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# Scheduling Mammogram and Physical Exam for a Healthy Woman

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## Opinion

As the technology and science advance every day, we live longer than previous generations; and long life may bring with it more chronic diseases. Breast cancer is one of these, which could be detected early by screening technology and treated effectively. In 2019, there will be an estimated 268,600 new breast cancer cases in the US, which is about 15.2% among all new cancer cases; and a woman's lifetime risk of having breast cancer is about 12.8% [1].

Breast cancer screening for women was initiated in the 1960s. The first randomized controlled mass screening was the Health Insurance Plan of the Greater New York [2]. Since then, many randomized controlled breast cancer screening had been carried out, such as, the Canadian National Breast Screening Study [3], the Swedish two-county trial [4], etc. With the improvement of screening technology or modality, more and more breast cancer cases were detected and diagnosed. The US Preventive Service Task Force recommends biennial screening for women between 50 to 74 years old; and for women from 40 to 49, the decision to have breast cancer screening or not is an individual choice [5]. However, this guideline may not be beneficial to individuals, especially to those superficially healthy women with a family history of cancer.

What I am interested is to develop a statistical method to help a physician and a currently looks-healthy woman to decide when to come back for the next screening of breast cancer. Think about this scenario: A woman has just completed a mammogram and a physical exam, and got negative result; so at this moment, she is cancer-free. However, when should she come back for the next exam? Should she come back in two years according to the recommendation if she is in the 50 to 74 age groups? Alternatively, should she come back earlier if she has some close relative who had breast cancer? This very practical problem needs a clear answer.

In this statistical method, we will use probability of incidence as a criterion; to make sure that if she would develop breast cancer in the next couple of months, her chance of incidence will not be larger than 10% (or some small value of risk that she can tolerate) [6,7]. That is, if she follows the scheduled time for her next screening, then, with 90% possibility that her cancer would be detected at the next exam, and she would not end up in hospital with clinical symptoms before the scheduled exam. The factors in the model are: a woman's current age, her screening history, screening sensitivity, sojourn time, and transition density. The last three are called the three key parameters in cancer screening, since all other terms in the screening model are functions of the three.

Let us go over the factors in the model. About the screening history, it means the number of previous screening exams with negative screening results, and the woman's ages at the past exams. Screening sensitivity is the probability of getting a positive result if someone is in the pre-clinical state (a time interval when one has the target cancer that a screening exam can detect), it depends on the accuracy of screening modality, for women's breast cancer, it is decided by (digital) mammogram and physical exam. The sojourn time is the time duration in the pre-clinical state. Finally, the transition density is the probability distribution of the time duration in the disease Free State. So where the personal risk of breast cancer is? It could be built in the transition density and the sojourn time. For a woman with a family history of breast cancer, or if she has breast cancer genes such as BRCA1 and BRCA2; the mean transition density and the mean sojourn time should be shorter than the average females.

It turns out that the probability of incidence before the next screening exam is an increasing function of the time interval. That is, we can find a numerical solution of the time interval (from now to the next exam) by pre-selecting a small value for this probability of incidence. Therefore, if you want to keep the probability of incidence to be 5%, or 10%, or 20% (any number between

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zero and one), there is a unique solution for the future screening time corresponding to it. And after this optimal screening time is found, we can further estimate the distribution of lead time (i.e., the diagnosis time advanced by screening), and the probability of over diagnosis and probability of true early detection. These numbers will provide useful predictive information to potential patients and physicians when they try to schedule the next screening exam.

These are some results regarding breast cancer based on simulations using screening data and our method [7]. It shows that higher sensitivity and longer sojourn time in the preclinical state means that a potential patient can come back later for the next exam. The next screening time increases with one's current age and the pre-selected probability of incidence (called incidence risk). It slightly increases if the historic screening interval decreases; which means, if someone screened more frequently in the past, then she could come back later, comparing with those who did not screened frequently. For example, to keep the incidence risk within 20%, a 60-years old woman should come back in 12 months, while a 70-years old woman should come back in 13 months, if they were both screened annually in the past. The 60-years old woman should come back in 10.5 months, while the 70-years old should come back in 12.5 months if they were screened once every two years in the past. The estimated lead time is negatively correlated with one's current age and the pre-selected incidence risk. The median lead time is between 10.3 and 11.6 months, and the mode of lead time is between 3.4 and 5.9 months. The probability of over diagnosis is very small, 2% to 5%. However, since we do not have personal data, and screening technology has improved fast over the years, these numbers need to be adjusted to reflect the truth.

Finally, the method could be modified to add more variables. In summary, we hope that we can build upon this method to provide more accurate and practical information to physicians and individual patient regarding her future screening schedule, especially for those women with high risk.

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