

Ethical, Social and Economic Issues in Familial Breast Cancer: a compilation of views from the E.C. Biomed II Demonstration Project

Michael Steel^{1,#}, Elizabeth Smyth¹,
Hans Vasen², Diana Eccles³, Gareth Evans⁴,
Pål Møller⁵, Shirley Hodgson⁶,
Dominique Stoppa-Lyonnet⁷, Jenny Chang-
Claude⁸, Maria Caligo⁹, Patrick Morrison¹⁰
and Neva Haites¹¹

¹*School of Biology, Division of Medical Science and Human Biology, University of St Andrews, Fife KY16 9TS, Scotland, UK*

²*Foundation for the Detection of Hereditary Tumours, c/o University Hospital, Rijnsburgerweg 10, 2333 AA Leiden, The Netherlands*

³*CRC Genetic Epidemiology Research Group, Wessex Regional Genetics Service, Southampton, SO9 4HA, UK*

⁴*Department of Medical Genetics, St Mary's Hospital, Hathersage Road, Manchester M13 0JH, UK*

⁵*The Norwegian Radium Hospital, N-0310, Oslo, Norway*

⁶*Division of Medical and Molecular Genetics, Guy's Hospital, London Bridge, London SE1 9RT, UK*

⁷*Unité de Génétique Oncologique, Institut Curie, Section Medicale, 26 Rue d'Ulm, 75231 Paris cedex 05, France*

⁸*Division of Epidemiology, German Cancer Research Centre, Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany*

⁹*Institute of Pathology, University of Pisa, Via Roma 57, 56126, Pisa, Italy*

¹⁰*Department of Medical Genetics, City Hospital, Belfast BT9 7AB, UK*

¹¹*Department of Medicine and Therapeutics (Medical Genetics), Aberdeen University Medical School, Foresterhill, Aberdeen AB25 2ZD, Scotland, UK*

ABSTRACT: Demand for clinical services for familial breast cancer is continuing to rise across Europe. Service provision is far from uniform and, in most centres, its evolution has been determined by local conditions, specifically by local research interests, rather than by central planning. However, in a number of countries there is evidence of progress towards co-ordinated development and audit of clinics providing risk assessment, counselling, screening and, in some cases, prophylactic intervention. Much important information should emerge from continued observation and comparative assessment of these developments.

In most countries for which relevant data are available, there is a distinct bias towards higher social class among those who avail themselves of clinic facilities (in line with findings from many other health-promotion initiatives). This should be addressed when considering future organisation of clinical services.

Molecular genetic studies designed to identify the underlying mutations responsible for familial breast cancer are not generally regarded as part of the clinical service and are funded through research grants (if at all). Economic considerations suggest that there is a case for keeping this policy under review.

Familial cancers throw into sharp relief certain ethical and legal issues that have received much recent attention from government advisory bodies, patients' representatives, professional commentators and the popular media. Two are of particular importance;

Correspondence: Dr. Michael Steel, School of Biology, Division of Medical Science and Human Biology, University of St Andrews, Fife KY16 9TS, Scotland, UK

first, the right to gain access to medical records of relatives, in order to provide accurate risk assessment for a given family member, versus the right to privacy in respect of personal medical information and, second, the obligation (or otherwise) to inform family members of their risk status if they have not actively sought that knowledge. The legal position seems to vary from country to country and, in many cases, is unclear. In view of pressures to establish uniform approaches to medical confidentiality across the EC, it is important to evaluate the experience of participants in this Demonstration Programme and to apply the principle of “non-maleficence” in formulating regulations that should govern future practice in this field. Data on economic aspects of familial breast cancer are remarkably sparse and outdated. As evidence accrues on the influence of screening and intervention programmes on morbidity and mortality, there is a strong case for evaluating the cost-effectiveness of different models of service provision.

INTRODUCTION

Although the existence of familial forms of common cancers, including breast, has been recognised for over a century, the medical profession, with a few notable exceptions, has paid little attention to the clinical implications until the present decade. Suddenly, heritable cancer risk has become an issue of concern not only within the narrow field of clinical genetics but in the public domain, as demonstrated by the proliferation of articles in the popular press, programmes on radio and television and pressure from families, who believe themselves to be at increased risk, for access to appropriate counselling and screening services.

In most countries, health services were ill prepared to meet the surge in demand. This applies to North America [1] as well as to Europe. “Cancer Family Clinics” have therefore evolved, in piecemeal fashion, from a variety of starting points, often based on research activity in academic centres [2]. In several instances, national and regional plans are now being formulated to extend services to a wider population [3]. For example, the development of cancer family clinic networks under the UK National Health Service followed reports from

advisory committees set up for England and Wales [4] and, separately, for Scotland [5]. Comparable activity in several other European countries is recorded in a number of papers elsewhere in this volume. A major purpose of this Demonstration Programme has been to collate experience from centres that have been operating under a variety of different circumstances, to identify potential solutions to common problems.

ORGANISATION OF CLINICS

Since cancer family clinics must serve multiple purposes — ascertainment of those at risk, risk assessment, counselling about screening or intervention options, organising screening programmes, offering molecular diagnosis, identifying and responding to psychological needs of cancer families, auditing the outcome of their own activities, educating healthcare professionals and the public and undertaking research [2,6–8] — it might seem that they need to be set up as multi-disciplinary organisations. The availability, on a single site, of specialist geneticists, surgeons/gynaecologists, radiologists and psychologists, closely associated with a molecular diagnostic laboratory, certainly provides all the requirements for an excellent service. However that is not always a practical possibility and it would be counterproductive to suggest that no service should be introduced until all these elements are together under one roof. In many centres there are separate but well-established genetics clinics, breast screening programmes, clinical psychology services and molecular biology laboratories whose remits can be extended to meet the needs of cancer families without necessarily re-housing any of them.

There is, however some danger that the mere existence of these individual components may be presumed to constitute an adequate breast cancer genetics service. It should therefore be made clear that special provision must be made for co-ordination. For example, if a patient is assessed in the genetics clinic as requiring regular clinical and radiological surveillance, then there must be

a mechanism for ensuring that this will happen and, further, that the outcome of screening is recorded along with the genetic findings. In other words, someone must have overall responsibility for keeping track of what is happening to that patient (and her family) and the record should be maintained in a manner that will permit audit of the service as a whole. In relation to mammography, there are specific additional responsibilities — to ensure appropriate quality control, to retain serial films for comparative purposes and to regulate radiation exposure [9].

CHARACTERISTICS OF CLINIC CLIENTELE

One feature that seems to be common to breast cancer family clinics in several countries is a strong bias towards higher social class among their clientele. This had been noted in seven out

of twelve clinics surveyed: only two believed there was no such bias in their population while three could not make an assessment. In south-east Scotland the bias takes the form of a considerable excess of university graduates (including a substantial proportion of healthcare professionals) and a significant deficit of the most deprived group [10] (Figure 1). While similar patterns are well recognised in other health-promotion programmes [11], it does appear to be more extreme in this particular setting. To some extent, this is understandable, given that, in the early days of the service, women had to be uncommonly “aware” of the specific health issue of familial breast cancer in order to find their way to the clinics. However, a survey of European centres within this Demonstration Programme suggested that there has been only a slight trend towards levelling-out across the social spectrum as services have become better established. An interesting

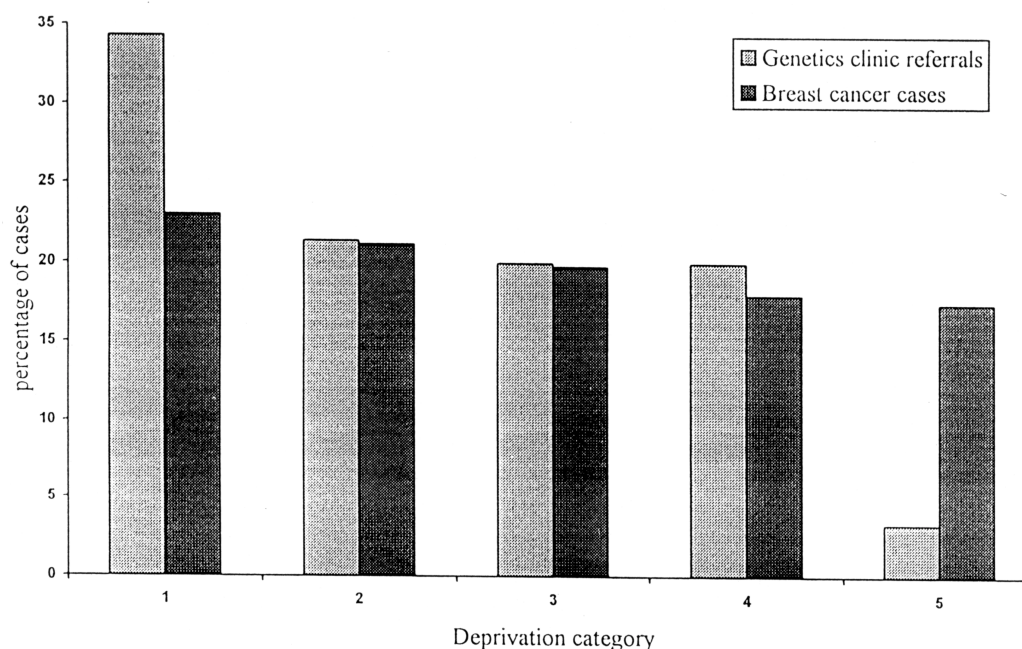


Fig. 1. Distribution of 425 consecutive women attending the Edinburgh breast cancer family clinic (“Genetics clinic”) according to deprivation category (1 = least deprived, 5 = most deprived. Carstairs and Morris, *Deprivation and Health in Scotland*. Aberdeen University Press, 1991). The corresponding distribution for women with breast cancer, seen by the symptomatic breast service over the same period, is shown for comparison. Note the striking deficit of women from deprivation category 5 and the relative over-representation of those from deprivation category 1 among the genetics clinic referrals.

suggestion, from formal psychological assessment of the Edinburgh clinic population, is that those classified as “Blunters” on the Miller behaviour scale (i.e. who tend to cope with issues by avoidance or denial) seem much less likely to be referred to the clinic by their family doctor if they belong to a socially deprived group. This may imply that, at present, GP’s are not able to identify the less articulate subgroup of at-risk women.

Despite the well-known trend for breast cancer to be commoner in women of high social class, the distorted social mix of breast cancer family clinic patients should be addressed if the service is to reach all those in need. Information campaigns directed both at primary healthcare workers and at women from lower social groups may be necessary. There could be a specific “outreach” role for genetics nurse specialists and perhaps some adjustment of clinic times and sites (e.g. evening clinics in community centres) to accommodate women in low-status jobs. This topic does appear to merit further study, perhaps evaluating some of the approaches indicated above.

THE ECONOMICS OF MUTATION SEARCHING

In most centres, the service element of molecular laboratory work is confined to screening individual members of families where a specific germline mutation has already been found. Searching for new mutations is regarded as a research activity and can be funded only from competitive grants [3]. As the efficiency of mutation-detection improves, the case for regarding it as “pure research” becomes weaker and the economic argument for allocating some service resources for this purpose becomes stronger [12].

A reasonable estimate of the new referral rate of families at substantially increased genetic risk of breast cancer is about 450 per year per million population. These, in the main, will be women requiring annual screening between the ages of 35 and 50. A “steady state” will then be achieved

after 15 years, when 450 women aged 50 will cease to require screening and another 450 (spanning the full age range) will replace them. The total number receiving an annual clinical examination and mammogram will be around 6000 and the total annual cost something over 1 million Euros. An effective mutation-detection protocol might lead to some 30% of these patients being discharged from further follow-up because they can be shown not to be at risk [13]. Obviously, the figures presented are somewhat speculative and depend, to a great extent, on the population frequency of recurring founder mutations [12] but it would seem wise to keep under review the economics of molecular laboratory input to this area.

MEDICAL INFORMATION: PRIVACY AND LEGITIMATE ACCESS

In recent years there have been many attempts to formulate an acceptable ethical and legal framework that protects the privacy of individual records yet permits necessary epidemiological and clinical research [14–23]. These are often characterised by indecision or vagueness when addressing specific, real-life situations. In the field of genetics there is the special issue of whether information about heritable factors can be regarded as the “property” of any one individual rather than belonging to all who share the same inheritance. At one extreme, it might be suggested that taking a family history in the clinic infringes the rights of relatives who have not given explicit permission for their illnesses to be divulged. In that case, is it the doctor who asks the questions or the patient who answers who is at fault? Of course we descend rapidly into absurdity in pursuing this argument. Nevertheless, when assessment of risk and decisions about management rest on a family’s medical history, the onus is on the doctor to ensure that the information on which he/she is acting is as accurate and complete as possible. This often requires seeking confirmation of diagnosis in a relative from hospital records.

In the majority of instances, relatives are

willing, indeed eager, to authorise access to their health records and there is no question that the preferred route to such information is through the family member who has been referred to the clinic and who can raise the issue with her relatives before a formal approach is made for written consent. However, problems can arise when there is little personal contact within a family or where the family tree is unusually extensive so that distant relatives whose medical histories may be relevant, are not known personally to the proband. Then questions arise about the justification or otherwise for taking steps to verify the medical information. We may not know, until the information has been obtained, whether it falls into the category of genetic data “jointly owned” by all the family; yet, particularly in such a sensitive area as breast/ovarian cancer, to ask a relative — not in direct contact with the proband and possibly unaware of any concern about familial cancer — for access to her medical records, could often cause unwarranted distress. Furthermore, the logistic problems of tracing relatives or their next of kin before proceeding to verify family histories provided in the clinic would add enormously to the workload (and cost) of a cancer family service.

While the law remains very uncertain in most European countries, there are pressures to reach a common policy, one which places a very high premium on the concept of privacy [21]. As indicated above, such a policy, if enforced, could operate to the detriment of good medical practice, specifically, though not exclusively, in the field of genetics. It is worth noting that in existing legal codes, privacy is never paramount [17,21,24]. Provision is invariably made for disclosure of medical information in the interests of public safety (e.g. in the case of “notifiable” infections) and, revealingly, to counter fraudulent claims where healthcare is provided through private insurance! The public interest might be better served by an approach to legislation that deals very severely with abuse of confidential medical information rather than placing barriers in the way of accessing that information for legitimate purposes. All health care professionals

explicitly accept the duty to respect the confidentiality of medical information and deal with sensitive information every day. Exchange of data about patients is a common and necessary part of routine practice in virtually every speciality and professional standards of confidentiality are taken for granted in such exchanges. There is at least a case for recognising the legitimacy of this practice in genetics. The principle of “non-maleficence” would seem to be appropriate, meaning that individuals should be protected from the harm that might come from release of their medical details but there should be no automatic prohibition of activities which cause no harm [25].

DUTY OF CARE

There remains the vexed question of “the cousin in Australia”, subjecting the geneticist to competing ethical pressures; on the one hand, to respect the wish for privacy on the part of those family members with whom the clinic has direct contact but, on the other, to recognise that more distant relatives have the right to be advised of possible genetic risk to themselves. As evidence grows for the benefits of early detection (or prevention) of cancer through recognition of genetic risk, it becomes increasingly likely that a relative who has not been advised of her possible risk status might bring a case for negligence against a geneticist (or his/her employing authority) who has known of the existence of that risk but who has not taken reasonable steps to warn all potentially affected members of the family [17,22,25,26].

From the preceding discussion, it should be clear that unwillingness on the part of the original patient to share with her family information about genetic risk is unlikely to be an adequate defence. In other words, if risk is recognised and especially if there are risk-reduction measures available, then there is a duty to transmit that information. But how far does that duty extend? Does it apply only to those family members known to the original patient or does the clinic

need to put in place mechanisms for extending family trees through access to public records of births, marriages and deaths — by advertising in the press or by circulating bulletins to General Practitioners? Who should bear the cost of these measures?

There are no simple answers to these questions but there may be an opportunity now to address them calmly before we are faced with an actual case that could set a precedent, exacerbating an already difficult problem.

COST EFFECTIVENESS

Finally, while the motivation for establishment of cancer genetics services is not primarily economic, it is prudent to examine the cost-effectiveness of any new development in health care. The overall costs of breast cancer family clinics are not very difficult to calculate and can be modified, for example, by altering the criteria for eligibility (i.e. the age range of patients and/or the numbers of affected relatives, their ages of disease onset and the closeness of the family relationship). Screening frequency may also be a relevant variable and introduction of more expensive techniques such as MRI could enter the equation. Greater use of nurse specialists and genetics associates may play some part in containing costs. The other side of the calculation — the savings to be made by prevention or early detection of breast/ovarian cancer — is much more difficult to work out. There are surprisingly few data on current costs of managing advanced breast cancer in young women. The two most commonly cited papers [27,28] predate the development of very expensive drugs such as the taxanes or modern aggressive approaches to chemotherapy with autologous bone marrow reinfusion. Young breast cancer patients are the most likely candidates for these regimes. Some account should also be taken of the “social” cost of prolonged illness and death in young women who have responsible jobs and/or who are bringing up young children. However, we require data of the type now emerging from this Demonstration

Programme to begin realistic modelling of the reductions in morbidity and mortality to be anticipated from cancer family clinics. Attention should therefore be given very soon to a thorough economic appraisal of this development in health care.

Acknowledgements

The authors are grateful to the many families in all participating centres who co-operated generously in the establishment and assessment of breast cancer family services. We also acknowledge the constant help and advice of professional colleagues too numerous to identify individually.

References

- [1] Thompson, J.A., Weisner, G.L., Sellers, T.A. et al. Genetic services for familial cancer patients: a survey of National Cancer Institute centers. *J. Natl. Cancer Inst.* **87**, (1995) 1446–1455.
- [2] Vasen, H.F., Haites, N.E., Evans, D.G. et al. Current policies for surveillance and management in women at risk of breast and ovarian cancer: a survey among 16 European family cancer clinics. *Eur. J. Cancer* **34**, (1998) 1922–1926.
- [3] Hodgson, S., Milner, B., Brown, I., Bevilacqua, G., Chang-Claude, J., Eccles, D., Evans, G., Gregory, H., Møller, P., Morrison, P., Steel, C.M., Stoppa-Lyonnet, D., Vasen, H. and Haites, N. Cancer genetics services in Europe. *Disease Markers* **15**, (1999) 3–13.
- [4] Harper, P.S. Genetics and Cancer Services: Report of a working party for the Department of Health for England and Wales. DoH London (1997).
- [5] The Scottish Office Department of Health: Priority Areas Cancer Team/Genetics Subcommittee of the Scottish Cancer Co-ordinating and Advisory Committee. Cancer Genetics Services in Scotland. Edinburgh. (1998).
- [6] Ponder, B.A.J. Setting up and running a familial cancer clinic. *Brit. Med. Bull.* **50**, (1994) 732–745.
- [7] Schneider, K.A., Patenaude, A.F. and Garber, J.E. Testing for cancer genes: decisions, decisions. *Nature Med.* **1**, (1995) 302–303

- [8] Eeles, R. Testing for the breast cancer predisposition gene, BRCA1. *BMJ* **313**, (1996) 572–573.
- [9] Law, J.A. Cancers detected and induced in mammographic screening: new screening schedules and younger women with family history. *Br. J. Radiol.* **70**, (1997) 62–69.
- [10] Smyth, E. Evaluation of a new clinical service for women with a family history of breast cancer. MD thesis, University of Edinburgh. (1999).
- [11] Roberts, M.M., Alexander, F.E., Andersen, T.J. et al. Edinburgh trial of screening for breast cancer: mortality at seven years. *Lancet* **335**, (1990) 241–246.
- [12] Heimdal, K., Maehle, L. and Møller, P. Costs and benefits of diagnosing familial breast cancer. *Disease Markers* **15**, (1999) 167–173.
- [13] Peelen, T., Cornelis, R.C., Van den Vliet, M. et al. The majority of Dutch high-risk breast cancer families are due either to BRCA1 or BRCA2. *Eur. J. Hum. Genet.* **4**, (1996) 225–230.
- [14] Royal College of Physicians of London working group. Ethical issues in clinical genetics. London (1991).
- [15] Nuffield Council on Bioethics: Genetic screening; ethical issues. London (1993).
- [16] Newcombe, H.B. Cohorts and privacy. *Cancer Causes and Control* **5**, (1994) 287–291.
- [17] McLean, S.A.M. The new genetics: a challenge to clinical values? *Proc. Roy. Coll. Phys. Edin.* **26**, (1996) 41–50.
- [18] Pembrey, M. and Anionwu, E. Ethical aspects of genetic screening and diagnosis. Ch32 in Emery and Rimoin's Principles and Practice of Medical genetics. Churchill livingstone, New York. (1996).
- [19] Rothenberg, K., Fuller, B., Rothstein, M. et al. Genetic information and the workplace: legislative approaches and policy challenges. *Science* **275**, (1997) 1755–1757.
- [20] Reilly, P.R., Boshar, M.F. and Holzmann, S.H. Ethical issues in genetic research: disclosure and informed consent. *Nature genet.* **15**, (1997) 16–20.
- [21] Vandenbroucke, J.P. Maintaining privacy and the health of the people. *BMJ* **316**, (1998) 1731–1732.
- [22] ASHG statement: Professional disclosure of familial genetic information. *Am. J. Hum. Genet.* **62**, (1998) 474–483.
- [23] Wadman, M. Privacy bill under fire from researchers. *Nature* **392**, (1998) 6.
- [24] Reilly, P.R. Legal issues in genetic medicine. Ch 33 in Emery and Rimoin's Principles and Practice of Medical Genetics. Churchill Livingstone, New York. (1996).
- [25] Harris, J. The use of information (autonomy and confidentiality). *Disease Markers* **10**, (1992) 195–198.
- [26] Offit, K. Clinical Cancer Genetics: Risk Counseling and Management. Wiley-Liss. New York. (1998).
- [27] de Koenig, H.J., van Ineveld, B.M., van Oortsmarsen, G.J. et al. Breast cancer screening and cost-effectiveness; policy alternatives, quality of life considerations and the possible impact of uncertain factors. *Int. J. Cancer* **49**, (1991) 531–537.
- [28] Richards, M.A., Braysher, S., Gregory, W.M. and Rubens, R.D. Advanced breast cancer: use of resources and cost implications. *Br. J. Cancer* **67**, (1993) 856–860.