Counting the cost: researchers create model to help life insurers calculate breast cancer survivors' risk of death more accurately

EBCC PRESS RELEASE: **Barcelona, Spain:** As early detection and treatment of breast cancer improves, more and more women are surviving the disease. However, they still face challenges, which include determining the moment when it might be reasonable to state they are "cured" of the disease, and obtaining life insurance.

"In the Netherlands, most applications for life insurance are accepted, but not for cancer survivors. A lot of former breast cancer patients are rejected for life insurance or subjected to higher insurance premiums," said Ms Marissa van Maaren, a researcher at the Netherlands Comprehensive Cancer Organisation (Utrecht, The Netherlands), at the 11th European Breast Cancer Conference today (Thursday). "Others might not even apply for life insurance because they might think they do not have a chance of being accepted. Former cancer patients in other countries may face similar problems.

"At the request of the Dutch Association of Insurers and the Dutch Federation of Cancerpatient Organisations (NFK), we have created a model for predicting the extra risk of death of breast cancer patients and survivors for up to ten years after their diagnosis. Importantly, this model takes into account that survival rates improve as each year passes by. This should provide patients and their clinicians with increased insight into their prognosis, and medical advisors with a more reliable basis on which to make their decisions."

Ms van Maaren and her colleagues matched 23,234 women diagnosed with breast cancer in 2005 and 2006 with the general Dutch population. Information on the patients, including age, year of diagnosis and stage of breast cancer, was taken from the Netherlands Cancer Registry. There were 10,101 women diagnosed with stage I cancer, 9,868 with stage II and 3,265 with stage III.

"We were interested in the excess risk of death for breast cancer survivors, so the risk of death in the patient population minus the risk of death in the general Dutch population. We also wanted to take into account the number of years survived after diagnosis," she explained.

Then she built 30 models, ten for each of the three stages of breast cancer for each year of survival after diagnosis up to ten years. The models were adjusted to take account of important prognostic factors that might influence the risk of death, such as type of breast cancer, whether or not the cancer had spread to lymph nodes, age at diagnosis, type of surgery, and if treatments such as radiotherapy, chemotherapy, hormone therapy and other targeted treatments were used.

"All the separate models were integrated into one model that, for every stage of disease, shows the extra

risk of death in the first ten years compared to the general Dutch population, conditional on the number of years survived after diagnosis," she said.

To give an example, the model can show that a particular patient with certain characteristics who applies for life insurance two years after diagnosis might have a 5.8% extra risk of dying within ten years compared to the general Dutch population, but if she applies five years after diagnosis her risk may be reduced to 4.2% and after nine years it may be 0.6%.

"This could result in lower premiums as the years go by, although the exact premium may vary depending on the insurance company," said Ms van Maaren. "It's also important to bear in mind that treatments for breast cancer have improved a lot since 2005 to 2006 when these women were diagnosed."

The researchers tested the accuracy of the 30 underlying models and found that they had a reasonable to good ability to predict the outcome and to discriminate between the risk of dying or staying alive. In addition, validation on an external population showed similar outcomes.

Now, Dutch insurance companies are testing the newly-developed model, comparing its results with those from old data, and calculating how it might affect whether or not someone is accepted for life insurance and the effect on their premiums. Then it will be discussed with all patient organisations and working groups involved in the project, and when everyone agrees that the model is valid enough to use, it could be implemented.

As the model is based on the Dutch population, other countries would need to validate it against their own populations before it could be used. "However, we do not expect that the extra death rates, in other words the difference between breast cancer survivors and the general population, will be very different," said Ms van Maaren.

"Currently, insurance companies in The Netherlands are using international data to assess breast cancer patients' and survivors' risk of dying, which may not be specifically targeted at the Dutch population. In addition, every insurance company is free to use other information on which to base their decision. We think it is unjustified to reject patients based on data that may not predict the risk for a Dutch breast cancer patient or survivor correctly. At present, the life insurance application process is not transparent and this results in a lot of uncertainty and incomprehension among breast cancer patients and survivors. We hope insurance companies will use this model and be more transparent with patients regarding the outcome of their life insurance applications."

She said the model could support decisions made by clinicians, insurance companies and patients but would not automate the process. "Clinicians and insurance companies take account of a number of other variables not included in this model, such as the presence of other diseases and conditions. But it could provide clinicians with a basis on which to deem a patient cured of the disease, and insurance companies have a more reliable basis for their life insurance application process that is based on more recent Dutch clinical data," she concluded.

Co-chair of the European Breast Cancer Conference, Professor Isabel Rubio, director of the Breast Surgical Unit at Clinica Universidad de Navarra (Spain), who was not involved with the research, commented: “This is an interesting study; however, it is just based on the Dutch population and would need to be re-worked for populations in other countries. It does appear to be a useful tool that might help former patients lead more normal lives and caregivers could use this information to better inform survivors about their actual prognosis.”

Abstract no: 9, “When will a breast cancer patient be cured? A prediction model predicting the conditional extra risk on mortality” **Thursday,** “After the primary treatment of breast cancer, then what?” clinical science session, 10.05 hrs, Goya room.

The research was partly funded by the Dutch Association of Insurers. It was commissioned by the Dutch Federation of Cancerpatient Organisations (NFK), and all results were discussed with the breast cancer patient organisation BVN (Borstkankervereniging Nederland), AYA international, the Cancer Survivors Taskforce in The Netherlands, and the National Breast Cancer Working Group (NABON).

Women with breast symptoms are at higher risk of cancer diagnosis in between regular screening visits

EBCC PRESS RELEASE: **Barcelona, Spain:** Women who report symptoms such as lumps, nipple retraction or nipple discharge during their regular breast screening appointments, are at higher risk of developing breast cancer during the interval before their next visit in two or three years’ time as part of a national screening programme.

In new research presented today (Thursday) at the 11th European Breast Cancer Conference, Dr Deependra Singh, a researcher at the Finnish Cancer Registry, Helsinki, Finland, said that even though women were more likely to be recalled for further investigations after their mammogram if they had breast symptoms, cancer could still be missed in a significant number of these women, and they were more likely to have cancer diagnosed either before or at the time of their next standard screening visit.

“We found that women with a lump had a three-fold increased risk of cancer being diagnosed in the interval before their next scheduled screening, and approximately two-thirds increased risk of cancer being detected at the time of their next mammogram, when compared with women who had no symptoms,” he said.

Dr Singh and his colleagues found that for every 1000 screening visits, two cancers per 1000 women were found within six months of the visit among women who had a lump at the time of their mammogram;; whereas, among 1000 women without symptoms at the time of their screening, two cancers would be found within two years.

“This means that women with breast symptoms should undergo further assessment irrespective of mammography findings. In addition, the higher risk of interval cancers means further assessment is not the complete solution;; mammography doesn’t detect all breast tumours and can miss about 35-40% of them. So women with symptoms, especially with a lump, should be invited at shorter intervals, before the normal scheduled date.”

In Finland the national breast cancer screening programme invites women for mammograms every two years between the ages of 50 and 69, although a few municipalities go up to the age of 74. The screening interval varies between European countries;; in the UK, for instance, women are invited every three years between the ages of 50 and 70, while in France women aged between 50 and 74 are invited every two years. In Spain, screening programmes vary between regions but tend to invite women every two years between the ages of 50 and 69.

The research presented today looked at women who participated in the Finnish National Breast Cancer Screening Program from 1992 to 2012. Women with or without symptoms and who went on to have breast cancer diagnosed were identified from the Finnish Cancer Registry. There were 51,332 women who had a lump when they attended screening, 40,917 had a retracted nipple, and 9,083 had discharge from a nipple. They were matched with a reference group of women who had no symptoms at the time of a screening visit.

Women who did have symptoms at their time of their visit for screening were more likely to be recalled for further investigations than women with no symptoms: about 15% were recalled if they had a lump compared to 3% of women with no symptoms. Women with a lump had a more than three-fold increased risk of breast cancer being detected in the screening interval before their next scheduled visit. Women with nipple discharge had two- fold risk and those with nipple retraction had a 1.5-fold risk.

“We know already that a substantial proportion of breast cancers, about 30-40%, are detected outside national screening programmes. There is room for improvement in the capability of mammography to detect cancer and our research shows this is particularly the case for women who have breast symptoms. Our findings can be extrapolated to other countries that have national mammography screening programmes, and we encourage these programmes to collect and analyse information on symptoms,” concluded Dr Singh.

Chair of the conference, Professor Robert Mansel, Emeritus Professor of Surgery in Cardiff University School of Medicine, Cardiff, UK, who was not involved with the research, commented: “This is important research that highlights the need for further, careful investigations if women attend their normal breast cancer screening appointment with breast symptoms such as a lump, nipple discharge or retraction, as they

have a higher rate of interval cancers. We know that survival is much better if breast cancer is detected in its early stages, and further research is indicated to determine the best way of monitoring these women more closely, including the possibility of shorter intervals between screening mammograms."

(ends)

Abstract no: 11, "Breast symptoms and risk of interval breast cancers in mammography-screening programme" **Thursday**, "Screening" proffered papers session, 15.35-16.35 hrs, Miro room.

The research was funded by a grant from the Cancer Foundation, Finland.

Women report fewer adverse side effects from partial or reduced breast radiotherapy: new results from IMPORT LOW trial

EBCC PRESS RELEASE: **Barcelona, Spain:** The average number of moderate or marked side-effects reported by breast cancer patients is lower if they are treated with radiotherapy to part of the breast or a reduced dose to the whole breast, rather than with standard radiotherapy to the whole breast, according to new findings presented at the 11th European Breast Cancer Conference on Friday.

The IMPORT LOW study of 2016 women in 41 centres in the UK has already shown that partial breast and reduced dose radiotherapy was as effective as whole breast radiotherapy in controlling the cancer at five years, and women in the partial breast and reduced dose groups reported fewer side-effects, including less change in the appearance of the breast.

These latest results, which focus predominantly on side-effects affecting the breast and also body image reported during the five years following radiotherapy, show that over half of patients in the study did not report moderate or marked side-effects at any point and that most side-effects reduced over time. The number of side-effects reported per person were fewer in the partial breast and reduced dose groups compared with the whole breast radiotherapy group.

Dr Indrani Bhattacharya, a clinical research fellow at the Institute of Cancer Research's Clinical Trials and Statistics Unit (London, UK), from where the IMPORT LOW trial was coordinated, told the conference: "The findings from this study are reassuring for women who are offered either whole breast or partial breast radiotherapy using this technique of radiotherapy, which is simple to deliver and already available in centres worldwide.

"This new information will help doctors discuss the risks and benefits of this type of radiotherapy with

patients and may improve shared decision-making, as well as enabling them to tailor treatment for individual patients."

The IMPORT LOW study randomised women to receive standard radiotherapy at a dose of 40 Gy to the whole breast (the control group), or 36 Gy to the whole breast and 40 Gy to the part of the breast that contained the original tumour (reduced dose group), or 40 Gy only to the site of the original tumour (partial breast group). The radiotherapy was given using hypofractionated intensity modulated radiotherapy (IMRT) – a technique that can deliver an even dose of radiation, minimising the chances of hotspots of unwanted high doses and reducing the cosmetic problems that can occur after breast radiotherapy.

More than half of the women (1265) took part in the sub-study that looked at patient-reported outcomes (PROMs). At the start of the study, after six months and one, two and five years after radiotherapy the women were asked about adverse side-effects, such as a hardening of tissue, pain, over-sensitivity of the treated area and build-up of fluid. Most of the side- effects reported by the women related to changes affecting the breast, and the commonest reported side-effect was "overall change in breast appearance".

The researchers found that women were more likely to report adverse side-effects if they were younger, had larger breasts, had a larger volume of breast tissue removed at surgery, if the cancer had spread to any of their lymph nodes, and if, at the start of the study, they were feeling anxious or depressed.

"Now that we can identify these patients who are at higher risk of reporting side-effects, this knowledge can be discussed with patients, may modify treatment and enable doctors to put in place more personalised and frequent monitoring if necessary. For example, patients with higher levels of anxiety and depression could be offered psychosocial support at the start of treatment, although we do not know from this study whether this would reduce the reporting of side effects," said Dr Bhattacharya.

"We have previously reported that partial breast radiotherapy is as effective as whole breast radiotherapy with similar or fewer side-effects over five years and can be safely delivered in a selected group of patients with low-risk breast cancers. This new analysis shows that patients requiring whole breast radiotherapy can be reassured about the low risk of side- effects affecting the breast and body image. The technique of radiotherapy used in IMPORT LOW is easy to implement and deliver as the equipment and expertise is available in all centres worldwide."

The IMPORT LOW trial is the largest randomised trial to study the use of IMRT to deliver partial or low dose breast radiotherapy compared to whole breast radiotherapy, and has provided the largest complete set of PROMs data for several points in time over five years.

"PROMs are very important for both women and clinicians as they describe side-effects from the patients' perspective and allow us to see the long-term effects of treatment as recorded by the patient. We know from this study and other studies that patients report more side- effects compared to doctors. This means that if we did not assess side-effects using PROMs, then the impact of the treatment-related side-effects on the patient may be underestimated," said Dr Bhattacharya.

Co-chair of the European Breast Cancer Conference, Professor Isabel Rubio, director of the Breast Surgical Unit at Clinica Universidad de Navarra (Spain), who was not involved with the research, commented: “Patient-reported outcomes are among the most important factors that we have added to assessments of outcomes in breast cancer in recent years. PROMs can improve relationships between physicians and patients, and enhance shared decision- making;; this strategy will impact on the final outcomes in the management of breast cancer patients. These latest results from the IMPORT LOW trial provide important and reassuring information for clinicians and patients about side effects after partial or reduced dose radiotherapy, and will help them to make the best choices in each individual case.”

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Abstract no: 3 (Best abstract), “A longitudinal analysis of patient reported outcomes over 5 years in the IMPORT LOW (partial breast radiotherapy after breast conservation surgery) phase III randomised controlled trial”, Friday, closing plenary session, 15.05-16.35 hrs, Picasso room.

The IMPORT LOW study was sponsored by The Institute of Cancer Research and was funded by Cancer Research UK. Dr Charlotte Coles at the ICR is the chief investigator of the trial.

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Fewer breast cancer patients need radical surgery if they are pre-treated with targeted drugs

EBCC PRESS RELEASE: **Barcelona, Spain:**

Extensive surgery involving mastectomy and removal of several lymph nodes can be safely avoided for more women with some types of breast cancer, if they receive targeted drugs before surgery, according to research presented at the 11th European Breast Cancer Conference.

The study focused on women with HER2 positive breast cancer, an aggressive form of the disease, who were given a targeted drug treatment to shrink their tumours before they had surgery.

Previous research has shown that women who have less extensive surgery suffer fewer long-term side-effects and enjoy better quality of life. The researchers say their work shows that even women with aggressive tumours can be safely treated with breast-conserving surgery, if the cancer responds to targeted treatment.

The research was led by Professor Isabel Rubio, Co-chair of the 11th European Breast Cancer Conference and former head of the breast surgical oncology unit at the breast cancer centre at Vall d'Hebron University Hospital in Barcelona, Spain, where she carried out the work.

She said: "In this study we have looked at women with HER2 positive breast cancer. This is an aggressive form of the disease but it is also one where a new class of drugs has successfully been developed. These drugs recognise and target HER2 receptors on the surface of cancer cells.

"We wanted to see whether the known benefits of these targeted drugs could be extended to spare women from the undesirable effects of radical surgery."

Surgery plays a vital role in treating breast cancer and it can involve removing only the area where the cancer is growing, or it can involve removing the whole breast as well as nearby lymph nodes, where the cancer may have spread. More extensive surgery is associated with more side effects such as pain and swelling that can last for many years.

The researchers studied a group of 160 women with HER2 positive breast cancer treated at Vall d'Hebron University Hospital between October 2007 and December 2016. Of these 129 (81%) were candidates for mastectomy based on the size of the tumour and other clinical characteristics.
All the patients were given a drug treatment before surgery including standard chemotherapy and at least

one anti-HER2 drug such as trastuzumab (Herceptin ®).

As a result, 61 women (47.2%) who might otherwise have been offered mastectomy, were instead treated with less extensive surgery. This meant that overall 92 out of 160 women (57.5%) were treated with breast conserving surgery.

The treatment also resulted in 71% of women having no signs of cancer in their lymph nodes, meaning they could have less extensive surgery on their lymph nodes.

Professor Rubio explained: “This study shows us that treating HER2 positive breast cancer with a targeted drug before surgery can mean fewer women need to undergo mastectomy and removal of several lymph nodes. It also shows us that we can use biopsies to see which cancers are responding best to anti-HER2 treatments and therefore which patients can be safely treated with breast conserving surgery.

“Breast cancer treatments have advanced tremendously in recent years. What this means is that surgery should evolve too so that it is tailored to the individual patient and takes account of the effects of their particular treatment.”

Professor Robert Mansel is chair of the 11th European Breast Cancer Conference and Emeritus Professor of Surgery at Cardiff University School of Medicine, UK, and was not involved in the research. He said: “Survival rates for breast cancer are improving and research continues to look for ways to build on that success. At the same time we need to understand the needs of individual patients and the differences between individual tumours.

“This research provides more information on which patients are likely to benefit from radical surgery and which could be safely treated with breast conserving surgery, bringing potential benefits in patients’ of quality of life.”

(ends)

Abstract no: 19, “Breast and axillary conservative surgery after neoadjuvant treatment in HER 2 positive breast cancer patients: The time is now” **Friday** 23 March, “Clinical Science Symposium: Local Treatment of the Breast After Excellent Response to Preoperative Systemic Therapy”, 11:05 hrs, Picasso room.

This research received no external funding.

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