Primary care level – quantify risk of cancer in 10-12 cancers with a poor evidence base, by individual studies using pre-existing records; and map the paths patients take between first symptom and eventual diagnosis for three cancers.
- At primary/secondary care interface – establish the threshold level of absolute risk for the three cancers that warrants urgent investigation from the perspective of patients; and model alternative investigative paths using the above info.

The programme includes three themes.

- Theme 1 – The symptom study. This is a cohort with a nested case-control qualitative study in Cambridge and Stockton-on-Tees, which will recruit 7,000 people with symptoms of lung, colorectal and pancreatic cancers. Data will be collected by: identifying patients as referred through various pathways (e.g. two-week-wait, to routine clinic); questionnaire; collecting information from primary and secondary care records; and some in-depth interviews.
- Theme 2 – Importing large data sets and analysis. This will involve quantifying risk of 13 cancer sites, and complements prior work by Willie Hamilton and NSPCR. It will also identify the pathways for colon, pancreatic and lung cancer, which complements work within the National Audit of Cancer Diagnosis in Primary Care.
- Theme 3 – patient views on testing for cancer. This will establish a threshold of risk beyond which people want to be tested for cancer. Volunteers will be asked questions based on 12 vignettes and four different levels of risk. Patients will be asked their willingness to pay for testing as a proxy for their desire for a test. This will all be conducted on iPads by patients in waiting rooms.

This evidence-based, systematic approach – along with the consensus development work presented by David Weller, the GPRD studies, ICBP, related NCAT and DH cancer policy initiatives and the PRU – will help the development of a broader, well-informed picture of early diagnosis.

DISCOVERY is currently one year into a five-year programme with the various research strands progressing well. There has been integration within theoretical and applied research and it has been a stimulus for further successful collaborative proposals and a vehicle for linkage within the NAEDI programme.

# The NAEDI Research Conference

**17th & 18th February 2011**
**British Library, Euston, London**

## Day 1 – 17th February 2011

| Times | Session | Speaker |
|---|---|---|
| 09.30 | Registration & Refreshments | |
| 10:20 | Welcome & Overview | **Sara Hiom**, Director of Health Information & Cancer Data, Cancer Research UK |
| 10:40 | **Keynote** - A complex but rewarding challenge: changing the time to diagnosis | **Prof Peter Vedsted,** Vice Director, Research Unit for General Practice, Danish Research Centre for Cancer Diagnosis in Primary Care |
| 11:20 | **NCRI/NAEDI Research Call Session** | Chair:<br>**Dr Jane Cope**, NCRI Administrative Director |
| 11:25 | Response to Call 1 and introduction to Call 2 | **Dr Ekaterini Blaveri**, Senior Research Funding Manager, Cancer Research UK |
| 11:40 | Brief presentations/outlines of funded NAEDI/ NCRI Call 1projects:<br>• Evaluating the acceptability and feasibility of a gynaecological cancer information leaflet. | **Dr Alice Simon**, Research Associate, Health Behaviour Research Centre, University College London |
| | • The effects of pain in mammography on reattendance for breast cancer screening: a systematic review. | **Ms Patsy Whelehan**, Senior Research Radiographer (Breast Imaging), Centre for Oncology & Molecular Medicine, Ninewells Hospital & Medical School, Dundee |
| | • ColoRectal Early Diagnosis: Information Based Local Evaluation (CREDIBLE). | **Dr Tom Marshall**, Senior Lecturer in Public Health, University of Birmingham |
| 12:30 | Lunch & poster viewing | |
| 13:30 | **Epidemiology and Cancer Outcomes Session** with Q&A | Chair:<br>**Prof Michel Coleman**, Professor of Epidemiology and Vital Statistics, Cancer Research UK Cancer Survival Group |
| | **Keynote** - Colorectal cancer: why has survival improved, and what more can be done? | **Prof Jean Faivre,** Professor of Oncology, Dept of Hepatogastroenterology, Dijon University Hospital Director of the Burgundy Colorectal Cancer Registry, Dijon |
| | International Cancer Benchmarking Partnership (ICBP)<br>• Overview<br>• Focus on survival and ovarian cancer | **Catherine Foot**, Cancer Research UK ICBP Programme Director/ Senior Fellow, Kings Fund<br>**Dr John Butler,** ICBP & Clinical Advisor to Professor Sir Bruce Keogh, Department of Health |
| 15:10 | Refreshments & poster viewing | |
| 15:30 | **Introduction to the new Policy Research Unit** (PRU) on cancer awareness, screening & early diagnosis | **Dr Russell Hamilton**, Director of Research & Development, Department of Health |

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| **15:40** | Director's Overview | **Prof Stephen Duffy**, Director of the PRU & Professor of Cancer Screening, Wolfson Institute of Preventive Medicine, Barts & the London School of Medicine & Dentistry |
| **15:55** | Cancer awareness | **Prof Amanda Ramirez**, Professor of Liaison Psychiatry & Director of Promoting Early Presentation Group, King's College London |
| **16:05** | Cancer survival: from small-area to international comparisons | **Prof Michel Coleman** |
| **16:15** | Screening efficacy | **Prof Peter Sasieni,** Professor of Biostatistics & Cancer Epidemiology, Wolfson Institute of Preventive Medicine, Barts & the London School of Medicine & Dentistry |
| **16:25** | Screening accessibility and coverage | **Prof Jane Wardle**, Deputy Director of the PRU & Director, Cancer Research UK Health Behaviour Research Centre, University College London |
| **16:35** | Early diagnosis and primary care | **Prof Una Macleod,** Professor of Primary Care, University of Hull |
| **16:45** | Inequalities and early diagnosis | **Prof Rosalind Raine,** Professor of Health Care Evaluation, UCL Dept of Epidemiology & Public Health |
| **16:55** | Close | |
| **17:00** | Poster viewing & networking reception | |

## Day 2 – 18th February 2011

| **Times** | **Session** | **Speakers** |
|---|---|---|
| **09:30** | **Grantsmanship session** | |
| | • Applicant's and committee member's perspective | **Prof Peter Sasieni** |
| | • Community's perspective | **Prof Clare Wilkinson,** Professor of General Practice CU & Director of Research in the North Wales Clinical School, Cardiff University |
| | • Funder's perspective | **Dr Ekaterini Blaveri** |
| **10:30** | Refreshments & poster viewing | |
| **11:00** | **Keynote** – Research to policy and practice Q&A | **Prof Sir Mike Richards,** National Clinical Director for Cancer, Department of Health |
| **11:45** | **Cancer in Primary Care research session** Methods in early diagnosis research: Raising the standard | **Chair & Speaker:** **Prof David Weller,** Head of General Practice, Division of Community Health Sciences, University of Edinburgh |
| | Time to diagnosis in symptomatic cancer: Does it have an effect on clinical outcomes? Systematic review. | **Dr Richard Neal,** Clinical Senior Lecturer in General Practice, Department of Primary Care & Public Health, School of Medicine, Cardiff University North Wales Clinical School |
| | DISCOVERY – a programme of research to optimise diagnosis of symptomatic cancer | **Prof Greg Rubin,** Professor of General Practice & Primary Care, Durham University |
| **13:15** | Sandwich lunch & networking | |