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ASSESSING LIFESTYLE INTERVENTIONS TO IMPROVE CARDIOVASCULAR HEALTH USING AN AGENT-BASED MODEL

Yan Li, Nan Kong, Mark Lawley

Weldon School of Biomedical Engineering
Purdue University
206 S. Martin Jischke Drive
West Lafayette, IN 47907, USA

José A. Pagán

Center for Health Innovation
The New York Academy of Medicine
1216 Fifth Avenue
New York, NY 10029, USA

ABSTRACT

Cardiovascular disease (CVD) is the leading cause of death in the United States (US) and places a heavy economic burden on the healthcare system. Recognizing the importance of CVD prevention, in recent years the American Heart Association (AHA) began to emphasize the need to increase awareness of key risk factors of CVD and proposed a new concept called ideal cardiovascular health. Based on this concept, we developed an agent-based model that is designed to capture individual health progression and study emergent CVD-related population health outcomes (diabetes, myocardial infarction, stroke and death) over a specified time period. We present some preliminary numerical results, which demonstrate the predictive validity of the model and show how the model could be used in practice by assessing the impact of a set of hypothetical lifestyle interventions on CVD-related health outcomes. Our model is designed to help policy-makers assess and compare different intervention programs targeting CVD prevention for the population of their interest.

1 INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in the United States (US) and the world (Alwan 2011). More than 2,150 people die of CVD in the US each day, and the direct and indirect costs associated with CVD have been estimated to be more than $312 billion in 2009 (Go et al. 2013). Recognizing the increasing prevalence of CVD and the importance of prevention, the American Heart Association (AHA) established an impact goal which aims to improve the cardiovascular health of all Americans by 20% while reducing deaths from CVD by 20% by 2020 (Lloyd-Jones et al. 2010). To better measure and monitor cardiovascular health, the AHA—for the first time—developed the concept of ideal cardiovascular health. The AHA definition of ideal cardiovascular health centers on a person not having CVD while also not smoking, being physically active, eating a healthy diet, having a normal body weight and maintaining optimal levels for blood glucose, blood pressure and cholesterol (Lloyd-Jones et al. 2010). The number of ideal cardiovascular health behaviors and factors has been shown to be a strong predictor of reduced mortality due to CVD (Ford, Greenlund, and Hong 2012). However, only about 3% of American adults meet the ideal cardiovascular health definition set forth by the AHA (Fang et al. 2012).

In this study, we develop an agent-based model (ABM) based on the ideal cardiovascular health concept. In particular, our model can generate a user-specified population, capture the dynamics of each individual's health behaviors and factors, and report a set of health outcomes and mortality over a time horizon of interest. ABM is a bottom-up modeling approach that has been applied to understand real-world systems in which the representation of behaviors of individuals is important and population interaction exists (Rahmandad and Sterman 2008; Siebers et al. 2010). By using simple rules of behavior and action, ABM can be used to model social and health systems in an intuitive way that is appealing to policymakers (Macal and North 2010). Although ABM is still a relatively new modeling approach, it has been applied to solve complex problems in several different disciplines such as economics, other social sciences and healthcare operations management (Barnes, Golden, and Price 2013; Bruch and Atwell 2013; Fagiolo, Moneta, and Windrum 2007).

A systematic literature review in 2006 identified 42 CVD policy models and discussed their strengths and limitations (Unal, Capewell, and Critchley 2006). Recently, the Rotterdam Ischemic Heart Disease and Stroke Computer Simulation model was developed and demonstrated good validity by matching data from two European prospective studies (Van Kempen et al. 2012). However, most of these models are Markov-based micro-simulation models, and they have limited capability in capturing population heterogeneity and modeling individual behavior and disease progression in detail. ABM has the potential to overcome these limitations by creating and growing a heterogeneous population and describing the state change of each individual in a less restricted manner. Thus, we develop an ABM that is used to model cardiovascular health or CVD as defined by the AHA concept of ideal cardiovascular health. Our model also provides a framework for future similar modeling efforts.

In addition to developing an ABM for cardiovascular health, we show how the model could be used in practice by assessing the impact of a set of hypothetical lifestyle interventions on CVD-related health outcomes. People with healthy lifestyle behaviors (i.e., those not smoking, following healthy diet and being physically active) have been shown to have reduced mortality from all causes and CVD (Ford et al. 2012; Ford and Capewell 2011). The importance of promoting healthy lifestyle behaviors has also been emphasized by the AHA to strengthen the prevention of CVD (Lloyd-Jones et al. 2010). The model developed here provides a convenient tool for policy-makers to gain new insights about the expected relative effectiveness of different programs (e.g., lifestyle interventions) without the need to spend substantial resources testing and implementing different programs in the field.

2 METHODOLOGY

2.1 Model Structure

We develop an ABM in which the CVD-related health behaviors and health factors of individuals are simulated, and the emergent health outcomes and mortality for a certain population are observed and studied. In the model, each agent (person) is defined according to three health behaviors (smoking, physical activity and diet) and four health factors (body weight, cholesterol, blood pressure and blood glucose) as well as by age, gender and by having a history of myocardial infarction (MI) or stroke. These factors were selected based on the AHA definition of ideal cardiovascular health as described in Section 1.

In our model, age and gender are intrinsic factors (i.e., not affected by other factors). We use one year as the basic time unit in the simulation, so age increases by one at each time step. Each individual's behaviors and health factors evolve simultaneously and interactively depending on his/her characteristics and the intervention(s) implemented. As Figure 1 shows, we develop eight parallel state charts to capture behavior changes (e.g., transitions between "smoking" and "not smoking"), health factor changes (e.g., transitions between "normal weight" and "overweight") and CVD-related health outcome changes (e.g., transitions from "no CVD history" to "history of MI", "history of stroke" or "death") at each time step. Among all the states shown in Figure 1, "not smoking" means the person never smoked or quit smoking for more than one year, "healthy diet" means the person ate five or more fruits/vegetables per day, "physically active" means the person had more than 150 minutes per week of moderate physical activity, and "normal weight" means the person had a body mass index (BMI) lower than 25 kg/m^2. Previous studies have shown close relationship between these health behaviors and factors and CVD-related health outcomes (Ford, Greenlund, and Hong 2012; Ford et al. 2012).

Transitions within some state charts are correlated with the states in other state charts. For example, changes in body weight are determined not only by the normal progression of body weight but also by the diet and physical activity status. Some transitions are also independent of all the other state charts (e.g., changes in smoking status are only affected by intrinsic factors such as age). Transitions within the CVD state chart are affected by all the behaviors and health factors, as well as by age and gender.

Our model also provides an interface that allows users to define the population size, the simulated time horizon and a set of basic demographic and health characteristics of a simulated population. After the initial population is generated, users can easily track and visualize population health outcomes and mortality over a given period of time. Then users can compare the effectiveness of different interventions on the population of their interest.

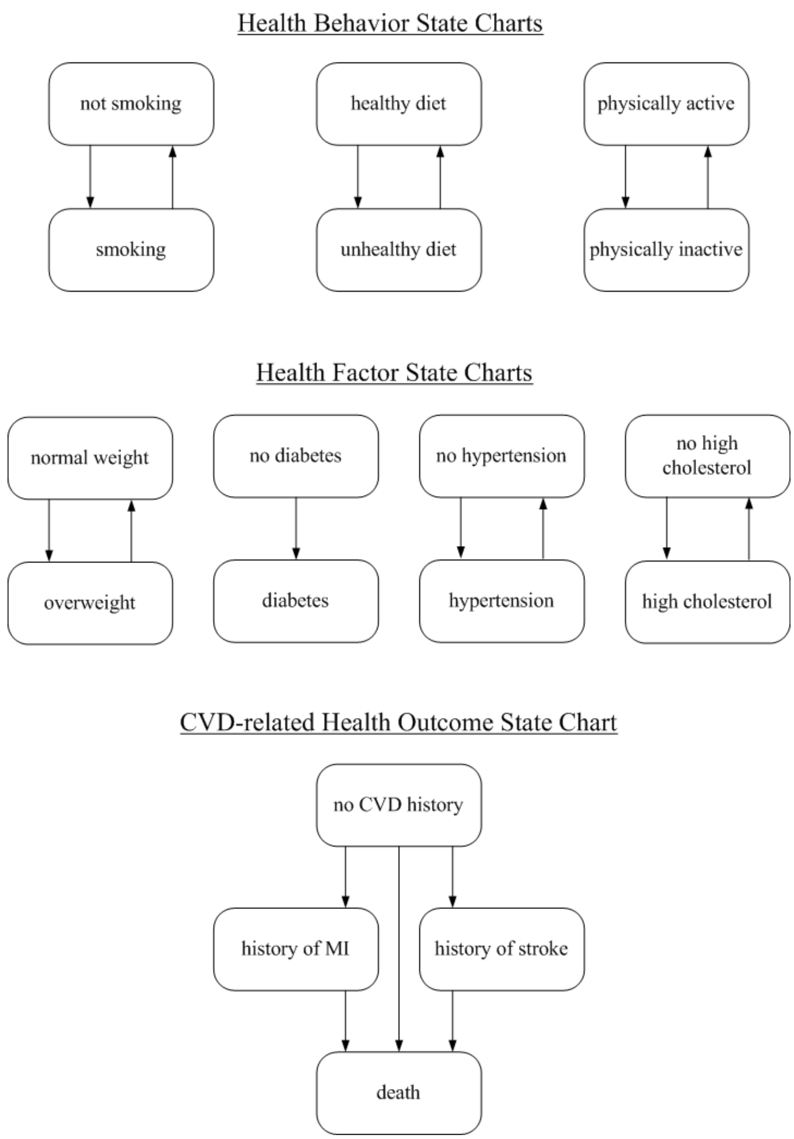

Figure 1: Eight parallel state charts capturing individual health progression.

2.2 Parameter Estimation

Transition probabilities for all the state charts and the correlations among different health factors are estimated from published studies. It is worth noting that the specification of parameter values is a time-consuming process and requires a large-scale literature review and synthesis to make the model useful. Some transition probabilities are estimated using age-specific incidence rates, and some are point estimates for all ages based on results from clinical trials. When there are two or more sources for estimating a specific transition probability, we adopt the one published more recently. Table 1 summarizes the parameters used in the model and the corresponding data sources. We present the detailed parameter estimation process in the following subsections.

Table 1: Data sources for major parameters.

Parameters	**Data Sources**
Smoking initiation and cessation	(Escobedo et al. 1990; Gilpin and Pierce 2002)
Change of diet status	(Dalziel and Segal 2007)
Change of physical activity status	(Dalziel, Segal, and Elley 2006)
Body weight progression	(Ogden et al. 2007; Kaukua et al. 2003; Pan et al. 2011)
Effect of diet status on body weight	(He et al. 2004)
Effect of physical activity status on body weight	(Hu et al. 2003)
Blood glucose progression	(Bonora et al. 2004)
Blood pressure progression	(Vasan et al. 2002)
Cholesterol progression	(Panagiotakos et al. 2008)
Risks of CVD	(Anderson et al. 1991)
Mortality rates	(Heron et al. 2009)

2.2.1 Parameter Estimation for the Health Behavior State Charts

The three health behavior state charts are independent of each other in our model. For the smoking state chart, we estimate the annual transition probabilities from "not smoking" to "smoking" based on the age-specific smoking initiation rates (Escobedo et al. 1990). Similarly, we estimate the annual transition probabilities from "smoking" to "not smoking" based on the age-specific smoking cessation rates (Gilpin and Pierce 2002). For the diet state chart, the annual transition probability from "unhealthy diet" to "healthy diet" is estimated to be 0.03 for people of all ages (Dalziel and Segal 2007). We assume the transition probability from "healthy diet" to "unhealthy diet" is also 0.03, which reflects the fact that people are reluctant to change their health behaviors and thus would not maintain the new behavior for long. For the physical activity state chart, we also assume that the transition probabilities for both directions between the states "physically active" and "physically inactive" are equal, which is estimated to be 0.049 for people of all the ages (Dalziel, Segal, and Elley 2006).

2.2.2 Parameter Estimation for the Health Factor State Charts

The four health factor state charts are correlated and also affected by changes in health behaviors. Annual transition probabilities for the body weight state chart are estimated based on three recent studies (Ogden et al. 2007; Kaukua et al. 2003; Pan et al. 2011). Research has shown that both healthy diet and sufficient physical activity reduce the risk of being overweight (Pan et al. 2011). We capture this effect by multiplying the annual transition probabilities from "normal weight" to "overweight" by the corresponding relative risks associated with having a healthy diet and being physically active (Hu et al. 2003; He et al. 2004). The transition probabilities for the blood glucose, blood pressure and cholesterol state charts are estimated based on age-specific annual incidence rates for diabetes, hypertension and high cholesterol (Bonora et al. 2004; Vasan et al. 2002; Panagiotakos et al. 2008). Obesity is related to the risk of high cholesterol, hypertension and diabetes and, thus, we estimate the relative risks associated with being overweight and adjust the transition probabilities accordingly (Thompson et al. 1999).

2.2.3 Calculation of CVD Risk and Mortality

In the CVD-related health outcome state chart, the initial distribution of population in the states of "no CVD history", "history of MI", and "history of stroke" is determined by the input from users. The transition probabilities from "no CVD history" to "history of MI" or "history of stroke" are calculated using the Framingham CVD Risk Calculator (Anderson et al. 1991). Note that these probabilities are updated at each time step during simulation and reflect a dynamic CVD risk profile determined by all the health behaviors and health factors. Once a person has a history of MI or stroke, he/she will have a higher risk of dying due to CVD. Although it is possible that a person has a history of both MI and stroke, we do not consider this scenario in our model since it is unclear how having a history of both diseases would change the mortality rate based on the published studies.

In our model, "death" could be due to CVD or other causes. The overall age- and gender-specific mortality rates for the general US population are obtained from the US vital statistics data (Heron et al. 2009). The transition probabilities from "history of MI" or "history of stroke" to "death" (i.e., mortality due to CVD) are calculated based on the Framingham Risk Calculator (Anderson et al. 1991). The transition probabilities from "no CVD history" to "death" (i.e., mortality due to other causes) are then calculated by subtracting the mortality rates due to CVD from the overall mortality rates. Note that "death" is an absorbing state and people in the "death" state are removed from the population.

2.3 Validation Procedures

We followed published principles (Weinstein et al. 2003) to conduct model validation. Our examination of model structure, mathematical equations and programming code by the development team and through consultations with CVD experts demonstrates that the model has consistent internal validity and face validity, as well as satisfactory predictive validity (Li et al. 2014). No cross-validation has been conducted due to the lack of accessible or similar simulation models linking health behaviors and factors, cardiovascular health and CVD. We present additional validation results in Section 3.2.

3 RESULTS

3.1 Input Modeling

Table 2 summarizes all the input parameters for our model. In the numerical studies, we obtained nationally representative data from the Behavioral Risk Factor Surveillance System (BRFSS) (Centers for Disease Control and Prevention (CDC) 2014a; Centers for Disease Control and Prevention (CDC) 2014b). The BRFSS is a telephone survey targeting American adults living in households, and the survey includes standard core questions related to preventive health practices and chronic health conditions. BRFSS uses a disproportionate stratified sample design. As such, all our estimations took into account the complex survey design (i.e., differences in the probability of selection into the survey, noncoverage and nonresponse adjusted through sampling weights; poststratification adjustments). We used the BRFSS data to identify the population profile needed for input modeling in our ABM. We extracted data from the 2007 BRFSS for all American adults between ages 20-79. We then divided the population into three groups by age (i.e., Age 20-39, Age 40-59, Age 60-79) and four mutually exclusive groups by race/ethnicity (i.e., non-Hispanic White, non-Hispanic Black, non-Hispanic Asian and Hispanic). We present the demographics and health profiles for the general American adult population and the selected subgroups in Table 3.

Table 2: Input parameters.

Basic demographic characteristics
- Population size
- Age (mean, standard deviation, min, max)
- Proportion of women (%)

Health behaviors
- Proportion of people who are not currently smoking (%)
- Proportion of people who are physically active (%)
- Proportion of people who eat a healthy diet (%)

Health factors
- Proportion of people who do not have diabetes (%)
- Proportion of people who do not have hypertension (%)
- Proportion of people who do not have high cholesterol (%)

CVD
- Proportion of people who have a history of MI (%)
- Proportion of people who have a history of stroke (%)

Other
- Simulation time horizon (years)

Table 3: Population characteristics from 2007 BRFSS.

	All	Age 20-39	Age 40-59	Age 60-79	White	Black	Hispanic	Asian
Mean Age	45.5	30.1	48.8	68.1	47.1	44.0	40.2	43.7
Female (%)	51.1	49.9	50.9	53.6	51.5	54.3	49.6	46.0
No currently smoking (%)	80.0	76.8	79.3	87.5	79.5	77.6	83.5	90.4
BMI < 25 (%)	34.2	39.7	30.7	30.8	35.6	24.5	28.3	61.7
Physically active (%)	36.9	38.2	36.6	35.2	40.1	28.2	29.6	25.8
Healthy diet (%)	24.4	23.3	24.3	26.7	24.3	23.3	23.8	29.4
No diabetes (%)	91.7	98.1	91.3	80.3	92.4	87.0	91.2	94.3
No hypertension (%)	73.1	90.1	71.1	45.3	72.8	63.4	79.0	83.6
No high cholesterol (%)	70.5	87.7	65.6	47.8	68.1	73.9	78.2	74.6
History of MI (%)	3.7	0.6	3.1	10.9	3.9	3.7	2.8	1.5
History of Stroke (%)	2.3	0.6	1.9	6.5	2.2	3.9	1.7	1.0

3.2 Normal Progression

We generated 10,000 hypothetical persons for each population group based on the demographic and health characteristics presented in Table 3 and simulated the population for five years without including any specific intervention. We compared the simulated results with the actual statistics estimated from the BRFSS 2012 for three major health outcomes (i.e., the proportion of people with diabetes, a history of MI and a history of stroke). We also conducted binomial probability tests for the actual and simulated normal progression results. Table 4 summarizes the actual and simulated health outcomes in 2012.

As Table 4 shows, the difference between the actual and simulated results is reasonably small for most of the health outcomes among these population groups. Also, 13 out of 24 binomial probability tests comparing actual with simulated normal progression for the proportions of people who have diabetes, a history of MI, or a history of stroke from 2007 to 2012 have *p* values larger than .05. Thus, in 13 out of 24 tests we fail to reject the hypothesis that the simulated proportions for these three health outcomes in 2012 are equal to the actual statistics. More specifically, our model shows a five-year predictive power in the proportion of people having a history of MI or stroke for the general population of adults. The model also predicts well in the proportion of people with diabetes for the Hispanic and Asian population groups and in the proportion of people with a history of MI or stroke for the relatively young population groups and all the ethnic/racial groups except Asians. Table 4 also shows the population groups in which our model does not make reasonable predictions. For example, our model overpredicted the incidences of diabetes, MI, and stroke for elderly population, which is potentially of the most interest to health policy makers. Further research work will be required to look into the calibration of the relevant parameters to enhance the prediction power of the model.

Table 4: Comparison between actual and simulated normal progression results in 2012.

	Diabetes (%)			**MI (%)**			**Stroke (%)**		
	Actual	**Simulated**	***p***	**Actual**	**Simulated**	***p***	**Actual**	**Simulated**	***p***
All	11.4	13.9	<.001	4.9	5.2	*.165*	3.1	3.1	*1.000*
Age subgroups									
Age 25-44	3.9	4.1	*.301*	1.1	0.9	*.055*	1	0.9	*.339*
Age 45-64	13.5	15.3	<.001	5.2	4.7	*.024*	3.2	2.5	<.001
Age 65-84	22.1	27.8	<.001	11.9	13.7	<.001	7.2	8.3	<.001
Race subgroups									
White	10.2	13.4	<.001	5.3	5.5	*.372*	3.1	3	*.587*
Black	15.7	18.4	<.001	4.5	4.9	*.057*	4.4	4.6	*.329*
Hispanic	13.3	13.1	*.567*	3.4	3.7	*.098*	2	2.2	*.153*
Asian	9.7	9.6	*.748*	1.9	2.4	<.001	2.1	1.5	<.001

3.3 Effect of Lifestyle Interventions

We assessed how five hypothetical lifestyle interventions (i.e., "quit smoking", "promote healthy diet", "improve physical activity", "reduce obesity", and "comprehensive") would reduce the number of people with diabetes, a history of MI and a history of stroke in 5, 10, 15 and 20 years. Among these interventions, "quit smoking", "promote healthy diet", "improve physical activity" and "reduce obesity" are the lifestyle programs implemented to reduce by half the proportion of the initial population who smokes, eats less than five fruits and vegetables/day, exercises less than 150 minutes/week and has a BMI of 25 or more, respectively. The "comprehensive" lifestyle program is the combination of the above four programs. Thus, these five hypothetical lifestyle interventions only change the initial health behaviors and factors of the simulated population, and they do not change the transition probabilities among different health states. We again generated 10,000 persons based on the general adult population characteristics in the BRFSS data and simulated the progression of the three health conditions with no intervention and with different lifestyle programs over 5, 10, 15, and 20 year periods. Figure 2 reports the reduced number of people with different health conditions by implementing the lifestyle programs as opposed to not implementing any interventions.

As the first bar chart in Figure 2 shows, for diabetes, rankings among all the lifestyle programs from the most effective to the least effective are "comprehensive", "reduce obesity", "quit smoking", "improve physical activity", and "promote healthy diet". Within the 10,000 randomly generated persons, the "comprehensive" lifestyle program may result in a reduction of about 200 people with diabetes in 5 years and more than 450 people with diabetes in 20 years. As the lifetime direct cost of treating diabetes is approximately $85,200 (Zhuo, Zhang, and Hoerger 2013), the reduced proportion of the population with diabetes after implementing the "comprehensive" lifestyle program for 20 years may translate into a saving of over $600 billion when considering all adults in the US population.

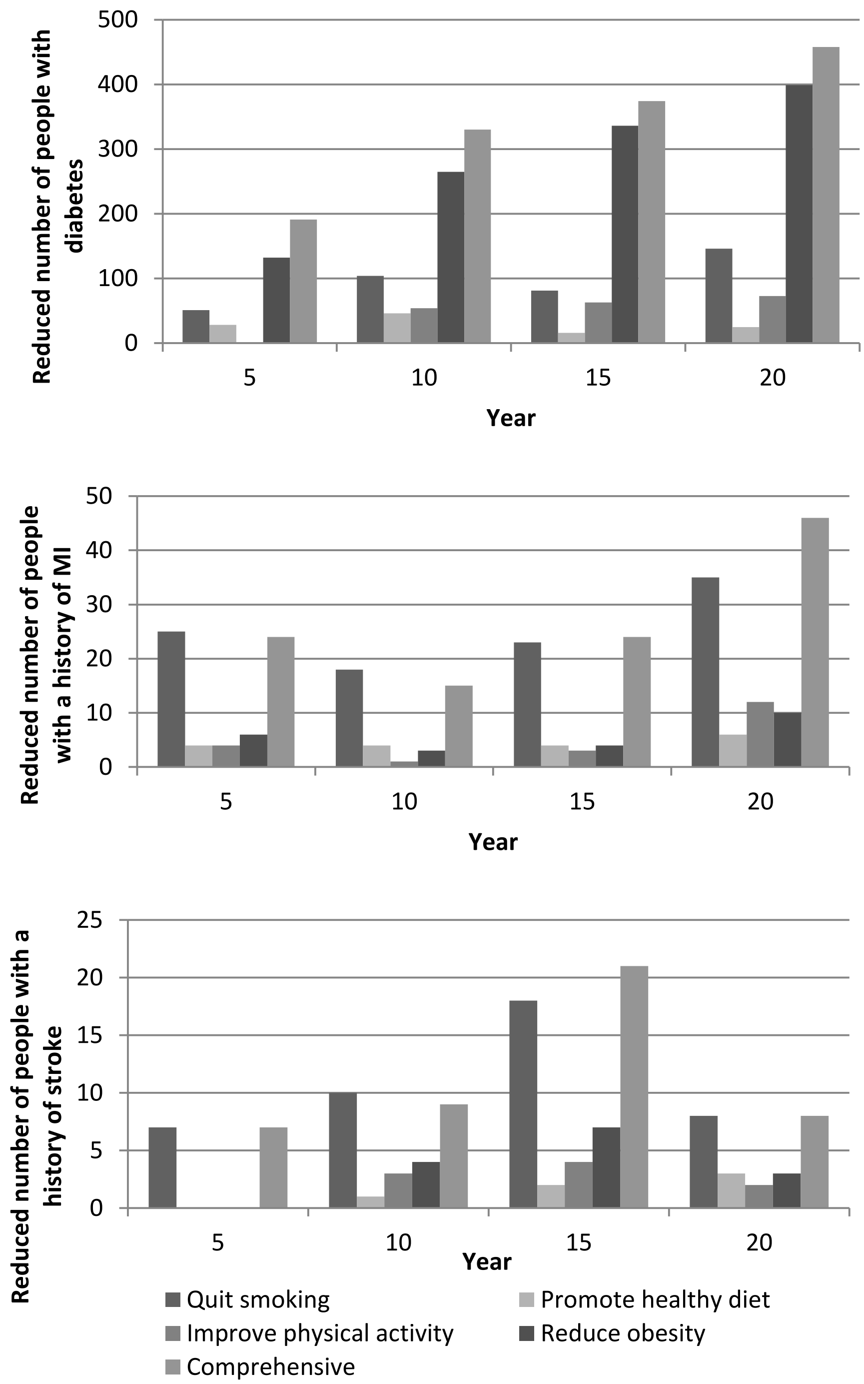

Figure 2: Prevention effects of the five lifestyle intervention programs (i.e., quit smoking, promote healthy diet, improve physical activity, reduce obesity and comprehensive) on three health outcomes (i.e., the number of people with diabetes, a history of MI and a history of stroke) in 5, 10, 15 and 20 years.

Among all the single interventions, "reduce obesity" is shown to be a very effective intervention in preventing diabetes, but "promote healthy diet" and "improve physical activity" have relatively small preventive effects, as both interventions resulted in a reduction of less than 80 people with diabetes in 20 years.

The second and third bar charts in Figure 2 show the effect of lifestyle programs on the number of people with a history of MI and stroke. In general, the preventive effect of lifestyle programs on MI and stroke is less significant than that on diabetes. It seems that "quit smoking" is the most effective non-comprehensive lifestyle program for reducing the incidence of MI and stroke. In 20 years, the "quit smoking" program may prevent 35 people and 8 people from having MI or stroke, respectively, and these two numbers would be 45 and 8, respectively, under the "comprehensive" program. In comparison with the "quit smoking" and the "comprehensive" programs, the other three lifestyle programs (i.e., "promote healthy diet", "improve physical activity" and "reduce obesity") have a less significant effect in preventing MI and stroke. Less than 10 MI cases and less than 5 stroke cases may be prevented by implementing any one of these three interventions over 20 years.

4 CONCLUSIONS AND FUTURE RESEARCH

In this study, we develop an agent-based model for cardiovascular health and demonstrate the potential use of the model by assessing the impact of a set of hypothetical lifestyle programs on incidences of diabetes, MI and stroke. The model parameters are estimated from the best available published evidence, and the simulated populations are generated based on the population characteristics obtained from nationally representative survey data. The numerical results reveal that improving different behaviors and health factors may have differential impacts on health outcomes. As such, this information could be useful when allocating limited resources for disease prevention. The agent-based model developed here also provides a framework for modeling other chronic health conditions (e.g., cancer and diabetes) and may inform future modeling efforts.

We plan to extend the model in the following directions. To improve the disease simulation model, we will expand each of the eight behavior and health factor state charts to capture individual health progression more realistically. This may further improve the predictive validity of the model and would allow us to study other health outcomes, such as complications from diabetes. Also, we are interested in modeling social influences on some health behaviors and factors. For example, research has identified how social influences may be strongly connected to the incidence of smoking and obesity (Christakis and Fowler 2007; Christakis and Fowler 2008). If this is the case, then ignoring these effects may result in biased estimates of disease incidence. To strengthen the analysis of the simulation results, we are interested in including cost and quality of life outcomes so that the model can be used for cost-effectiveness analysis. This is of interest to health policy analysts who may want to compare the cost and benefit of different programs and interventions over time.

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AUTHOR BIOGRAPHIES

YAN LI is a research assistant and Ph.D. candidate in the Weldon School of Biomedical Engineering at Purdue University. He had a research internship in the Center for Health Innovation at The New York Academy of Medicine. He holds a M.S. in Manufacturing Engineering from the University of Texas-Pan American. His email address is li528@purdue.edu.

NAN KONG is Associate Professor in the Weldon School of Biomedical Engineering at Purdue University. He received a Ph.D. in Industrial Engineering at the University of Pittsburgh. His email address is nkong@purdue.edu.

MARK LAWLEY is Professor in the Weldon School of Biomedical Engineering at Purdue University. Before joining Biomedical Engineering in 2007, he served nine years as Assistant and Associate Professor of Industrial Engineering, also at Purdue, and two years as Assistant Professor of Industrial Engineering at the University of Alabama. As a researcher in academia, he has authored approximately 100 technical papers including book chapters, conference papers, and refereed journal articles, and he has won four best paper awards for his work in systems optimization and control. He received his Ph.D. in Mechanical Engineering from the University of Illinois at Urbana Champaign in 1995 and is a registered Professional Engineer in the State of Alabama. His email address is malawley@purdue.edu.

JOSE A. PAGAN is Director of the Center for Health Innovation at The New York Academy of Medicine. He is also Adjunct Senior Fellow of the Leonard Davis Institute of Health Economics at the University of Pennsylvania. He received his Ph.D. in economics from The University of New Mexico. Dr. Pagán was a Fulbright Scholar in Mexico, a Robert Wood Johnson Foundation Health & Society Scholar at the University of Pennsylvania, and the recipient of an Investigator Award in Health Policy Research from the Robert Wood Johnson Foundation. He is a member of the Board of Directors of the American Society of Health Economists. His email address is jpagan@nyam.org.