Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health technology assessment (HTA) of surveillance of women aged less than 50 years at elevated risk of breast cancer

Advice to the National Cancer Control Programme

19 March 2013

Safer Better Care

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is the independent Authority established to drive continuous improvement in Ireland's health and personal social care services, monitor the safety and quality of these services and promote person-centred care for the benefit of the public.

The Authority's mandate to date extends across the quality and safety of the public, private (within its social care function) and voluntary sectors. Reporting to the Minister for Health and the Minister for Children and Youth Affairs, the Health Information and Quality Authority has statutory responsibility for:

- **Setting Standards for Health and Social Services** – Developing person-centred standards, based on evidence and best international practice, for those health and social care services in Ireland that by law are required to be regulated by the Authority.

- **Social Services Inspectorate** – Registering and inspecting residential centres for dependent people and inspecting children detention schools, foster care services and child protection services.

- **Monitoring Healthcare Quality and Safety** – Monitoring the quality and safety of health and personal social care services and investigating as necessary serious concerns about the health and welfare of people who use these services.

- **Health Technology Assessment** – Ensuring the best outcome for people who use our health services and best use of resources by evaluating the clinical and cost effectiveness of drugs, equipment, diagnostic techniques and health promotion activities.

- **Health Information** – Advising on the efficient and secure collection and sharing of health information, evaluating information resources and publishing information about the delivery and performance of Ireland's health and social care services.

Foreword

Breast cancer is the most common invasive cancer diagnosed in women in Ireland and the second most common cause of cancer death in women. Although the majority of breast cancers are sporadic, it is estimated that 25% of cases relate to a familial risk with 5% to 10% of all cases specifically relating to a genetic predisposition. Cancers relating to genetic predisposition have a median age of onset more than 20 years earlier than the general population. The lifetime risk of developing breast cancer is 10% to 11% for the general population; for female carriers of mutations of the *BRCA1* and *BRCA2* genes, average lifetime rates of up to 60% to 80% are reported.

Screening and surveillance are secondary preventive measures that aim to detect breast cancer at the earliest possible stage in order to reduce the rate of breast cancer death. Screening refers to monitoring those at average risk of a disease; surveillance refers to the monitoring of those known to be an increased risk of the disease. Internationally recommended surveillance imaging options include digital mammography, magnetic resonance imaging (MRI) or a combination of the two. However, there is currently no consensus as to the optimal design of a surveillance programme.

The Director of the National Cancer Control Programme (NCCP) in the Health Service Executive (HSE) requested that the Health Information and Quality Authority (the Authority or HIQA) undertake a health technology assessment (HTA) in relation to a potential national surveillance programme for women aged less than 50 years at elevated risk of breast cancer due to a familial or genetic predisposition. The purpose of this HTA is to examine the safety, effectiveness, cost-effectiveness, budget impact, and resource implications of a surveillance programme based on digital mammography, magnetic resonance imaging (MRI) or a combination thereof.

Work on the assessment was undertaken by an Evaluation Team from the HTA Directorate of the Authority. A multidisciplinary Expert Advisory Group (EAG) was convened to advise the Authority during the conduct of this assessment.

The Authority would like to thank its Evaluation Team, the members of the EAG and all who contributed to the preparation of this report.

Dr Máirín Ryan,
Director of Health Technology Assessment,
Health Information and Quality Authority

Advice to the National Cancer Control Programme

This health technology assessment (HTA) examined the potential provision of a national surveillance programme for women aged less than 50 years at elevated risk of breast cancer due to a genetic predisposition or a strong family history. Evidence of the safety and effectiveness of digital mammography and magnetic resonance imaging (MRI) were assessed as well as the cost-effectiveness, budget impact and resource implications of various surveillance options.

The key findings of this HTA which precede and inform the Authority's advice are:

a) Based on a 10-year risk of breast cancer between age 40-50 years of less than 3% as average risk, between 3% and 8% as moderate risk, and greater than 8% as a high risk, the estimated percentage of women in Ireland aged less than 50 years in these risk groups is 92.4%, 5.7% and 1.9%, respectively. Women at high risk of breast cancer contribute disproportionately to the incidence of early breast cancer. Although comprising less than 2% of the population, women at high risk are estimated to contribute 10% of incidence of breast cancer in women aged less than 50 years.
b) There is limited evidence directly comparing surveillance MRI, film mammography and digital mammography in women aged less than 50 years at an elevated risk of breast cancer. MRI is more sensitive, but less specific than mammography for the target population. Combined MRI plus mammography improves sensitivity further, with a minimal decrease in specificity. Although uncommon, frequent exposure to radiation through a mammography-based surveillance programme from a young age may induce breast cancers.
c) The overall effectiveness of a surveillance programme for women at elevated risk of breast cancer depends on the combination of age range, imaging technology and frequency of surveillance. International practice varies, although use of mammography is usually avoided in women aged less than 30 years and the role of MRI has to date often been limited to that of an adjunct to mammography. While there is evidence of a mortality reduction in average risk populations through earlier detection and treatment, there is a lack of data specific to women aged less than 50 years at elevated risk of developing breast cancer. Surveillance has effects that are both positive (e.g., early detection leading to less toxic treatment) and negative (e.g., radiation-induced carcinoma, overdiagnosis, and unnecessary biopsies).

d) At present, some women aged less than 50 years considered to be at elevated risk of developing breast cancer are offered surveillance, although the frequency, type of imaging and starting age vary considerably. Women with *BRCA1* and *BRCA2* mutations will typically be offered annual MRI from age 30 with the addition of annual digital mammography from age 30 or 35. Many women at high familial risk with no identified genetic mutation and those at moderate risk receive annual or digital mammography every two years from the age of 30 or 35.

e) The analyses conducted for this HTA show that, in Ireland, organised surveillance is cost-effective compared to no surveillance for women aged less than 50 years with an identified high penetrance genetic mutation based on a threshold of €45,000/QALY. For women aged less than 50 years with either high familial risk and no identified genetic mutation or those at moderate risk, standardised surveillance is not cost-effective by traditional standards when compared to no surveillance.

f) For women aged less than 50 years with identified high penetrance genetic mutations, standardised surveillance offers a significant opportunity to reduce mortality. Annual MRI from age 30 to 49 is recommended for those with *BRCA1* and *BRCA2* mutations. The addition of annual digital mammography from age 40 to 49 could be offered to maintain accordance with current international practice although this is more costly and unlikely to result in a substantial clinical benefit. For women with an identified *TP53* mutation, annual MRI surveillance from age 20 to 49 is the recommended strategy.

g) For women at high familial risk with no identified genetic mutations, surveillance before the age of 40 is not recommended on the basis of cost or clinical effectiveness. While surveillance from age 40 to 49 is not cost-effective compared to no surveillance, providing annual MRI-based surveillance is less costly than existing ad hoc surveillance and offers the potential of a minor mortality reduction. If it is considered impractical to offer MRI-based surveillance to such a large cohort, but offering some form of standardised surveillance is considered desirable, then annual digital mammography from age 40 to 49, in accordance with current international practice, would be less costly and more effective than existing surveillance.

h) For women at moderate risk, surveillance before the age of 40 is not recommended on the basis of cost or clinical effectiveness. Similar to women with high familial risk, surveillance is not cost-effective from ages 40 to 49 compared to no surveillance. However, providing annual MRI-based surveillance is less costly than existing ad hoc surveillance and offers the potential of a minor mortality reduction. If it is considered impractical to offer MRI-based surveillance to such a large cohort, but offering some form of standardised surveillance is considered desirable, then annual digital

mammography from age 40 to 49 would be less costly and more effective than existing surveillance.

i) In exceptional individual cases, it may be appropriate to commence surveillance at an earlier age than for the risk group generally, given the individual's particular family history and context.

j) The known population of women aged less than 50 who are at elevated risk of developing breast cancer is relatively small and hence, the incremental budget impact of different surveillance strategies for this cohort tends to be small. A strategy of no surveillance would cost approximately €1.7 million over five years arising from the management of symptomatic cases. Relative to this, the proposed strategies will have an incremental five-year budget impact of €819,000. This compares with an estimated incremental five-year budget impact of €908,000 for the existing ad hoc surveillance. Of note, the known population of women at elevated risk of developing breast cancer is only a small proportion of the estimated true population, however, in the absence of any change to how women at elevated risk are identified, it is not anticipated that the known population will increase substantially in the short to medium term on foot of introducing standardised surveillance.

k) The modelling approach in this HTA took full account of the uncertainty associated with the various parameters used. Scenario and sensitivity analyses were used to test the robustness of the results to different assumptions regarding the data.

l) The main ethical issues associated with provision of a formal surveillance programme for women aged less than 50 years at elevated risk of breast cancer include informed consent, equity of access and allocation of resources. Those invited for surveillance should receive sufficient information to enable them to fully understand the benefits and risks of surveillance and to understand the alternatives.

m) Ad hoc surveillance is currently offered to a variable extent at a local and regional level. In the absence of a structured programme, there may be inconsistencies in the availability and type of surveillance offered, resulting in inequitable care.

n) An organised surveillance programme will improve equity of access; it should have quality key performance indicators (KPIs) to measure performance against targets or expectations.

As economic models incorporate a number of assumptions and are dependent on the quality of data available, the results are subject to a degree of uncertainty. Bearing in mind the estimates and assumptions that were used in this analysis and arising from the findings above, the Authority's advice to the National Cancer Control Programme is as follows:

- Surveillance is cost-effective compared to no surveillance for women aged less than 50 years with an identified high penetrance genetic mutation. For women aged less than 50 years with either high familial risk and no identified genetic mutation or those at moderate risk, surveillance is not cost-effective by traditional standards when compared to no surveillance.
- For women aged less than 50 years with identified high penetrance genetic mutations other than *TP53*, annual MRI from age 30 to 49 is recommended. The addition of annual digital mammography from age 40 to 49 could be offered to maintain accordance with current international practice.
- For the subgroup with a *TP53* mutation, annual MRI surveillance from age 20 to 49 is recommended.
- For women at high familial risk with no identified genetic mutations, annual digital mammography from ages 40 to 49 is preferable to existing ad hoc surveillance.
- For women at moderate risk, annual digital mammography from ages 40 to 49 is preferable to existing ad hoc surveillance.
- An organised surveillance programme will improve equity of access; it should have quality key performance indicators (KPIs) to measure performance against targets or expectations.

Published by the Health Information and Quality Authority.

For further information please contact:

Health Information and Quality Authority
Dublin Regional Office
George's Court
George's Lane
Smithfield
Dublin 7

Phone: +353 (0) 1 814 7400
URL: www.hiqa.ie