Breast cancer screening rates have increased considerably in recent years worldwide. However, breast cancer continues to be the principle cause of cancer deaths and by far the most frequent cancer among women (23% of all cancers), with an estimated 465,000 deaths and 1.3 million new cases in 2007, in both developing and developed countries. More than half of these new cases occur in developed countries—about 408,000 in Europe (31.3%) and 260,000 in North America (20%) [1].

Mammography is the most effective modality to detect preclinical breast cancers and decrease breast cancer deaths. Nevertheless, mammography is not perfect and has several potential risks, particularly risks associated with false positive mammograms, which may lead to unnecessary diagnostic follow-up (e.g., additional imaging and invasive procedures such as biopsy), associated morbidities, psychological distress including anxiety and depression, considerable amount of time loss, and as a result a significant reduction in quality of life. Yet, false positive mammograms are not rare (10.7% per mammogram) and the risk increases with increased screening frequency. For every 1,000 healthy women who undergo annual mammograms, about half will have a stressful false positive and nearly 200 of them will undergo an unnecessary biopsy within 10 years [2].

In addition, the efficacy of mammography in cancer detection and mortality reduction is contingent upon patient behavior (i.e. adherence to screening recommendations). Randomized clinical trials have demonstrated that routine screening mammography can reduce breast cancer mortality rates by 40%—45% among women between the ages of 40 to 69 [3]. Although rates for recent mammography screening are increasing, adherence to screening recommendations remain low. A recent national mammography survey indicates that 50.9% of US women had a mammogram within the last year, but many of them did not follow the screening recommendations to get their routine screening mammograms [4]. For example, a review of regional studies reports that the average percentage of routine screening mammography in women aged 50 years (using screening intervals from 12 to 24 months) is only 53% [5]. Therefore, recent attention has focused on moving women from having initial mammograms to maintaining adherence to recommended mammography schedules [6]. The Institute of Medicine identifies...
adherence to mammography screening recommendations as an area to improve the quality of health care [7].

The existing mammography screening guidelines worldwide do not fully capture the dynamics of mammography screening. Specifically, 1) these guidelines consider only age, which is just one of the risk factors associated with breast cancer, when making policy recommendations. However, the evidence suggests that other risk factors (e.g., family history, body mass index, ages at menarche, menopause, and first birth) may also be important for balancing the benefits and risks of a breast cancer screening policy. As noted by the 2005 Institute of Medicine report, understanding that women at the same age groups do not have uniform breast cancer risks suggests that screening strategies that are tailored to individual risks may be more beneficial in increasing life-savings in high-risk women while decreasing unnecessary complications in low-risk women. 2) The existing mammography screening guidelines do not consider adherence behavior of patients when making policy recommendations. In other words, the existing guidelines assume 100% adherence to screening recommendations by patients, an assumption which is not supported by observed screening rates.

A review of the literature indicates that no prior study has considered the effects of adherence on screening efficacy. On the other hand, numerous studies have explored effectiveness (but not cost-effectiveness) of adherence-enhancing interventions such as health promotion checklists, mailed reminders, computer-generated reminders, and physician counseling [8]. However, adherence-enhancing interventions use scarce resources in both developing and developed countries; therefore, they should be informed by theory to improve access to affordable quality care [9].

The purpose of this study is to develop a modeling framework to evaluate the effects of adherence on individualized mammography screening policies. Specifically, 1) we analyze how mammography screening decisions change for individual patients when adherence is explicitly considered in the decision process, and 2) we investigate the cost-effectiveness of adherence-enhancing interventions (i.e. the effects of adherence-increasing investments on screening efficacy) in a mammography screening program. To the best of our knowledge, this is the first analytical study that considers explicit modeling and investigation of the effects of patients' adherence rates on mammography screening policies.

For this purpose, we formulate a discrete-time, finite-horizon partially observable Markov decision process (POMDP) model, which is a generalization of a Markov decision process that allows sequential decision making when the information regarding the true state of the system is incomplete. POMDPs allow capturing partial observability of the disease progression and imperfect test results, making them ideally suited to health care problems. In this modeling framework, there is a single decision maker such as a physician whose aim is to maximize the total expected quality adjusted life years (QALYs) of the patient. Each time a patient is screened, the physician recommends the patient the next time to be screened, depending on the patient's current risk of breast cancer and her adherence rate based on her prior screening history. However, due to the imperfect adherence, the patient may not adhere to the physician's recommendation for the next screening. We structurally analyze this POMDP model and solve it using real data.
Our primary source of data for parameter estimation comes from a validated computer simulation model of breast cancer epidemiology in the US developed at the University of Wisconsin-Madison, which we refer to as the University of Wisconsin Breast Cancer Simulation (UWBCS). The UWBCS is developed as part of the Cancer Intervention and Surveillance Modeling Network (CISNET), a National Cancer Institute (NCI)-sponsored consortium focusing on statistical modeling of the impact of cancer control interventions and optimal cancer control planning. Some of the CISNET breast cancer models, including the UWBCS, have been used to investigate the optimal population-based mammography screening strategies and provided evidence for policy recommendations [10]. The UWBCS is a highly detailed simulation model designed to replicate breast cancer natural history, detection, treatment, and mortality rates in the US population. The model is able to replicate population-level US cancer surveillance data by simulating the individual life histories of women aged 20 years or older in proportion to their prevalence in the US population. The UWBCS is calibrated to the breast cancer statistics reported in the NCI's Surveillance, Epidemiology, and End Results program and cross validated against the Wisconsin Cancer Reporting System. Separate analyses based on the UWBCS yield results that are congruent with the results of other natural history models for breast cancer. Detailed descriptions of model design, assumptions, and validation have been described elsewhere [11].

Our preliminary results show that incorporating adherence into the problem of designing a breast cancer screening program might result in significantly different screening recommendations than the existing guidelines. Specifically, we demonstrate that the optimal screening decisions are determined by the trade-off between a woman's breast cancer risk and her adherence rate to the screening recommendations, neither of which are considered by the existing guidelines. For example, consider two women who are at the same age and have identical breast risks with different adherence rates. We find that the woman with low adherence should be recommended more frequent screening. We also find that low-risk women with high adherence rates should be recommended significantly less screening than most of the existing guidelines suggest. We compare our proposed policies to the existing guidelines suggested by various countries and health organizations, and find that our proposed policies result in higher expected QALYs while reducing the total expected number of mammograms significantly. In addition, we specify mammography screening threshold risks for different adherence rates, which might be of particular help in clinical practice. Furthermore, we show that depending on the budget limits of a country, the magnitude of optimal investment amounts in adherence-enhancing interventions might change.

Medicine often balances patient and population benefits. When designing national guidelines for lethal diseases, this balance is often determined by the resources that a country has. In resource-rich settings, such as the US, the balance might shift towards the individual patients' benefits, whereas in resource limited settings such as sub-Saharan Africa, maximizing population benefits becomes more important. Depending on the available resources of a country, these pressures sometimes conflict. We build an analytical framework to determine the effects of adherence on a mammography screening program and how much to invest in adherence to increase the life-savings to the national health targets. Our model provides insights to improve affordable quality care depending on the health targets and resource constraints of a country. Furthermore, our POMDP framework can be used to investigate the issues related to adherence in screening for other diseases (such as prostate and colon cancers, and HPV) and address the differing priorities of resource-rich or resource-limited countries.
References.