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M.S. Dissertation in Engineering

Modeling Online Interventions for the Prevention of Diabetes Type II
Targeting Individual Behavior for Weight control

August 2018

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Abstract

Modeling Online Interventions for the Prevention of Diabetes Type II

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Recent socio-economic changes are increasing the incidence of chronic diseases, challenging the efficacy of the traditional healthcare system. Thus, the healthcare paradigm should shift from cure to prevention. Online strategies, such as apps or webpages, increase access to information and facilitate real-time monitoring. However, modifying outcome is a difficult endeavor in the context of healthcare due to its complex adaptive nature. An agent-based model is proposed which considers the complexity of healthcare, to optimize the design of online intervention strategies for the prevention of diabetes type II. These interventions are designed to promote weight control in the population, to tackle obesity, which is one of the main causes diabetes type II. The model was calibrated with individual-level data to increase robustness in prediction. Simulation results were used to evaluate different intervention methods and their impact on diabetes type II incidence in the United States. Results show diabetes incidence and its associated costs could be reduced by adopting web-based interventions with random targets.

Keywords: diabetes, obesity, prevention, complex adaptive system, agent-based modeling.

Student Number: 2016-26097
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1. Introduction

Several socio-economic changes challenge the efficacy of healthcare delivery. An important change hindering sustainability is the inversion of the population pyramid in developed countries, where a fast aging population is coupled with labor shortage and an increase in the usage of health services (Hewitt 2002). The current healthcare model, which was designed for a different population distribution, might soon be no longer affordable. This should encourage countries to reduce the cost in healthcare without reducing the quality of the service provided (Reilly 2014). Accordingly, the World Health Organization (2012) calls for a paradigm shift in healthcare delivery. The new goal is to keep healthy people healthy (prevention). In the context of rapid technological advances, prevention strategies can benefit from IT-based solutions, which facilitate access to care information (World Health Organization 2010), through cost reductions and improvement of service outcome.

Diabetes is a chronic disease, which affects an alarmingly growing percentage of the global population. In 1980, 108 million people were affected. That number rose to 422 million in 2014 (N. C. D. Risk Factor Collaboration 2016). It is predicted to become the 7th most frequent cause of death by 2030 (Mathers and Loncar 2006). Between 90 and 95% of the diabetic population are affected by diabetes type II (American Diabetes Association 2014). Diabetes type II, impairing the cells’ ability to utilize insulin, is often called insulin-resistant diabetes. Thus, treatment for diabetes
type II is difficult, costly and, in its chronic nature, lengthy. On the bright side, the development of this condition can be prevented with regular exercise and a healthy diet (Eriksson and Lindgärde 1991). A prevention strategy is the best solution to reduce incidences of diabetes type II (which is referred to from here onwards as “diabetes”). Most of the existing solutions target the population who is already suffering from diabetes. Changing the paradigm of healthcare delivery also requires new prevention interventions designed to target the population at risk or even the healthy population.

Due to the wide spread of information technology (IT), prevention strategies can also benefit from IT. IT-based solutions do not only reduce the distance and costs but also facilitate access to information, enable feedback tools, and can exploit network benefits. Consequently, IT-based strategies, such as self-tracking devices (Hansen and Margaret 2012) or online social networks interventions (Hilliard et al. 2015; Toma et al. 2014), have been designed. These strategies assume that the causes of diabetes impact the outcome linearly. These approaches yield biased conclusions by failing to look at the whole picture (Martin and Sturmberg 2009).

Modeling realistic outcome, however, is a difficult endeavor in the context of healthcare. The reason is the complex adaptive system (CAS) nature of healthcare: The healthcare “system” is a set of connected or interdependent stakeholders; Its attribute “Complex” comes from the diversity and the wide variety of elements; Its attribute “adaptive” refers to the capacity of the healthcare system to learn from the experience of the activities of the stakeholders (Begun et al. 2003). In other words, this system is better studied
as a living organism than a static machine. Consequently, intervention strategies for diabetes need also to be designed with a CAS system (i.e., a nonlinear system) approach in mind.

The CAS nature of healthcare creates important interrelatedness among these factors. These relationships are as important as the factors themselves. This CAS view provides a comprehensive approach to evaluate potential Online intervention mechanisms, to reduce the incidence of diabetes in the population. It also allows for long-term understanding of the consequences of an implemented strategy. It offers the opportunity to combine available parameters from empirical literature and study the relationships among components. Thus, it would improve the outcome of the devised intervention strategy.

Following the idea of the CAS approach, the research objective is to model in detail the scenario of diabetes prevention by weight control promotion, so that more realistic results about the effect of preventive activities can be obtained. Based on this objective, the research questions were formulated as follows:

1. How does a comprehensive model of diabetes type II looks like?
2. Can the effects of interventions for the prevention of diabetes type II be predicted?
3. What are the implications of the modeling for policy makers?

These questions were addressed by building an agent-based model (ABM). The ABM is used to simulate different scenarios of diabetes prevention. In
detail, in the first step, the components and interdependencies in the system were carefully analyzed, assuming that the later have as big of an impact on outcome (incidence of diabetes) as the former. In the second step, this conceptual model was translated to a computer-simulated ABM, and the outcomes of the simulations of different scenarios of diabetes prevention were studied. Finally, these results were used to evaluate the health and economic impact of each method.

The results of this research are a model to find the optimal Online intervention strategy to reduce obesity by promoting weight control for the prevention of diabetes type II. This model with its focus on diabetes type II, considers the CAS nature of healthcare by studying changes in the macro-pattern through micro-motivations. The intervention would alter individual behaviors (e.g., healthy eating and exercising), which would eventually result in new patterns of behavior. The IT nature of the intervention is reflected in the model by including the effects of increased access to information, feedback mechanisms, and propagation of information within the stakeholder network. The significance of the last one is particularly important, considering that one of the main causes of diabetes, namely obesity, is a behavior which is imitated within the social network of people (Christakis and Fowler 2007). Therefore the learning of healthy habits from the social network of people can prevent diabetes (Centola 2013). Targeting the appropriate stakeholders in the network is essential for this.

The contribution is to look at diabetes prevention from the perspective of complexity science. Studying healthcare as a CAS, the importance of its
multiple components and the way they affect each other is highlighted. A tool to estimate outcome from non-linear interactions is built and used to compare different scenarios of active diabetes prevention. While empirical alternatives are commonly used to research healthcare interventions, simulation has some strengths that are absent in an empirical research. First, a simulation can be carried out in a much shorter time than an empirical research. That way, several scenarios can be rapidly tested to have a preliminary evaluation of those which should be further studied with an empirical setting. Second, empirical studies, such as randomized control trials, require a control group to which treatment is not provided. Simulation eliminates this necessity. Finally, simulations provide tools to understand the environment and external conditions of the setting, while in an experiment much of the heterogeneity might be hard to follow. Simulation results were used to evaluate different intervention methods and their impact on diabetes type II incidence in the United States. The model and results have important policy implications, as they are a tool for evaluation and a suggestion for prevention improvement, respectively.

The remainder of the paper is organized as follows. In the next chapter, I review the literature on the causes of diabetes, proposed online weight control interventions to prevent diabetes incidence, the characteristics of CAS, and models to study healthcare as a CAS. In chapter 3, I describe the model and methodology. In chapter 4, I present the results of the simulation. Then, I discuss the implications of the model as well as its potential applications in chapter 5. Chapter 6 closes the paper with a conclusion and guidelines for future research.
2. Literature Review

2.1. Health Care as a Complex Adaptive System

CAS are described by Rouse (2000) as a non-linear and dynamic system that is composed of independent agents, who act following certain socio-economic rules. As agents are heterogeneous, their goals and behaviors are likely to conflict. Agents are also intelligent. They can adapt and, therefore, self-organize, which results in the emergence of certain behavior patterns and, consequently, in the adaptation of the system. This is a consequence of the absence of a single point of control, which governs the system. Consequentially, CAS may be unpredictable and uncontrollable, which poses serious challenges to any management attempt. These challenges are best overcome by adopting a complexity science approach. As opposed to traditional science, this methodology is characterized by its holist view, the importance of relationships, the study of variation (time component, no averages) and the assumption that behavior emerges from the micro-level (Dent 1999).

The theoretical framework developed by Rouse (2008) describes the main implications of viewing healthcare as a CAS. His work emphasizes the heterogeneity of agents’ goals, as well as their free will. Thus, the main challenge in the management of health is that the system will never stop redefining itself, changing with the environment. The author suggests that the limitations imposed on management can be alleviated by understanding this CAS nature and designing solutions accordingly. Therefore, solutions
should have a holistic scope and be able to adapt over time. Even more, the misalignment of system’s goals and the agents’ goals should be corrected in a bottom-up direction by influencing individuals’ objectives (Begun et al. 2003). However, traditional policy design methods target a single cause of the problem in a top-down fashion, expecting linear positive responses. By ignoring the non-linear nature of healthcare, policies often obtain counterintuitive results. This phenomenon is known as policy resistance and is an important concern for the management of complex systems (Sterman 2001).

2.2. Prevention as a Central Mean in CAS

When designing an intervention solution, one should consider that changes are originated at the micro-level and communicated upstream until they reach the macro-level, starting small and snowballing to the rest of the system (Afek et al. 2009). Thus, the behavior should be the main target of any designed prevention method in the context of CAS. Evans and Stoddart (1990) proposed a model of health consumption, which includes the ideas of emergent patterns and locates patient behavior in a critical position.

Although there is a progressively increasing literature on healthcare as a CAS, including studies to increase value (Nesse et al. 2010), integrate care (Edgren 2008), or to evaluate National Health Services (Papadopoulos et al. 2001), there is little on prevention. While earlier research on healthcare as a CAS has already studied prevention from the complexity perspective (Miller et al. 1998), the scope was constrained to the clinic environment and the follow-up period was short. These two characteristics are antagonist to the
holistic and dynamic nature of CAS and, thus, limit the interpretation of results.

Previous studies on prevention focused on linear relationships disregarding the complex characteristics of the system or studied complexity from a narrow point of view. These approaches yield biased conclusions by failing to look at the whole picture.

2.3. Existing Online Strategies for Diabetes Management

Several online solutions to treat or prevent diabetes have been proposed by previous literature. O’Connor et al. (2011) studied the application of IT in the form of Electronic Health Records (EHR) to improve clinical support. They found improvements in most clinical markers of diabetes, such as blood pressure. Of special interest for the study in hand is the application of IT to influence patient behavior, such as engagement. Goldzweig et al. (2009) and Berikai et al. (2007) found evidence that increased engagement and access to information has a positive effect on outcome. In particular, Or and Tao (2014) obtained promising results on outcome improvement with the use of consumer health IT in diabetes. Different ways in which engagement and information can be promoted are online information resources (Adams et al. 2017), health-specific applications (Lithgow et al. 2017), self-tracking devices (Paton et al. 2012), online social networks (Hilliard et al. 2015; Toma et al. 2014), social media (Harris et al. 2013) and message-based reminders (Hanauer et al. 2009).

This is just a brief summary of the many solutions, which have been proposed regarding diabetes management. However, they illustrate an
interesting point. The use of IT still focuses on the treatment of diabetes. Thus, the paradigm has not yet shifted towards prevention. Very similar applications could be potentially used for the prevention of diabetes, targeting the population at risk instead of the already sick population.

2.4. Factors Impacting Diabetes Incidence

The factors impacting diabetes incidence can be classified into two. The first group corresponds to non-modifiable factors, which cannot be altered by intervention methods. Among these, genetics (including ethnicity), sex, height (through the Body Mass Index) and age are physical factors inherent to the individual (NIDDK 2016). Other non-modifiable factors include those that indirectly impact diabetes incidence through obesity development, such as the type of relationships (Christakis and Fowler 2007) and the area of residence (Tseng et al. 2014); and those that indirectly affect the quality of healthcare provided and the effectiveness of prevention. These are the ease of access to the healthcare system, the confidence and trust in the healthcare system, the type of work, the income, the education years, among others.

On the other hand, modifiable factors are induced by health-related habits such as exercise and nutrition, and include weight, waist circumference and blood glucose level (NIDDK 2016). Several studies have shown that modifying individual behavior substantially decreases the risk of developing diabetes, regardless of their non-modifiable factors (Knowler et al. 2002; Tuomilehto et al. 2001). In particular, by promoting weight control diabetes incidence can be significantly reduced (DPP Research Group 2009). The prevalence of diabetes is closely related to obesity (Leong and Wilding 1999),
which has become a worldwide problem in the past years. In the developed world, it is no surprise that lower levels of activity and a diet rich in fat and carbohydrates has caused obesity to be on the rise or already at alarming levels (Prentice 2006). What surprises is the high prevalence of obesity in the developing world due to nutrition transition. This term refers to the shift experimented in developing countries from their traditional diet to a “Western diet”, which is characterized by a high amount of fat, refined carbohydrates, and sedentarism (Popkin 2001). To address this worldwide problem, it should become a priority to target prevention of obesity and diabetes by encouraging people to eat healthy and exercise, which has proved to be more effective than prevention with drugs (Diabetes Prevention Program Research Group 2002).

2.5. Healthcare Utilization Behavior

The final factor to consider for the design of a successful intervention method is the extent to which individuals will be willing to use the service. This can be studied with Andersen Healthcare Utilization Model (Andersen and Newman 2005). This model explains the factors that determine the use of healthcare services. According to the authors, these factors are of three types. The first ones are the societal determinants, which include technology and norms. This implies that an improvement in the technology or in the societal norms will in turn increase the use of healthcare services. The second type of factors are those related to the health service system, namely resources (volume and distribution) and organization (access and structure). These include the number and density of health resources (such as doctors or
hospitals) and what the system does with these resources (how the patients enter the system and what is being done upon entry). Finally, the use of healthcare services will also be determined by individual characteristics. These are divided in three: predisposing, enabling and need. Predisposing factors include demographics, such as age, societal, such as education, and beliefs, such as the attitude towards the healthcare system. Enabling factors include family-related, such as income, and community-related, such as the individual’s region. Finally, need factors are those related to the illness level, both perceived and real.

These factors will have an impact on healthcare utilization. Consequently, it is important to know the extent to which they can be modified to increase the levels of participation. Andersen and Newman (2005) define this as mutability. Highly mutable factors are those that can be easily changed. The authors identified enabling factors (e.g. family and community-related) to be the ones with the highest mutability. Tackling these factors and taking into account those with low-mutability is crucial to increase the utilization of the proposed health service. In the context of this thesis, the components of the Andersen Model will affect the participation in the intervention services to prevent the incidence of diabetes type II through the promotion of healthy habits for weight control.

3. Methods

3.1. Literature Search Methodology

This model on diabetes was constructed based on literature research on

In particular, using these literature references, components, in which diabetes is embedded, and the relationships among the components of the healthcare system were identified. In a first step, literature on healthcare as a CAS was used to extract the main components and the most significant relationships for the model to be consistent with complexity theory. Some of the identified components were environment, networks, type of technology and types of agents (e.g. state of the agent). Afterwards, literature research was carried out to identify the main causes of diabetes type II, namely obesity, age, gender, income and other components explained in previous chapters. Modifiable factors of obesity are diet and sedentarism.

In the second step, combinations of the factors were used as keywords for another round of online literature search (e.g. environment obesity). The search results helped identifying specific relationships among components.

The third step involved the identification of literature on online strategies to
manage diabetes or to prevent its development (by tackling its causes). Used keywords were diabetes, obesity, diet, and exercise combined with (social) network, (social) media, message, email, smartphone and web.

3.2. Diabetes CAS Model

The model is built on the ideas of prevention (healthy people are kept healthy), individual behavior (not everyone will seek for help), and healthcare efficacy (or success of healthcare). The second concept was thoroughly studied by Evans and Stoddart (1990), who proposed a model to understand the use of health services, based on a number of variables, which included individual behavior, such as perceived need for health services. They also included in the model the important concept of “personal health practices”. Even though the authors’ goal was to study use of health services, the relationship with prevention can be found, since a decrease in the use of health services can be also a consequence of improved practices generated by effective prevention.

It is worth noting that the idea of prevention does not exclude sick patients from the healthcare system. This group is, and will always be, a key target of healthcare providers. Focus on prevention only implies that the proportion of people in this state could be potentially reduced by modifying the approach of care delivery. More interestingly, those who have already entered the “diabetic” state are likely to become advocates on the consequences of the disease. They experience in first person the burden of the disease, and might be therefore more efficient in transmitting the value of prevention. Accordingly, their presence is not only maintained under this view, but
enhanced under the new perspective of collective preventive efforts.

Figure 1 provides a holist view of the different components impacting the incidence of diabetes. The emergent behavior (i.e., diabetes occurrences in the population) arising from the self-organization of the system (adaptive nature) is a result of the interaction of the components shown in the figure. The individual presents traits that increase their predisposition to develop diabetes, as well as their attitude towards prevention mechanisms. The physical world limits the observed behavior, as it determines the availability of enabling resources, such as the accessibility to healthy food (Tseng et al. 2014). Social network relationships determine the speed of behavior diffusion, either amplifying it or dampening it (Centola 2010). Finally, IT-infrastructures facilitate feedback to the system. Upon feedback emission, the components of the system can adapt and show new emergent patterns of behavior based on self-organization (Begun et al. 2003).
3.2.1. Micro-Level of the Diabetes CAS Model

At the micro-level the interest lies in individual characteristics and behavior, as well as in biological characteristics of diabetes development. While the causes for diabetes type I have a strong genetic component, the risk of diabetes type II (as per actual research) mainly increases with “age, obesity, and lack of physical activity” (American Diabetes Association 2014). As such, the model includes agents’ age, weight, age, gender, obesity and diabetic status and their exercising and nutritious behavior, as well as the probabilities to adhere to each intervention method. Adherence to a mobile
application to lose weight was 93% as opposed to websites with 55%, and offline alternatives with 53% (Carter et al. 2013). Stronger adherence reduces the risk of prevention dropout (Scherer et al. 2017). The last two parameters in the micro-level account for the nature of diabetes development. Obese adults have an odds ratio of 7.37 to develop diabetes (Mokdad et al. 2003). An adult is considered to be obese if the body mass index (BMI) is above 30 and to be at risk, if it is over 25 (U.S. Department of Health & Human Services). The body mass index is the ratio of weight to height and it was a common resource to diagnose obesity.

Figure 2 shows the states, in which an individual can be found. Each box represents a state in which an agent can be in the model (e.g. non-obese diabetic, non-obese non-diabetic, obese diabetic and obese non-diabetic diabetic). Red arrows indicate flow from one state to the other. Agents move in the direction of the arrows. Green arrows represent the flow promoted by prevention mechanisms. At any point \( t \) in time, the population of individuals at the micro-level can be divided into subgroups representing the status of health of the individual (mutually exclusive and completely exhaustive). Figure 2 shows also the process, through which individuals can potentially enter the third state: diabetic. As chronic diseases cannot be cured, these patients are locked in this state, which iteratively increases demand for health care service and, thus, cost. The number of chronic patients in the model is determined by the incidence of diabetes type II.
Actions presented in the literature target the population at the chronic state, in order to help them manage the disease. This falls under the traditional view of healthcare, in which only sick people are treated. The treatment that they receive helps them managing the disease. Diabetes is treated in this way mainly by controlling glucose levels. As showed previously, this can effectively be done with the help of online solutions. This, however, does not solve the problem of having more people entering the chronic state. This is of particular importance in the case of diabetes type II, which commonly goes undiagnosed for many years, as the disease does not cause the classic symptoms of diabetes at earlier stages (American Diabetes Association 2014). Active prevention would therefore be more efficient than action upon (late) diagnosis.

The micro-level of the model considers all alternatives. It also includes the possibility to target the population at high risk of developing diabetes by the healthcare system with prevention strategies and intervention strategies (green arrows in Figure 2). While prevention could be offered in a myriad of
ways, this study focuses on online strategies and consider the network, in which the individual is. Both ways are part of the meso-level and macro-level.

At the micro-level not only the agents’ states (e.g. obese, non-obese and diabetic) are defined but also their individual characteristics that might have an effect on their likelihood to develop the disease. These are age, weight, age, gender, exercising and nutritious behavior, adherence to intervention, and likelihood to develop diabetes after being diagnosed as obese. This is shown in figure 3.

### 3.2.2. Meso- and Macro-Levels of the Diabetes CAS Model

Under the assumption that people can flow from one state to the other (Figure 2), those transitions need to be defined. We, therefore, need a multidimensional view to fully understand the effects of the implemented online intervention and to optimize its design accordingly.

The micro-level of the model is thus complemented with multiple dimensions of two more levels (Figure 3). The dimensions are the environment and healthcare at the macro-level, and networks of individuals at the meso-level. Each dimension includes components which have been related to diabetes in previous research. The components are, at the macro-level, the access and confidence in the healthcare system and the obesogenicity of the agent’s region. The latter was estimated based on the region’s sports facilities, food retailers, sports guidelines, regulations and policies regarding nutrition and exercise and the density of farmers markets.
At the meso-level the components are the number of friends and their state (obese/non-obese) and the marital status as well as their partner’s state (obese/non-obese).

Figure 3. Levels of the diabetes CAS model, showing the dimensions and components for each level.

The integration of these components in a single model provides a more comprehensive view of the impact of intervention on individual behavior and consequences on macro-levels, as the health of an entire population. This would enable the study of interactions of different phenomena, which would only be possible through an empirical approach conducted over a very long time period and substantial cost. The modular nature of the model allows for easy updating of parameters when new results are published. The model
could also be adapted to study conditions other than diabetes.

In detail, Figure 3 is a schematic representation of the three dimensions and the corresponding components. Starting from the top, the macro-level is divided in two: environment and healthcare. The first one is common to all individuals living in the same region. For each region, the environment is represented through its obesogenicity index value, which groups the area's sports facilities, retailers, meeting sports guidelines, regulations, and farmers markets. This represents whether the region where a person lives constraints or enhances their tendency to become obese. The healthcare system is evaluated through the ease of access to health care and the confidence in the healthcare system. The former represents the experience of individuals with respect to the ease of access to healthcare, while the second stands for the trust they have in the healthcare system. Under the healthcare system, prevention was also evaluated.

This is the model’s component of interest, as it allows designing, incorporating, and testing new creative methods. For example, methods, with which engagement and information can be promoted, are online information resources (Adams et al. 2017), health-specific applications (Lithgow et al. 2017), self-tracking devices (Paton et al. 2012), online social networks (Hilliard et al. 2015; Toma et al. 2014), social media (Harris et al. 2013) and message-based reminders (Hanauer et al. 2009). Methods of intervention of focus in the model are offline, web-based, and app-based prevention methods.

At the meso-level, effects from network relationships are visible. Networks are an important part of CAS and their structure has direct impacts in
behavior and outcome (Koohborfardhaghighi and Altmann 2014; Koohborfardhaghighi and Altmann 2016; Koohborfardhaghighi et al. 2017). Network effects are not only considered but also exploited for the sake of the intervention’s success. This is based on the premise that both obesity (Christakis and Fowler 2007) and healthy habits (Centola 2013) are contagious, in the sense that they spread through the network. The component of network influence refers to the rate of obesity spread in the network, its parameters were obtained from the studies by Christakis and Fowler (2007) and Centola (2013). The second component, network connections, is the way agents are connected to each other. Two types of relationships were considered: marital and friendship.

3.3. Agent-Based Modeling Methodology Applied to the Diabetes CAS Model

The Diabetes CAS model was implemented in NetLogo, which is software optimized for Agent-Based Modeling (ABM) (Wilensky 2008). ABM is a simulation methodology, in which a multi-agent system is studied (Klügl and Bazzan 2012). Each agent has a set of simple rules and can interact with the environment and other agents. In each iteration of the simulation, new patterns of behavior emerge from the decisions made by the agents. In this Diabetes Modeling Methodology, each agent has its own characteristics and individual behavior and makes decisions, which are also affected by the setting of the meso-level and macro-level. These decisions cause individuals (agents) to gain weight, lose weight, or keep their weight in each iteration. An iteration represents the period of a week. At the end of a year, all
individuals go through a diabetes diagnosis. The emergent pattern of behavior is the percentage of diabetes incidence.

3.3.1. Agent-Based Model Dynamics

The first step in the simulation (Step 1 in Figure 4) is the initialization of agents’ attributes, relationships, and intervention status. The first two correspond to the components shown above in figure 3. The intervention status depends on the type of intervention selected for a scenario as well as on the likelihood a certain individual would be targeted for intervention. Initialization finishes by calculating the effect of prevention on the agent’s gain or loss of weight. This is a measure of the impact the agent’s attributes would have on decision making and are calculated according to equation 1:

$$\text{eff-prev} = ((1 + \text{interv})* (\text{acc} + \text{conf} + \text{exerc} + \text{nutr} + \text{obs} + \text{edyr} + \text{inc} ) - (1 - \text{interv})* \text{WH}),$$

where $\text{interv}$: value of intervention, $\text{acc}$: level of healthcare access, $\text{conf}$: level of confidence in the healthcare system, $\text{exerc}$: individual’s behavior towards exercising, $\text{nutr}$: behavior towards healthy dieting, $\text{obs}$: obesogenicity of the agent’s environment, $\text{edyr}$: years of education attained, and $\text{inc}$: income of the agent, and $\text{WH}$: working hours of the agent. All variables are on a scale from 0 to 5, being 0 the lowest level and 5 the highest. This scale was chosen so that all variables are consistent with the survey’s structure, were 0 would be chosen by respondents if they strongly disagreed with the answer and 5 if the strongly agreed with it. Since the model was calibrated with real-world data, scaling a few variables would not
distort the results in a highly significant way.

Upon initialization, the model iterates between Step 2 and Step 3 (Figure 4). Each iteration corresponds to a week. Each iteration, individuals make decide whether they take action to reduce their weight or not. The decision-making process is facilitated by a calculation of points that evaluate the agent’s willingness to take healthy decisions. In Step 2, the overall points are calculated with equation 2. The equation takes the health status of the agent’s connections into account. As agents are inevitably influenced by their friends and family, these points are therefore updated every iteration. The equation is:

\[ \text{Points} = \text{eff-prev} + (1 + \text{interv}) \times (\text{fr}_M \times \text{number-healthy-friends-M} + \text{fr}_F \times \text{number-healthy-friends-F} + \text{gender-factor} \times \text{healthy-spouse}) - (1 - \text{interv}) \times (\text{fr}_M \times \text{number-unhealthy-friends-M} + \text{fr}_M \times \text{number-unhealthy-friends-F} + \text{gender-factor} \times \text{unhealthy-spouse}), \]

(2)

where \( \text{eff-prev} \): variable calculated as per equation 1, \( \text{interv} \): value of intervention, \( \text{fr}_M/\text{fr}_F \): effect that female/male friend’s weight will have on the agent’s weight, \( \text{number-healthy-friends-M/F} \): number of non-obese male/female friends an agent has, \( \text{number-unhealthy-friends-M} \): number of obese male/female friends an agent has, \( \text{gender-factor} \): effect the spouse’s weight will have on the agent’s weight, which defers by gender, and \( \text{healthy/unhealthy-spouse} \): spouse is non-obese or obese. The possible values for \( \text{interv}, \text{fr}_M, \text{fr}_F \) and \( \text{gender-factor} \) are shown in table A1 in the appendix.

Once points are calculated, agents make decisions regarding their health,
which are represented with a gain or loss of BMI (Step 4 of Figure 4). If points are above the upper threshold, the agent will lose an amount of BMI. If points are below the lower threshold, the agent will gain BMI. Most agents will neither gain nor lose weight as their points will be within the neutral range. The points’ threshold was calibrated as explained in the last section of this chapter.

Finally, every year (52 weeks or iterations) diabetes is diagnosed (Step 4 of Figure 4), and the overall outcome is recorded as total number of diabetic individuals (Step 5 of Figure 4). Diagnosis is simulated with the probability that an obese individual will become diabetic of type II.
### 3.3.3. Data to Populate the Agent-Based Model

Although most ABMs are used to understand relationships among components, only a few studies have populated the models with real-world data for improving the accuracy of the predictions. An example of a data-driven agent-based model is the one developed by Venkatramanan et al. (2017) to predict the emergence of the infectious disease Ebola. Inspired by this model, data was gathered to populate all components (Figure 3) with real-world data and constructed one variable for each component. Environment variables were constructed from data gathered by Centers for Disease Control and Prevention (2018) and all other variables by combining answers to the International Social Survey (ISSP Research Group 2015). With increasing accessibility to data, the model can be adapted to specific countries. Table 1 in the appendix describes in detail the variables and their data sources.

Relationships were constructed in two ways. On the one hand, marital relationships were randomly built among adults, who had reported married status in the International Social Survey Program (ISSP Research Group 2015). On the other hand, friendship relationships were constructed with Barabasi-Albert’s algorithm (Barabási and Albert 1999). The algorithm creates a scale-free network following the power-law distribution, which best fits a friendship network.

Table 1 shows the descriptive statistics of the data. All variables were constructed from the International Social Survey (ISSP Research Group 2015), except for obesogenicity, which was constructed from data gathered...
by Centers for Disease Control and Prevention (2018). Sex, marriage, obesity and diabetes are dummy variables. Weight, height, BMI and age are unbound variables. All other variables have been normalized between 0 and 5, being zero the worst value with respect to health. For example, a high point value in *access to healthcare* has a strong effect on health. The right-most column indicates the level, at which these variables are located in the model. The color code is consistent with the diagram in figure 3.
Table 1. Descriptive statistics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td>0</td>
<td>1</td>
<td>0.4329</td>
<td>0.49564</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Married</strong></td>
<td>0</td>
<td>1</td>
<td>0.44774</td>
<td>0.49742</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Weight (Kg)</strong></td>
<td>36</td>
<td>248</td>
<td>80.096</td>
<td>19.656</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>137</td>
<td>203</td>
<td>169.73</td>
<td>10.329</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>13.223</td>
<td>76.543</td>
<td>27.714</td>
<td>5.9817</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Obese</strong></td>
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<td>0.2871</td>
<td>0.45255</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Diabetic</strong></td>
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<td>1</td>
<td>0.13419</td>
<td>0.34097</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Access to HC</strong></td>
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<td>1.75</td>
<td>0.90137</td>
<td>0.25648</td>
<td>Macrolevel</td>
</tr>
<tr>
<td><strong>Confidence in HC</strong></td>
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<td>0.60674</td>
<td>Macrolevel</td>
</tr>
<tr>
<td><strong>Working Hours</strong></td>
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<td>1.233</td>
<td>1.2004</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Education years</strong></td>
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<td>5</td>
<td>0.70431</td>
<td>0.18994</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>20</td>
<td>89</td>
<td>49.637</td>
<td>17.099</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Exercise habits</strong></td>
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<td>5</td>
<td>3.5123</td>
<td>1.321</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Nutritious habits</strong></td>
<td>0</td>
<td>5</td>
<td>4.1145</td>
<td>1.1085</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Income</strong></td>
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<td>5</td>
<td>1.7161</td>
<td>1.4873</td>
<td>Microlevel</td>
</tr>
<tr>
<td><strong>Obesogenicity</strong></td>
<td>0.9664</td>
<td>2.3402</td>
<td>1.8466</td>
<td>0.41456</td>
<td>Macrolevel</td>
</tr>
</tbody>
</table>
3.3.4. Agent-Based Model Calibration

The empirically measured level of diabetes incidence (Statista 2018) was used as a baseline case, in order to calibrate the ABS and find the best value for the parameters, which were not available in the literature, namely the values for the thresholds and increments of BMI. Since the model starts at a low level of diabetes incidences, calibration started at the year, in which both outcomes were similar.

Figure 5 shows the output of the best fitting, calibrated model and the empirically measured values of diabetes incidences, which were reported by Statista (2018). This output of the best fitting, calibrated model was found by black-box calibration, through which several combinations of unknown variable values were introduced in the model. For each combination, the output curve was compared against the reference curve through least squares minimization. The combination of variable values yielding the minimum least squares distance were selected and fixed for further modeling with the model. Upon calibration, the model performs with a minimum sum of squared residuals of 74.47.
Figure 5. Calibration of model variable values against the empirical diabetes incidence curve.

3.3.5. Validation

Upon calibrating the model, its robustness was further validated by replicating two studies. The first study was conducted by the Diabetes Prevention Program Research Group, which belongs to the Centers for Disease Control and Prevention in the US. This study is of great importance, as they proved that a change in lifestyle had higher chances to reduce diabetes incidence than a medicine alternative (Diabetes Prevention Program Research Group 2002). The intervention was in person and targeted
individuals with a BMI above 25. The experiments were carried out in different centers in the United States. Among the intervention group, 4.8% developed diabetes every year. To replicate the experiment, the simulation was set for an offline intervention targeting individuals at risk in different regions of the country. 439 individuals were targeted in the simulation. After a year, 29 individuals in this group developed diabetes. This corresponds to 6.6% of the intervention group. The difference of 1.8% arises from differences in the individual traits of participants, as well as the environment where they live.

The second study assessed the efficacy of a diabetes prevention program delivered through a mobile app (Fukuoka et al. 2015). They studied 30 overweight individuals (BMI > 25) who used an app which encouraged them to take up healthy habits to reduce their weight. After two years of participation in the program, the intervention group had lost an average of 6.2 Kg. The study took place in California. In order to replicate the experiment with the model, 30 overweight individuals (8% initial intervention) living on the west coast (region 9) were targeted with an app-based intervention. The initial average weight of these individuals was 83.64 Kg. After two years, the average weight was 74.18. This corresponds to a loss 9.46 Kg. There is a small difference of 3.26 Kg between the experimental and the simulated result. This difference might account for the simplification of the simulation scenario, as well as the different individual traits between the subjects of study.

In both replications the simulation result was very close to the observed
experimental result, with difference explained by the inherent simplification of a simulation of reality. This validates the model and increases the confidence on results predicted with the simulation.

3.4. Simulation Setup

The simulations ran with 1550 agents living in different regions of the US. The reason to choose this country was the availability of data to populate the model. Running time was 1040 weeks, corresponding to 20 years. All variables were fixed throughout the simulation, with values as indicated in Table 1 of the appendix. Each scenario is a combination of intervention method and target of intervention, yielding 13 different intervention strategies: no intervention (none), offline intervention with random target (off rand), offline intervention targeting obese individuals (off ob), offline intervention targeting individuals at risk of obesity (off risk), offline intervention targeting agents with a strong friendship (i.e., high clustering coefficient; off nw), web-based intervention with random target (web rand), web-based intervention targeting obese individuals (web ob), web-based intervention targeting individuals at risk of obesity (web risk), web-based intervention targeting agents with high clustering coefficient (web nw), app-based intervention with random target (app rand), app-based intervention targeting obese individuals (app ob), app-based intervention targeting individuals at risk of obesity (app risk) and app-based intervention targeting agents with high clustering coefficient (app nw).

Scenarios differ by the type of intervention method and the target of such an intervention. The former is measured by the variable interv, which takes the
values 0.95, 0.55 and 0.53 for app, webpage or offline interventions, respectively (Carter et al. 2013). The target of intervention defines the agents of the model who will be targeted in each scenario. For those who are targeted, the value \( \text{interv} \) will be 0.95, 0.55 or 0.53, and for all others, zero. Random target refers to the scenario where targets are chosen at random, including healthy patients. In other scenarios targets are those agents who are obese (BMI > 30), who are at risk of obesity (BMI > 25) or who have a high clustering coefficient. For each scenario, the yearly number of incidences of diabetes has been recorded, which allows us to compare different strategies and evaluate the optimal intervention.

Some assumptions were made in the construction of the model. First, individuals do not die during the 20 years of study and new individuals are not born. Second, only the effect of weight on diabetes is studied. Other factors such as genetics, gender or age are modeled with stochastic behavior. Third, it was assumed that agents would behave according to the empirical studies used to identify parameters. Finally, it is assumed that diabetic individuals will require treatment from the healthcare system.

4. Results

4.1. Predicting the Effects of Intervention

Figure 6, shows the evolution of diabetes incidence for all scenarios. The vertical axis measures the number of diabetic individuals, while the horizontal axis indicates time.

This figure is useful to get an overall idea of the relative effectiveness of
different methods. The most meaningful idea to note from this graph is that most intervention methods yield a lower number of diabetic than having no intervention at all (black line). The only method which is worse than no intervention was found to be offline prevention with obese targets. This can be explained by the phenomenon of policy resistance, by which top-down implementation of policies can have the opposite effect (Sterman 2001). With offline interventions targeting obese people, the person is imposed guidelines by an authority – the doctor. As such, confidence in the system are important to avoid policy resistance (Sterman 2001). The agents in the system have low average confidence (2.6 over 5) as reported in the survey.

Figure 6. Comparison of diabetes incidences for each intervention method and target.
Figures 7-9 are detailed views of the graph above. Each graph depicts the evolution of diabetes incidences for different intervention methods. The first one shows the relative effectiveness of offline methods, that is, preventive intervention which is carried out exclusively in person.

![Graph showing comparison of diabetes incidences: offline intervention.](image)

**Figure 7.** Comparison of diabetes incidences: offline intervention.

In this case, the best outcome would be obtained by targeting people at risk and the worst would be to target obese people. This result is interesting, as most preventive strategies for diabetes type II are targeting obese individuals and carrying out personal sessions (Centers for Disease Control and Prevention 2016).

Figure 8 depicts the incidences of diabetes when a webpage-based intervention is applied. According to the results, choosing both random targets or targets who are highly connected to the network, would yield the best results.
These results support the comments made above, by which targeting obese individuals or those at risk, while intuitive, seems to have worse results than directing the intervention towards other people. The explanation is that targeting these two groups leaves out non-obese individuals which might become obese in the future. As such, methods which include healthy individuals are not only reversing the effect on some obese individuals but also preventing healthy people from gaining unhealthy weight, ultimately outperforming methods that only focus on obese individuals.

Figure 9 shows similar results when an app-based intervention is carried out. Once again it is not as effective to target obese people or individuals at risk to become it. The main difference between this graph and the two previous ones is that random targets yield similar outcomes than those with a high body mass index.
Figure 9. Comparison of diabetes incidences: app-based intervention.

The nature of the technology appears to have a stronger effect in network propagation of habits, in such a way that targeting agents with a high clustering coefficient is the most effective approach.

Figures 10-13 give a different perspective of the outcomes by grouping up scenarios with the same target and different intervention method. This allows us to compare methods by type of target. Figure 10 shows outcomes with random targets. The best outcome is the webpage-based intervention, while the worst is to have no intervention at all.
It is important to consider the scenario for random targets because it is the fastest and cheapest targeting strategy, as there would be no cost and time devoted to the identification of targets. For example, if one wished to target obese people, one would first need to diagnose obesity. According to the results, randomly targeting individuals to prevent them from developing diabetes type II would be most effective by means of a webpage.

Figure 11 shows the case in which individuals at risk of obesity are the target of intervention. In this scenario the most effective intervention would be offline, while the least effective would be to have no intervention at all, followed by an app-based intervention.
Figure 12 depicts the case in which obese individuals are the target of intervention. It shows how all types of intervention yield similar results, apart from offline intervention, which is even worse than having no intervention at all.
When obese agents are intervened for the prevention of diabetes type II, there seems to be no difference in the chosen method. Recalling previous graphs, it is seen that, in fact, no matter which method is chosen, targeting obese individuals will yield the worst results. Once again it is important to note that while obesity is the main indicator of diabetes type II (Leong and Wilding 1999), the model suggests that focusing on obese agents is the least effective method to reduce the incidences of the disease. This might be because once a person has become obese, it might be too late to reverse it, or at least it is slower than just preventing healthy people from gaining weight.

Figure 13 shows the case in which the target of intervention are those agents with the highest clustering coefficient. Results suggest that this type of targeting is best when online strategies are used, namely webpages or apps.

Figure 13. Comparison of diabetes incidences: targeting agents with high clustering coefficient.
While these targets are the most difficult to identify, the fact that online strategies are the best-suited is good news. With the help of social media and the internet, it would be easier to detect targets with many friends, and implement the intervention strategies with them.

Figure 14 sums up the results by showing the incidences of diabetes (in percentage of total adult population) in the year 2020, which is the final year of prediction.

![Prediction of diabetes incidence in 2020](image)

**Figure 14.** Comparison of diabetes incidences at the end of the period of study for each intervention method and target.

Most intervention scenarios finished with a lower percentage of diabetic than having no intervention (11.74%), except for offline intervention targeting obese individuals (12.13%). The best outcome was for webpage-based
intervention with random targets (10.9%) followed by highly connected targets with webpage-based (10.97%) and app-based (11.1%) interventions.

### 4.2. Sensitivity Analysis

A sensitivity analysis was performed for the parameter “percentage of initial intervention”. Outcome values were averaged over 100 simulations with parameters ranging ± 5% points from the 30% used in the simulation. Figure 15 depicts the outcome in diabetes incidences for each percentage of initial intervention.

![Sensitivity analysis of initial % of intervention](image)

**Figure 15 - Sensitivity analysis of the parameter "percentage of initial intervention"**
As can be seen in Figure 15, the sensitivity analysis suggests that an increase of one percent point in the initial percentage of intervention would decrease the percentage of diabetes incidences 0.0064 points. As such, results may vary in real environments where the percentage of initial intervention differs by intervention type.

4.3. Cost Saving Estimate

The best scenario would reduce diabetes incidences in 0.84% by 2020, compared to the baseline of having no intervention. In the US, this percentage corresponds to 2.19 million less people developing the disease. This is shown in tables 2 and 3, which describe the diabetes incidences predicted for 2020 in the USA in percentage of adult population and in millions of adults, respectively. The baseline incidences corresponds to the scenario with no intervention, which was calibrated to fit real world data. For table 3, that baseline was calculated with population predictions, by which 78% of a total population of 334.5 million will be over 18 in 2020 (Colby and Ortman 2015).
Table 2. Diabetes incidences in percentage of adult population (predicted for 2020). In parenthesis: difference from baseline of no intervention (11.7419%)

<table>
<thead>
<tr>
<th></th>
<th>Random</th>
<th>Obese</th>
<th>Risk</th>
<th>Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offline</td>
<td>11.2903</td>
<td>12.1290</td>
<td>11.2903</td>
<td>11.6774</td>
</tr>
<tr>
<td></td>
<td>(-0.4516)</td>
<td>(0.3871)</td>
<td>(-0.4516)</td>
<td>(-0.0645)</td>
</tr>
<tr>
<td>Webpage</td>
<td>10.9032</td>
<td>11.5484</td>
<td>11.4194</td>
<td>10.9677</td>
</tr>
<tr>
<td></td>
<td>(-0.8387)</td>
<td>(-0.1935)</td>
<td>(-0.3226)</td>
<td>(-0.7742)</td>
</tr>
<tr>
<td>App</td>
<td>11.1613</td>
<td>11.6774</td>
<td>11.4839</td>
<td>11.0968</td>
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<tr>
<td></td>
<td>(-0.5806)</td>
<td>(-0.0645)</td>
<td>(-0.2581)</td>
<td>(-0.6452)</td>
</tr>
</tbody>
</table>

Table 3. Diabetes incidences in millions of adults (predicted for 2020). In parenthesis: difference from baseline of no intervention (30.6359 million adults).

<table>
<thead>
<tr>
<th></th>
<th>Random</th>
<th>Obese</th>
<th>Risk</th>
<th>Network</th>
</tr>
</thead>
<tbody>
<tr>
<td>Offline</td>
<td>29.4576</td>
<td>31.6459</td>
<td>29.4576</td>
<td>30.4676</td>
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<tr>
<td></td>
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<td>(1.0100)</td>
<td>(-1.1783)</td>
<td>(-0.1638)</td>
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<tr>
<td>Webpage</td>
<td>28.4476</td>
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<td>29.7942</td>
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<td></td>
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<tr>
<td>App</td>
<td>29.1209</td>
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<tr>
<td></td>
<td>(-1.5150)</td>
<td>(-0.1638)</td>
<td>(-0.6733)</td>
<td>(-1.6833)</td>
</tr>
</tbody>
</table>

The American Diabetes Association (2013) estimated the economic cost of diabetes including direct medical cost and indirect costs from lost productivity. They found that in 2012 the total cost of diabetes was $245 billion, where $176 billion were direct costs and $69 billion were indirect costs. Each diagnosed individual spent on average $7,900 in medical care directly related to diabetes. They also found that 20% of health care
expenditure in the USA was for the diagnosed population, who had a personal expenditure 2.3 times higher than in the absence of the disease. This study was conducted for an adult diabetic population of 22.3 million. Indirect estimated costs were divided by the number of diagnosed individual to have an estimate of indirect cost per person. Tables 4, 5 and 6 show direct, indirect and total costs for each scenario. Direct costs were calculated by multiplying diabetes incidences in millions of people times the $7.900 average expenditure obtained by the American Diabetes Association (2013). Individual indirect costs were estimated by dividing total indirect costs by the diabetes incidences in 2012, yielding an amount of $3094 per individual. For the best scenario, direct costs would be reduced in 17.29 billion USD, while indirect cost would decrease 6.77 billion USD. This is a total cost reduction of 24 billion dollars from the baseline of no intervention. In the case of offline intervention targeting obese people, the cost would not only increase as a result of the intervention, but also result in 11 billion dollars more cost derived from increased diabetes incidences.

Table 4. Direct costs of diabetes in billions of USD (predicted for 2020). In parenthesis: difference from baseline of no intervention ($242.0235).

<table>
<thead>
<tr>
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<th>Random</th>
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<th>Risk</th>
<th>Network</th>
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</thead>
<tbody>
<tr>
<td>Offline</td>
<td>232.7149 (-9.3086)</td>
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<td>240.6937 (-1.3298)</td>
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<td>226.0659 (-15.9576)</td>
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<td>230.0553 (-11.9682)</td>
<td>240.6937 (-1.3298)</td>
<td>236.7043 (-5.3192)</td>
<td>228.7255 (-13.2980)</td>
</tr>
</tbody>
</table>
Table 5. Indirect costs of diabetes in billions of USD (predicted for 2020). In parenthesis: difference from baseline of no intervention ($94.7874).

<table>
<thead>
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<th>Risk</th>
<th>Network</th>
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<tbody>
<tr>
<td>Offline</td>
<td>91.1418 (-3.6457)</td>
<td>97.9123 (3.1249)</td>
<td>91.1418 (-3.6457)</td>
<td>94.2666 (-0.5208)</td>
</tr>
<tr>
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<td>88.0169 (-6.7705)</td>
<td>93.2250 (-1.5624)</td>
<td>92.1834 (-2.6041)</td>
<td>88.5377 (-6.2497)</td>
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<td>App</td>
<td>90.1001 (-4.6973)</td>
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<td>92.7042 (-2.0832)</td>
<td>89.5793 (-5.2081)</td>
</tr>
</tbody>
</table>

Table 6. Total costs of diabetes in billions of USD (predicted for 2020). In parenthesis: difference from baseline of no intervention ($336.8109).

<table>
<thead>
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<th>Risk</th>
<th>Network</th>
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<tbody>
<tr>
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<td>347.9146 (11.1037)</td>
<td>323.8566 (-12.9543)</td>
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<td>Webpage</td>
<td>312.7530 (-24.0579)</td>
<td>331.2591 (-5.5518)</td>
<td>327.5579 (-9.2530)</td>
<td>314.6036 (-22.2073)</td>
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<tr>
<td>App</td>
<td>320.1554 (-16.6555)</td>
<td>334.9603 (-1.8506)</td>
<td>329.4085 (-7.4024)</td>
<td>318.3048 (-18.5061)</td>
</tr>
</tbody>
</table>

Each scenario has different associated costs depending on the type of intervention and the target of the intervention. Offline interventions have the highest associated costs, as they require human labor to implement the intervention strategy. The Diabetes Prevention Program Research Group (2012) reported a per capita cost of the offline intervention program of $4,572 over ten years, resulting in an average of $457 per capita per year. To estimate the cost of online methods it was compared with that of online-
based self-care for chronic patients, found to be 378€ per individual (Kennedy et al. 2007). In both cases, the individual was referred to the program by a doctor, in which case there would be no difference in cost for the different target groups. The main advantage of the online methods is that the cost per capita would be reduced when more individuals make use of the system.

5. Discussion

5.1. Theoretical Model

The proposed model provides a way to combine empirical studies into one, interrelated system. This respects the CAS nature of the healthcare system and enables observability of emergent behavior. It results in a collaborative compilation of data from existing literature combined to test online preventive strategies. This model has important implications for the decision-making process regarding prevention of diabetes type II. It is a tool to utilize data available in the literature to have a holistic view of the system and to understand the important interrelatedness among components. It also offers a way to study temporality. In a dynamic system, it is meaningful to understand variations in the environment and how these will impact change in individual behavior.

The theoretical model is a tool to understand the main components and relationships in the CAS of healthcare. As such, it is patient-centered, dynamic with non-linear relationships, evolving and dependent on previous states. It was designed to respect the main conditions to success in CAS,
namely that patient behavior (at the micro level) is key for an intervention to succeed (Rouse 2008) and that healthcare cannot be designed, only influenced (Begun et al. 2003). With these attributes, the model is a framework for the design of prevention campaigns which consider the nature of the healthcare system upon which they will be implemented.

While the accuracy of the prevention scenario is limited by the nature of the model, simulating is an additional tool in the design process of a prevention strategy. Modelling allows us to see the effect of different combinations of components in a short time and without the need of creating all prototype alternatives. In a short period of time, results would be visible and objective decisions on design could be made prior to empirical studies on efficacy and efficiency of the strategy. Therefore, it helps saving time and cost and implement the solution with best predicted outcome. This offers the opportunity to have long-term thinking in healthcare, with important implications for policy.

5.2. Agent-Based Model Simulation

The theoretical framework was implemented to an agent-based model, which was simulated in NetLogo by populating it with data from a real setting. The results of the simulation suggest that, as expected, intervention strategies could reduce the incidences of diabetes among adults in the US. Twelve scenarios were studied, each of which simulated an intervention strategy (i.e., offline, webpage-based and app-based) with different targets (i.e., random, obese, at risk of obesity and high clustering coefficient). Outcomes were compared with the baseline of having no intervention and observed that most
scenarios yielded a lower number of diabetic individuals than the baseline at the end of the simulation period.

For each type of intervention, targeting randomly or selecting as targets those individuals with a high clustering coefficient resulted in the lowest diabetes incidences. This suggests that targeting obese individuals or those at risk of obesity is less effective than including the healthy population in the prevention strategy. The explanation is that targeting these two groups leaves out non-obese individuals which might become obese in the future. As such, methods, which include healthy individuals, are not only reversing the effect on some obese individuals but also preventing healthy people from gaining unhealthy weight, ultimately outperforming methods that only focus on obese individuals.

While being less effective, targeting obese or at risk of obesity agents with the use of online prevention strategies reduced diabetes incidences between 0.06% and 0.32%. This is translated into 163,800-841,600 fewer individuals developing diabetes and a total cost reduction of 1.85-9.25 billion USD per year. Based on traditional linear thinking, prevention strategies in the US, such as the National Diabetes Prevention Program are targeting the obese population (Centers for Disease Control and Prevention 2016). Linear approaches focus on treating the cause, in order to minimize the outcome probabilities, in this case, directing efforts only towards those who have already become obese. The inefficiency of this approach might be a consequence of the complex adaptive nature of health, by which relationships between cause and effect are complex and non-linear. Even
more, these strategies might revert obesity among the treated patients but are not able to prevent the healthy population from becoming obese. As a result, only those interventions, which are highly effective at reverting obesity, will be able to keep up with the healthy population who is becoming obese. Results show that only online strategies, namely webpages and apps, would be more effective at reducing diabetes incidences when compared to having no intervention at all. In fact, an offline intervention targeting the obese population would result in an increase of 0.39% in diabetes incidences.

The aforementioned National Diabetes Prevention Program includes being overweight (BMI > 25) as an eligibility condition for their program (Centers for Disease Control and Prevention 2016). They have reported positive outcomes from the prevention program (Diabetes Prevention Program Research 2009), which might be a consequence of including people at risk of obesity. The program consists of sessions in which obese and people at risk are influenced to take up healthy habits. According to the model, targeting the population at risk with offline methods seems to be more effective, with a relative reduction in incidences of 0.45%. Interestingly, results suggest that offline methods have similar outcomes regardless of the target. This means that for the National Diabetes Prevention Program (NDPP) to yield better results, not only the target, but also the method of intervention, should be improved.

The obese population seems to be the optimal target, when the intervention method is webpage-based (0.19% reduction). Targeting the population at risk would yields the best results when using offline methods. The NDPP has
been therefore optimized for both offline interventions and people at risk as a target. However, when the target includes healthy population, the percentage decrease can be much higher. In the case of random targets, using a webpage or an app results in 0.84% and 0.58%, respectively. If the target specifies individuals with a high number of connections these percentages become 0.77% and 0.64%. This means that designing a webpage and letting anyone use it would help the NDPP decrease diabetes incidences from 0.45% to 0.84%. This is 1 million fewer diabetic and 12 billion dollars less. Even more, the design and maintenance of a webpage will most likely be less expensive than their current offline program; and randomly targeting the candidates for the intervention will be easier, faster and less costly than diagnosing patients to be eligible for the program.

5.3. Policy implications

The model suggests that investing in prevention can considerably reduce diabetes incidences, which in turn decreases healthcare costs and productivity losses. Furthermore, results showed that intervention method and target of intervention are important factors, which can drastically change outcomes. Online interventions, delivered through webpages or mobile apps, can be almost twice as effective as an offline intervention and yield results that are almost eight times better than having no intervention. Policymakers should also consider policy resistance and the inefficiency of only targeting the overweight population. According to the model, when the healthy population is included in the intervention program, diabetes incidences can have a twofold decrease. As such, the model is a useful tool for policymakers
to plan intervention strategies in their country or region. The National Diabetes Prevention Program, which is the current prevention system in the US, could decrease diabetes incidence in a million per year by adapting the intervention strategy and target according to our model’s results.

Results from the simulation are, however, an approximation of the outcome. In reality, introducing innovations in healthcare is not an easy task. First, socioeconomic characteristics of the patients will impact the preferences on health technology attributes, as well as the willingness to pay (or perceive value) for that product (Park et al. 2011). Second, innovation success is also limited by the different layers of the healthcare structure. Rouse and Cortese (2010) suggest considering the stakeholders involved in the change, and especially, what their reaction will be regarding such a change. In fact, the layered nature of the system requires approval of stakeholders at different levels (e.g. doctors, companies, government which might cause an important barrier to change. An example of negative reaction by a stakeholder is doctors’ reluctance to use Health Information services which challenge their long-established fee-for-service reward method (Park et al. 2015).

Third, at the highest layer, political resources are needed to smoothly implement change. This may sound contradictory with the fact that complex adaptive systems have no single point of control. However, as recalled by Rouse (2009), innovations implemented in a layer might be limited by actions on the layers above. This is supported by Niosi (2014), according to whom regulations and policies directly impact the success of a health technology. Thus, the actions of the government might be critical in the
implementation of technologies which target health. Consequently, despite not having total power to control the system, authorities can perform actions to generate the necessary cues for the environment to change and trigger the desired response in the system. Therefore, the involvement and interest of the government needs to be understood. If healthcare is at the base of development (OECD Indicators 2011), it would be natural to predict that governments will be interested in promoting health technologies. However, regardless of its importance, Batley and Mcloughlin (2015) showed that the inherent characteristics of preventive medicine usually cause politics to disregard them. This should be carefully considered when proposing prevention solutions.

Finally, resistance to innovation is an important cause of prevention strategies failure. Rouse (2009) stresses the importance of use being offset by cost for the innovation to succeed. From a wider perspective Herzlinger (2006) suggests that the intrinsic nature of the healthcare system (e.g., fragmentation, complicated value chain, long life cycle) creates barriers to innovation that result in inefficient solutions or even hindered innovation. Park, Chon et al. (2011) concluded that failure of telemedicine might be originated from information asymmetries caused by a lack of knowledge (e.g. in telemedicine) or by reduced interactions with healthcare providers. Resistance to innovation might pose challenges in the affordability of an online solution.

Barriers to innovation in healthcare exist and cannot be ignored, but the model shows that a simple change in the approach to prevention can
drastically reduce diabetes incidences. For the US, the model suggests that online strategies (e.g., webpage and app) which include the healthy population are the optimal configurations for the intervention, as they yield the lowest diabetes incidences by the end of the simulation period. Implementing these strategies would not only improve the health and quality of life of the population but also reduce the financial burden on the healthcare system.

5.4. Limitations

The accuracy of the results is limited by the nature of the model. Reality has been simplified to understand important relationships in the diabetes system. As such, these results shed light on the optimal prevention scenarios but cannot be as accurate as carrying out randomized control trials to test the different strategies. Our model is a good starting point to test different approaches before experimenting in the real world. The model could be improved by increasing the number of agents, for which a larger survey should be carried out. Further limitations include the simplification of health status, by which over 20 years only diabetes and obesity are considered, while all other characteristics remain the same; and the assumption that diabetic individuals will require treatment for the rest of their lives.

Another limitation of the model is the simplification of intervention strategies. A more comprehensive model should include attributes of each system. This would improve the accuracy of the adherence and efficiency measurements. For example, diabetic patients in Korea consider price, and comprehensiveness of service scope to be the most important attributes of a
telemedicine service to manage their disease (Park et al. 2011). Taking into account preferences of agents for the services would make the model more reliable.

Finally, another limitation is the data used to calibrate the model. First, this model was populated with data from the US, which is a heterogeneous country. As a consequence, the accuracy of the model is decreased, since the macrolevel is not homogeneous. Second, although many countries like the US or regions like the European Union have widely available data to readily fill in the model, other countries, especially in the developing world, are likely to lack studies in one or more of the fields that enable the usability of the model. In such cases, countries with similar characteristics can be used to approximate lacking parameters. Finally, other limitations include barriers to change from the stakeholders and resistance to innovation in the healthcare environment.

6. Conclusion

This thesis proposed a model to design and evaluate interventions for the prevention of diabetes type II. These interventions are designed to promote weight control in the population, in order to tackle obesity, which is one of the main causes of non-insulin dependent diabetes. The model is based on the idea that healthcare is a CAS and it was constructed upon considerations of the causes of diabetes, the layered nature of the system, the observable network effects, the characteristics of individual behavior evolution and the implications of using social networks. Based on extensive literature research,
a theoretical model for diabetes type II and its prevention was built. The model includes crucial components and their interrelatedness, as well as their relationships to outcome. This was built to understand the whole picture of diabetes and as a tool to answer important questions on how to prevent the disease. This theoretical framework was implemented in NetLogo and simulated as an agent-based model. Results from the simulation suggested that intervention strategies would considerably reduce diabetes incidences. Using a webpage or an app to deliver the intervention and including the healthy population in the strategies would further reduce diabetes incidences when compared to offline strategies with overweight targets.

The contribution was to look at diabetes prevention from the perspective of complexity science. Studying healthcare as a CAS, the importance of its multiple components and the way they affect each other was highlighted. A tool to estimate outcome from non-linear interactions was built and used to compare different scenarios of active diabetes prevention. Simulation results were used to evaluate different intervention methods and their impact on diabetes type II incidences in the United States. Possible improvements on target and type of intervention were discussed.

As for any simplification of reality, the accuracy of the prevention scenario is limited by the nature of the model. The model could be improved by more agents and more detailed information about the intervention methods. Further limitations include barriers to change from the stakeholders and resistance to innovation in the healthcare environment. In future work, more attributes to the intervention methods will be included, as well as cost
information to fully estimate optimal configurations for the prevention strategies. Populated with the appropriate data, the model could be used in different countries or regions and it could also be modified to study other chronic and preventable diseases or even serve as a base to inspire models in other complex fields, such as education. The model can also be a tool to evaluate the effect of new technologies on the treatment and prevention of diseases, such as wearable and connected devices.
Bibliography


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Diabetes Prevention Intervention Using a Mobile App: A Randomized Controlled Trial with Overweight Adults at Risk,


Wilensky, U. 2008. "Netlogo 4.0. 4,")

## Appendix

Table A1. Variables used in the model.

<table>
<thead>
<tr>
<th>Parameters common to all agents</th>
<th>Value</th>
<th>Source</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>% initial intervention</td>
<td>30</td>
<td>-</td>
<td>% of agents who will be intervened</td>
</tr>
<tr>
<td>Threshold</td>
<td>8</td>
<td>Calibrated</td>
<td>Points above which BMI increases</td>
</tr>
<tr>
<td>Increment</td>
<td>0.0015</td>
<td>Calibrated</td>
<td>BMI increment per week</td>
</tr>
<tr>
<td>Value of intervention</td>
<td></td>
<td></td>
<td>Impact of intervention on individual points.</td>
</tr>
<tr>
<td>• App</td>
<td>0.93</td>
<td>(Carter et al. 2013)</td>
<td></td>
</tr>
<tr>
<td>• Webpage</td>
<td>0.55</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Offline</td>
<td>0.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Network’s influence</td>
<td>0.57</td>
<td>(Christakis and Fowler 2007)</td>
<td>Influence of agent’s directly connected peer’s health status.</td>
</tr>
<tr>
<td>• Friends same gender</td>
<td>0.71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Friends diff gender</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Husband</td>
<td>0.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Wife</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI thresholds</td>
<td>18</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>------------------------</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>Healthy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Obese à diabetic       | 7% | (Mokdad et al. 2003) | Probability to become diabetic being obese. |

<table>
<thead>
<tr>
<th>Individual parameters (turtle’s own)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (Kg)</td>
<td>36 – 208</td>
<td>(ISSP Research Group 2015)</td>
<td>Self-reported weight in Kg.</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>137 – 203</td>
<td>(ISSP Research Group 2015)</td>
<td>Self-reported height in cm.</td>
</tr>
<tr>
<td>Gender</td>
<td>0 / 1</td>
<td>(ISSP Research Group 2015)</td>
<td>Female / Male</td>
</tr>
<tr>
<td>Obese?</td>
<td>0 / 1</td>
<td>Calculated from (ISSP Research)</td>
<td>Obese if BMI &gt; 30</td>
</tr>
<tr>
<td></td>
<td>Group 2015)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic?</td>
<td>0 / 1 Calculated from (ISSP Research Group 2015) (10% of chronic patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10% of individuals with chronic disease were initialized as diabetic.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Access</td>
<td>0 – 5 Calculated from (ISSP Research Group 2015)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Access to healthcare was computed with agent’s evaluation of V42(^1), V45(^2), V46(^3), V48(^4) on a scale from 0 to 5.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confidence</td>
<td>0 – 5 Calculated from (ISSP Research)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Confidence in healthcare was computed with agent’s evaluation of V7(^5), V16(^6), V18(^7), V32(^8) on a</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Times in the past year the agent visited a doctor.
2. Times in the past year the agent could not get a treatment because he/she could not pay for it.
3. Times in the past year the agent could not get a treatment because he/she could not take time off.
4. Times in the past year the agent could not get a treatment because the waiting list was too long.
5. Confidence the agent has on the US healthcare system.
6. Level of agent’s agreement to use public finding of preventive medical checkups.
7. Level of agent’s agreement to use public finding of obesity prevention.

69
<table>
<thead>
<tr>
<th>Variable</th>
<th>Range</th>
<th>Calculation Details</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working Hours</td>
<td>0 – 5</td>
<td>Calculated from (ISSP Research Group 2015)</td>
<td>Self-reported working hours were adjusted on a scale from 0 to 5.</td>
</tr>
<tr>
<td>Education years</td>
<td>0 – 5</td>
<td>Calculated from (ISSP Research Group 2015)</td>
<td>Self-reported education years were adjusted on a scale from 0 to 5.</td>
</tr>
<tr>
<td>Age (years)</td>
<td>20 – 89</td>
<td>(ISSP Research Group 2015)</td>
<td>Years from birth year.</td>
</tr>
<tr>
<td>Exercise</td>
<td>0 – 5</td>
<td>Calculated from (ISSP Research Group 2015)</td>
<td>Self-reported behavior towards exercise was adjusted on a scale from 0 to 5.</td>
</tr>
<tr>
<td>Nutrition</td>
<td>0 – 5</td>
<td>Calculated from (ISSP Research Group 2015)</td>
<td>Self-reported behavior towards nutrition was adjusted on a scale from 0 to 5.</td>
</tr>
<tr>
<td>Income</td>
<td>0 – 5</td>
<td>Calculated</td>
<td>Self-reported income was</td>
</tr>
</tbody>
</table>

---

8 Level of agent’s trust in doctors.

70
<table>
<thead>
<tr>
<th>Term</th>
<th>Value/Details</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesogenicity</td>
<td>0 – 5</td>
<td>Calculated from (Centers for Disease Control and Prevention 2018) Obesogenicity of agent’s living state was computed regions’ [facilities, retailers, meeting sports guidelines, regulations, farmers markets] and adjusted to a 0-5 scale.</td>
</tr>
<tr>
<td>Points</td>
<td>New each iteration</td>
<td>Algorithm of calculation Equations (1) and (2).</td>
</tr>
<tr>
<td>Network connections</td>
<td>Connected turtle’s name Randomly generated with AB algorithm</td>
<td>Algorithm in Matlab’s file <code>randomized_links.m</code></td>
</tr>
<tr>
<td>Intervened</td>
<td>Value of intervention (Carter et al. 2013)</td>
<td>Modulating points assigned to intervened individuals based on type of intervention chosen by user.</td>
</tr>
</tbody>
</table>
Abstract (Korean)

치료 중심의 전통적인 의료 시스템은 최근 사회 경제적 변화에 따라 증가하고 있는 만성 질환의 발병으로 인해 그 효과성과 효율성 이 도전 받고 있다. 의료 시스템의 패러다임이 치료에서 예방으로 전환되어야 한다는 것이다. 어플리케이션이나 웹페이지 등과 같은 온라인 채널은 정보의 접근성을 증가시키고, 실시간 모니터링을 용이하게 하지만, 의료의 복잡한 적응 특성으로 인해 이들을 이용해서 의료 분야에서 결과에 변화를 가져오는 것은 어렵다. II형 당뇨병의 예방을 위한 온라인 개입 전략을 최적화하기 위해 의료 시스템의 복잡성을 고려할 수 있는 에이전트 기반 모델을 제안한다. 이러한 전략은 II형 당뇨병의 주요한 원인 중 하나인 비만을 예방하고, 사람들의 체중 조절을 촉진하도록 설계되었다. 이 모델은 예측의 정확성을 높일 수 있도록 개인 수준의 데이터로 보정되었다. 시뮬레이션 결과는 여러 개입 전략과 이들이 미국에서의 II형 당뇨병 발생률에 미치는 영향을 평가하는데 사용되었다. 결과는 임의 대상에 대한 웹 기반 개입 전략을 통해 당뇨병 발병과 이와 관련된 비용이 감소될 수 있음을 보여 주었다.

주요어 : 당뇨병, 비만, 예방, CAS, ABM
학번 : 2016-26097