Appendix 15.1
Tobacco Control Simulation Models

Introduction

This Appendix covers the topic of models that simulate tobacco use, the determinants of tobacco use, and the consequences of tobacco control interventions and policies in populations. Such models are widely used in public health to, for example, model infectious disease epidemics and simulate the consequences of control measures, such as vaccination and quarantine (Epstein 2006; Leischow and Milstein 2006; Luke and Stamatakis 2012).

This Appendix begins with an overview of modeling, providing a broad introduction before turning to uses of the models in specific simulations related to tobacco control. The concluding section addresses future uses of models in tobacco control.

Simulation models in tobacco control are used in three main ways:

1. To *forecast* outcomes of interest under the assumption that the current tobacco control conditions will not change in the future (i.e., status quo). Outcomes could include tobacco consumption, prevalence of smoking, and tobacco-related mortality, and models could provide forecasts of such outcomes on subgroups of a population.

2. To *estimate* the values or relative values of outcomes of interest under future scenarios in which one or more new policies, programs, or interventions are introduced and/or implemented under ideal or different conditions (i.e., explore "what if" scenarios).

3. To *evaluate* the impact of past smoking control policies by contrasting the historical smoking trajectory with the estimated smoking pattern in the population, had those policies not been implemented.

Simulation modeling provides a set of strategic and heuristic tools to inform how interventions and policies can impact upon specific outcomes (e.g., prevalence of tobacco use behavior over time, health consequences of changes in tobacco use) that are influenced by a complex system of multi-level, dynamic interactions of influences (National Cancer Institute [NCI] 2007). Systems thinking and simulation have been adopted as important strategic priorities by the National Institutes of Health (NIH). These approaches are beginning to demonstrate their value for informing decision making on intervention and policy approaches in public health (Mabry et al. 2008, 2010; Milstein 2008; Milstein et al. 2010, 2011). For example,

such methods have been used to inform the World Health Organization's stance on polio (eradication versus control) (Thompson and Tebbens 2007), to develop a national plan that addresses the threat of emerging infectious diseases (Luke and Stamatakis 2012), to aid communities in implementing the most cost-effective policies for reducing cardiovascular events (Homer et al. 2010), and to understand and intervene with the obesity epidemic (Institute of Medicine [IOM] 2010).

Simulation models can also be helpful tools for forecasting the consequences of tobacco control policies, allowing for the evaluation and comparison of selected policies and policy options. The use of models in tobacco control is expanding and was the focus of *Greater than the Sum: Systems Thinking in Tobacco Control,* a monograph (number 18) from NCI (2007). The topic of models is included in this report because models will be used increasingly to explore strategies that will continue and accelerate the decline of tobacco use in the United States. Additionally, models offer an approach for projecting the public health consequences of new tobacco products and other products that deliver nicotine to their users. Chapters 15 and 16 address strategies for accelerating the decline of tobacco use, as emphasis shifts to the "endgame" for eventual elimination of tobacco smoking. Because decision makers increasingly will ask for advice about what may be an optimal mix of policy measures, modeling will be essential to planning and implementing such measures (NCI 2007). Thus, this Appendix provides background for the final two chapters of the 2014 Surgeon General's report and for future analyses in support of changes in tobacco control policy in the United States.

Why model? As Epstein (2008) stated:

"Anyone who ventures a projection, or imagines how a social dynamic—an epidemic—would unfold is running *some* model. But typically, it is an *implicit* model in which the assumptions are hidden, their internal consistency is untested, their logical consequences are unknown, and their relation to data is unknown. But, when you close your eyes and imagine an epidemic spreading, you are running *some* model. The choice, then, is not whether to build models; it's whether to build *explicit* ones. In *explicit* models, assumptions are laid out in detail, so we can study exactly what they entail. On these assumptions, *this* sort of thing happens. When you alter the

assumptions *that* is what happens. By writing explicit models, you let others replicate your results. You *can* in fact calibrate to historical cases if there are data, and can test against current data to the extent that exists" (Epstein 2006, 2008).

The tobacco control field has many policy questions that would benefit from modeling. The U.S. Food and Drug Administration (FDA), NIH, Centers for Disease Control and Prevention's [CDC] Office on Smoking and Health, and state and local tobacco control stakeholders are showing increased interest in tobacco policy and intervention modeling. At a Tobacco Policy Modeling Workshop in 2013 (NIH 2013), it was noted that modeling and simulation can:

- estimate a policy's impact quickly and at a much lower cost than waiting to learn what happens after a policy is implemented;

- estimate what would have happened if the policy had not been implemented;

- make mental models transparent;

- summarize evidence across disciplines at multiple levels;

- expose research gaps and prioritize them; and

- explore "what if" scenarios to identify effective approaches.

Models are heuristic, always approximate in nature (Epstein 2006). Although they are inherently "wrong" because they are representational, their findings are illuminating (Sterman 2002). By making model assumptions and parameters explicit and transparent, models can identify the conceptual foundations of their respective fields (Leischow and Milstein 2006), inform needs for data collection, suggest potential leverage points for intervention, and point to unintended consequences. More details about the basics of modeling can be found in Chapter 5 of the NCI Monograph, *Greater than the Sum: Systems Thinking in Tobacco Control,* where Richardson states:

"Today's tobacco control environment represents a complex and dynamic interrelated system of issues and stakeholders. In this dynamic environment, change is continuous and poses significant challenges for those who would anticipate change and prepare for its consequences. There is growing recognition that systems approaches need to be able to address this challenge of dynamics and to anticipate change. Modeling is one of the most prominent and promising approaches for addressing such problems and, in doing so, (modeling is) helping to achieve more effective integration of research knowledge and its practical implications" (NCI 2007).

The *Family Smoking Prevention and Tobacco Control Act* of 2009 requires the FDA to use a public health/population health impact regulatory standard for tobacco products instead of the traditional standard of safety and efficacy. FDA typically uses individual risk analysis to apply its standard for judging efficacy, but for tobacco products the agency must now consider overall population impact, taking into account users and nonusers of tobacco products and determining the likelihood of harms versus benefits at the population level. Thus, in this emerging new field of regulatory science (Villanti et al. 2011; Zeller 2012), simulation modeling will become an invaluable tool for FDA-related policymaking as it works with NIH, CDC, and other major science agencies to evaluate population impact of potential actions.

Table 15.1.1 provides a simplified overview of the main types of simulation models used in tobacco control, dividing them into aggregate and individual-level models. Models can take many forms to depict complex dynamic systems at different levels of granularity. Such divisions are somewhat arbitrary in that one can create hybrid models where individual-level units (agent based) can interact to produce an aggregate set of outcomes that can feed into compartmental or systems dynamic models. Thus, models of "systems within systems" can be developed as part of the general field of "systems thinking" and system dynamics (for more details, see pages 111–148 in NCI [2007]).

Compartmental models track groups within a population that are considered to be homogeneous for the purpose of examining a particular outcome of interest. In contrast, individual-based models represent each individual by him/herself without bundling individuals together into a group. Individuals in the model have their own unique characteristics and ways of relating to each other within their specific environments. Individual-based models include both microsimulation, in which the agents do not interact with each other, and agent-based models, in which the agents have the opportunity to interact with each other and their environments in ways that affect their future behaviors or characteristics. To date, individual-based models used in tobacco control have been almost exclusively agent-based.

Aggregate (compartmental) models track large groups, or compartments, within the populations being

Table 15.1.1   Main types of simulation models used in tobacco control research

Aggregate (compartmental) models	Individual (agent-based) models	Examples of inputs and outputs

Main characteristic: Keep track of aggregate quantities that describe homogeneous groups (e.g., total number of smokers in the population).	**Main characteristic:** Keep track of individuals as they interact with their environment and other individuals through their social networks.	• Example of inputs:
		   – Different smoking control policies, e.g., increased taxation for tobacco products.
		• Example of outputs:
		   – Estimates of future smoking prevalence.
		   – Estimates of smoking-related deaths.

Structure: • Stocks—Aggregate quantities of interest representing homogeneous groups (e.g., number of smokers). • Flows—Rates of transitions among stocks (e.g., rates of smoking initiation and cessation). **System Dynamics Model:** Type of aggregate model that is further characterized by complex, nonlinear interactions and feedback effects.	**Structure:** • Agents—Individuals with their unique traits that are followed throughout the simulation • Attributes—Individual traits of interest (e.g., smoking status, age, gender, socioeconomic status) • Rules—Specified behavior of the agents as they interact among themselves and with the environment (e.g., the interaction between a nonsmoking teen and a smoking teen increases the probability of the smoking initiation by the nonsmoking teen)	

studied. Groups may be defined by sociodemographic characteristics (e.g., race, gender, age, education, and income). Groups may be further distinguished by smoking status, quantity smoked, duration of smoking, or type of tobacco product smoked (e.g., menthol vs. nonmenthol, combustible or smokeless, other product characteristics, or brands).

Aggregate and individual-based models require assumptions about the relevant sociodemographic and smoking characteristics considered, and the choice of characteristics depends on several factors:

- features of the problem and how it is operationally defined;

- relevant characteristics—such as age, gender, and socioeconomic status—that affect the link between behaviors and health outcomes;

- sociodemographic characteristics that are associated with various smoking patterns;

- extent that the effects of policies vary by sociodemographic, smoking, or other characteristics;

- availability of data (e.g., can sufficiently accurate data be obtained that distinguish the population by potentially relevant characteristics); and

- complexity of the model, in terms of the number of different group classifications or individual characteristics included.

Compartmental models can include age as a characteristic in order to represent the relevant transitions of individuals over time, such as change in smoking status. Discrete time models allow individuals to move between different states (e.g., from current smoker at age *a* in period *t* to former smoker at age *a+1* in period *t+1*) at only fixed time intervals (possibly dependent on the state).

Over time, transitions between states or compartments depend on specific transition rules. In agent-based models, transition rules may apply to specific behaviors of individuals. By contrast in compartmental models, transitions depend on group characteristics—such as age, gender, and smoking status; the effects of policies and how they unfold over time; and the health outcomes under consideration. Transition rules may depend on individual or group characteristics in either type of model.

Central to models of smoking are the transitions into and out of smoking status. Transitions into smoking are described by rates of initiation, usually defined in terms of the proportion of never smokers in particular time period *t* becoming smokers by time period *t+1*. The definition should correspond to what the model considers to be a smoker. For example, if the model considers health effects for established smokers, defined as those who have smoked 100 cigarettes in their lifetime and are currently smoking, then rates of initiation must explain the transition to being an established smoker.

Smoking models may also consider cessation and relapse by representing each of these statuses separately. Cessation is generally considered over a fixed period of time, such as the past year, and relapse may be modeled as dependent on the number of months or years since quit-

ting smoking. Cessation and relapse may be collapsed into a measure of cessation net of relapse for simplicity when the issues surrounding relapse are not considered central to the problems addressed by the model.

Some models define situations that involve multiple subsystems. In such models, the actions applied to a particular subsystem may produce an effect that triggers a response in other subsystems, which may in turn affect the system that produced the original response. This circular cascade effect, known as feedback, is the hallmark of a more general characteristic of system dynamics models (Sterman 2000, 2006; NCI 2007). For example, policies may affect smoking rates, and changes in smoking rates may in turn affect social norms or the ability to implement policies.

Several distinct simulation models have been developed that can be used for tobacco control research. To date, simulation models have been used to evaluate several types of interventions and policies:

- taxation and price (Emery et al. 2001; Ahmad 2005b; Ahmad and Franz 2008; Mendez et al. 2013);

- media campaigns (Levy and Friend 2001; Tobias et al. 2010);

- educational programs (Dino et al. 2008);

- advertising bans and warning labels (Levy et al. 2006; Ferrante et al. 2007);

- youth access laws, such as increasing the legal smoking age (Ahmad 2005a,c; Ahmad and Billimek 2007);

- mandating coverage for cessation treatment (Levy and Friend 2002a,b; Warner et al. 2004);

- combining policies and interventions to boost population prevalence reduction (e.g., Abrams et al. 2010; Levy et al. 2010a,b,c);

- indoor clean air laws (Levy et al. 2001; Ong and Glantz 2004; Richiardi et al. 2009);

- making safer cigarettes (Sumner 2003; Tengs et al. 2004; Ahmad and Billimek 2005); and

- informing potential regulatory policies of the FDA, for example, banning menthol (Levy et al. 2011) and reducing the level of nicotine in cigarettes (Tengs et al. 2005; Cavana and Tobias 2008).

Simulation models have also been developed to assess the impact of various cessation treatments using cost-effectiveness frameworks. The impact of cessation treatments can be evaluated by inputting the treatment's effectiveness, as extracted from the literature, and then comparing the output of several treatment options, including no treatment. Cessation treatment can also be evaluated by varying the percentage of treatment uptake. For example, Apelberg and colleagues (2010) compared a constant increase in the uptake and use of nicotine replacement therapy, until a doubling of the rate was achieved, to a constant increase in the uptake of use of nicotine replacement therapy, until 100% use was achieved. Avila-Tang and colleagues (2009) evaluated the health benefits of nicotine replacement therapy and quit attempts by comparing constant rates to gradually increasing rates over time.

Types of Simulation Models Used in Tobacco Control

Aggregate (Compartmental) Models

Aggregate or compartmental models simulate the evolution of *stocks* and *flows*. In one form of compartmental modeling, the initial population (the stock(s)) is commonly grouped into nonoverlapping stocks of smoking status, most often "never," "current," and "former" (Figure 15.1.1) and may be disaggregated further by gender and age. Flows represent the active changes within the system that determine the values of the stocks (i.e., the percentages of never, current, and former smokers in the population). Flows commonly presented in tobacco control models are governed by rates of initiation, cessation, and relapse. These rates are applied to the stocks to determine the changes or outcomes (i.e., the percentage of never, current, and former smokers in the population; number of persons in each group who died) at a given point in time.

In the tobacco control literature, aggregate models generally take a population perspective and thus start with an initial population typically based on external data sources (e.g., the U.S. Census). In the simulation, the population undergoes life-cycle changes through births, deaths, aging, and net migration and other changes, such as smoking status. The rates of these population changes—such as age- and gender-specific smoking initiation, cessation, and relapse—are often derived from various external sources, including the Current Population Survey's Tobacco Use Supplement and the National Health Interview Survey (see Chapter 13). "Former"

Figure 15.1.1   Example of a stock and flow diagram
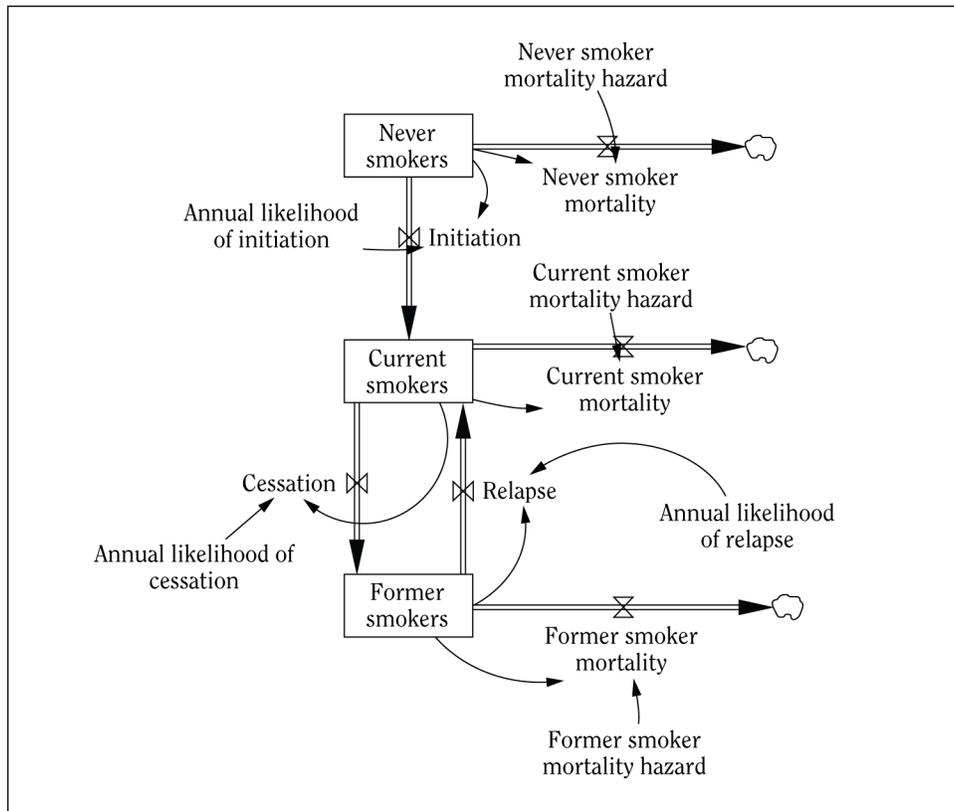
smokers may be disaggregated further by the number of years since quitting smoking. The initial smoking status for the population is derived from other data sources, such as the Behavioral Risk Factor Surveillance System, Youth Risk Behavior Survey, National Health Interview Survey, National Youth Tobacco Survey, and databases from departments of health.

System dynamics is an important specialization of the aggregate modeling approach, taking the perspective that the world is a complex system with interconnected components (Sterman 2001). System dynamics deals with internal feedback loops and time delays that affect the behavior of the entire system. What makes using system dynamics different from other approaches to studying complex systems is the use of feedback loops and stocks and flows. The elements of system dynamics diagrams are feedback, accumulation of flows into stocks, and time delays. The models include nonlinear processes that are characteristic within complex social phenomena, such as counterintuitive behavior of social systems and unintended consequences (Luke and Stamatakis 2012). Models solve the problem of simultaneity (mutual causation) by updating all variables in small time increments with positive and negative feedbacks and time delays structuring the interactions and control (NCI 2007).

Agent-Based Models

An agent-based model is a class of computational models for simulating the actions and interactions of autonomous agents (individual and collective entities, such as organizations or groups), with a view to assessing their effects on the system as a whole. The models simulate the simultaneous operations and interactions of multiple agents, in an attempt to recreate and predict the appearance of complex phenomena using heuristics or simple decision-making rules. The process is one of emergence from the lower (micro) level of systems to a higher level. Agents may experience "learning", adaptation, and reproduction. Most agent-based models are composed of: (1) numerous agents specified at various scales (typically referred to as agent-granularity), (2) decision-making heuristics, (3) learning rules or adaptive processes, (4) an interaction topology, and (5) a non-agent environment.

Agent-based models have been directed at the adoption of smoking behavior, in particular, and have assessed the impact of peer influences on this behavior. For example, Axtell (2006) modeled the adoption of smoking behavior in the context of adolescent social networks. Song (2006) incorporated addiction and cessation functions to estimate individual smoking probabilities, as well as peer networks, into an agent-based model of adolescent smoking behavior. Hybrid models that incorporate agent-based models within broader system dynamics models are also being developed (Osgood 2007).

The next section describes briefly the features and characteristics of aggregate compartmental and agent-based system dynamics models.

Types of Models and Modeling Approaches

Aggregate (Compartmental) Models

System Dynamics Models

System dynamics is a broad, evolving approach to understanding and managing complex systems. The origin of system dynamics lies in the pioneering work of Jay Forrester (of the Massachusetts Institute of Technology) (Forrester 1958, 1961). Since then, the toolbox of system dynamics has been refined and extended (Sterman 2000). System dynamics builds on elements from systems thinking and complex systems theory.

Several motivations are central to the system dynamics approach. The first is the conviction of the value of models that operationally express hypotheses about the causes behind system behavior. Such hypotheses can be termed "dynamic hypotheses," because they posit a particular causal structure for the system—"what affects what" in the system and the nature of that interaction—that has implications for the system's behavior over time and for its responses to interventions. Such models can be used to help explain diverse observed patterns (i.e., "behavior modes," such as a sudden rise in the rate of smoking initiation or a decline in tobacco-related mortality) and the impact of possible choices on the system. In many ways, system dynamics models serve as "thinking tools." A second motivation behind the practice of system dynamics lies in observing the ubiquity of *mental* models of this sort—that is, the act of routinely, but too often *implicitly*, constructing stylized mental models of the systems with which we interact. System dynamics seeks to make these models *explicit* (so that they can be shared, critiqued, and refined) and, where possible, to make them *quantitative* (so that computers can be used to secure a more reliable understanding of the models' logical implications for system behavior over time, and the impact of choices on that

behavior). A final source of motivation reflects the observation that the presence of feedback fundamentally shapes the behavior of many systems over time and complicates decision making regarding those systems. The historic record is replete with cases where people have overlooked feedback effects (Tenner 1996; Sterman 2000). Even when feedback is recognized, decision makers may suffer from poor intuition about skillfully interacting with feedback-rich systems. While feedback phenomena may pose dangers, they may also offer opportunities: some of the most powerful and effective interventions are those that seek to change the feedback structure of a system.

Model building is central to the system dynamics approach, particularly the need to build and simulate models of the system that capture operational hypotheses for "how the system works." Like other dynamic modeling techniques, quantitative system dynamics models provide formalisms to express quantitative relationships and dynamic hypotheses in an operational form that is useful for decision making. Such models can also help with theory generation (e.g., exploring possible hypotheses that might explain system behavior) and theory evaluation (e.g., thinking consistently through and scrutinizing the implications of those hypotheses in terms of their consistency with empirical observations, estimating components of the model in light of such observations, and offering information about important priorities for data collection or improving system understanding).

Basic Concepts of Feedbacks

Feedbacks are central to the concept of system dynamics. Feedbacks are causal sequences in which a change at one point in a system leads to a cascading series of changes that have a ripple effect to either amplify or push back the initial change. Altering the feedback structure of a system can also be of tremendous value in

helping to manage that system. Feedbacks are very common and can be observed in diverse aspects of daily life. They play a prominent role in shaping the impact of tobacco and tobacco control policies at the individual or societal levels.

Feedbacks can be characterized into two sorts: reinforcing (or positive) and balancing (or negative). In this case, the terms *positive* and *negative* do not carry their typical normative connotations. Instead, these terms reflect the fact that the response to the simulation creates a response relative to the original change in either the same direction (reinforcing or positive feedback) or the reverse direction (balancing or negative feedback).

Because balancing feedbacks push back original changes, such feedbacks can make a system stable and resistant to change. Sometimes this stability can be undesirable—such as when growing cravings drive a person trying to quit smoking to fall back into his or her habit. However, such feedbacks can also confer key benefits. In addition to their operation at the individual level, balancing feedbacks can also work at the societal level. For example, a rise in tobacco use among adolescents can trigger alarm, research, and policy action to reverse the worrying trend. Interventions to lower the burden of tobacco can lead tobacco companies to strategize and take action to maintain market share.

Like its balancing cousin, reinforcing (or positive) feedbacks are associated with situations in which an original change triggers a series of responses that cascade to interact with the original change. While the response in balancing feedbacks pushes the system in the opposite direction of the original change, reinforcing feedbacks trigger responses in the same direction as the original change, thereby amplifying the original change. When the direction of the change is deleterious, such feedbacks are frequently termed *vicious cycles*. At the individual level, for example, an increase in nicotine addiction on the part of an adolescent can trigger a series of changes (e.g., more frequent use of cigarettes or use of additional tobacco products) that further deepens the addiction. Such feedbacks are also common at the interpersonal level. For example, the initiation of smoking by one popular student can lead to copy-cat behavior in impressionable peers, triggering subsequent initiation by several other students. However, reinforcing feedbacks can also trigger virtuous cycles that cascade favorable change in the same direction. For example, smoking cessation by a popular person may lead to smoking cessation by several other parties. Some of the earliest research that applied systems modeling to smoking mapped out diverse feedbacks associated with tobacco use (Roberts et al. 1982).

Stocks and Flows

Structural Elements

Although the behavior of real-world systems is often complex, such behavior also frequently exhibits fundamental regularities. Certain types of factors in a system can change rapidly based on a change elsewhere in the system. For example, yearly initiation counts or the number of cigarettes being smoked by an individual each month may vary widely over time. But other types of variables, such as the count of smokers in the population or an individual's degree of nicotine addiction, may be capable of only very slow change. This latter variable type is typically associated with great "inertia," in which even dramatic changes in related variables elicit only slow changes in the variable of interest. As a result of this property, long delays can separate the propagation of changes from one part of the system to another. Another form of regularity in such a system is associated with sequential ("upstream-to-downstream") linkages that connect many different system components. In such cases, changes in the upstream components (e.g., a state policy that bans smoking indoors) lead slowly but surely to changes in downstream elements.

The differences between these two types of variables, and the nature of sequential linkages, can be captured neatly by distinguishing between two types of quantities: stocks and flows. Stocks (also called levels, state variables, or compartments) are accumulations. Being accumulations, stocks cannot change instantaneously. Instead they can change only over time due to influences from other factors (flows). Stocks serve as the system memory and collectively characterize the state of the system. The current values of stocks at any given moment drive the changes in the system to be experienced in the near future.

Stocks of relevance to tobacco-related models vary. At an individual level, potential stocks include an individual's level of addiction to tobacco, the cumulative damage caused by tobacco, and an individual's strength of conviction in the hazards of cigarettes. At a population level, potential stocks include people distinguished simultaneously by various stages of tobacco use (e.g., current, never, and former), by health states or categories of tobacco use, and by various demographic characteristics (e.g., almost 80% of African American adults smoke mentholated cigarettes). Potential other stocks of interest could include (possibly discounted) costs (e.g., accumulated health costs born according to different perspectives and accumulated intervention costs), quality-adjusted life years, and accumulated tobacco-related deaths. Some stocks could also be

associated with tobacco industry operations, such as the number of stores that sell tobacco products or the number of those in which the tobacco industry has enrolled in coupon programs. Figure 15.1.1 presents an example of a stock and flow diagram. In visual representations of stocks in system dynamics diagrams, stocks are shown as boxes. Figure 15.1.1 includes several stocks, including never, current, and former smokers.

By contrast, flows represent the rates of active change in the system and the conserved quantities that shift between stocks. In visual representations of flows in systems dynamics diagrams, flows are commonly depicted by valves and clouds. A cloud at one end of a flow indicates that the end of the flow lies outside of the scope of the model. Figure 15.1.1 includes several flows, including initiation, cessation, and relapse. Common flows within a tobacco control context would be those associated with these same indicators of rates of change.

Typically, a flow cannot be measured instantaneously, nor can it be quantified without mentioning a time unit. By its nature, a measurement of a flow reflects the change in a certain quantity over some period of time (e.g., a magnitude of 5 quitters per week or 60 quitters per year). The net flows affecting a stock determine the evolution of that stock. A positive net flow leads to progressive increases in the value of the stock over time, and a negative net flow decreases the value of that stock over time.

In general, the rates of flow at any given point in time are dependent upon the state of the system at that point—a state that is specified by the values of the stocks. For example, consider a stock of current smokers. Despite several outflows from this stock (e.g., representing death or smoking cessation), the number of people leaving the stock over a brief period of time cannot exceed the number currently in the stock. For this reason, the rate of outflow of a stock subject to depletion typically depends on the value of that stock. Such a flow may also depend on other stocks. For example, a modeler might posit that the risk that a never smoker will initiate smoking depends in some fashion (likely complex) on the prevalence of smoking among his or her peers and other factors. Reflecting this dynamic hypothesis, the magnitude of the "initiation" flow in Figure 15.1.1 might depend on the number of never smokers in that age group and also on the number of smokers (the value of the current smokers stock) in that or nearby age groups (via smoking prevalence). As a result, as the prevalence of smoking changes in the simulated population, the likelihood that a never smoker would initiate smoking will vary accordingly.

Stocks and flows also play important roles in feedbacks. The feedbacks depicted in causal loop diagrams link together stocks and flows. Figure 15.1.1 includes a number of such feedbacks, including those that link each stock with its outflow (thereby preventing depletion). Every feedback—no matter how rapid—is associated with some accumulation process that involves at least one stock. This process leads to at least a small delay between the original change and the consequent amplification or push-back.

Dynamics

The evolution of stocks over the next short period of time depends on the net of their flows over that interval. Specifically, viewing the magnitude of flows into a stock as being positive and the flows out as being negative, the rate of net change over time of a given stock (mathematically, its derivative) is equal to the sum of the values of its flows. Thus, the value of a stock of former smokers—in which there were 100 individuals quitting per week, 50 individuals relapsing per week, and 1 individual dying per week—would rise at a rate of 49 individuals per week ($100 - 50 - 1 = 49$). A stock rests in equilibrium when the sum of the rates of all inflows equals the sum of the rates of all outflows.

At a mathematical level, stock and flow models represent Ordinary Differential Equations, a powerful formalism used widely in applied mathematics across many application areas. This correspondence permits modelers to use a wide variety of analysis tools and to reason about the behavior of a system under a wide variety of conditions.

Feedbacks reflect cyclic causal linkages between stocks and flows. Because all changes in a system over time are caused by changes to stocks, and because the changes in those stocks are driven by flows, all feedbacks must involve at least one stock and one flow. The structure of the feedbacks gives rise to certain characteristics of emergent behaviors that can be categorized by two types of feedback loops: balancing feedbacks and reinforcing feedbacks, as described previously.

Many balancing feedbacks lead to stability and resistance to change. For example, many physical stocks (e.g., people, cigarette or tobacco inventories, addiction level) are subject to depletion and cannot physically become negative. Ultimately, if the stock contains nothing and all inflows are zero, then nothing can flow out and the values of the outflows must be zero. The outflows of such stocks are almost always associated with balancing feedbacks. Figure 15.1.2 presents a simple example of a balancing (or negative) feedback loop, in which people in a stock (e.g., current smokers) have a constant likelihood per unit of time of leaving that stock (e.g., a certain likelihood per month of quitting) via one or more pathways. As depicted

Figure 15.1.2   Example of a simple balancing (or negative) feedback loop
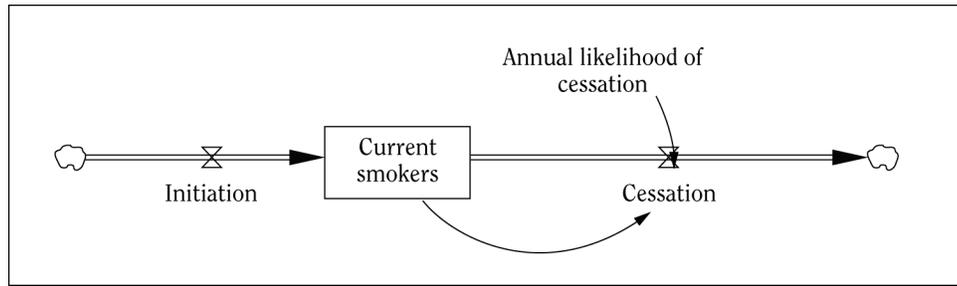

Figure 15.1.3   Several possible goal-seeking trajectories of the stock in Figure 15.2, given different initial numbers of current smokers
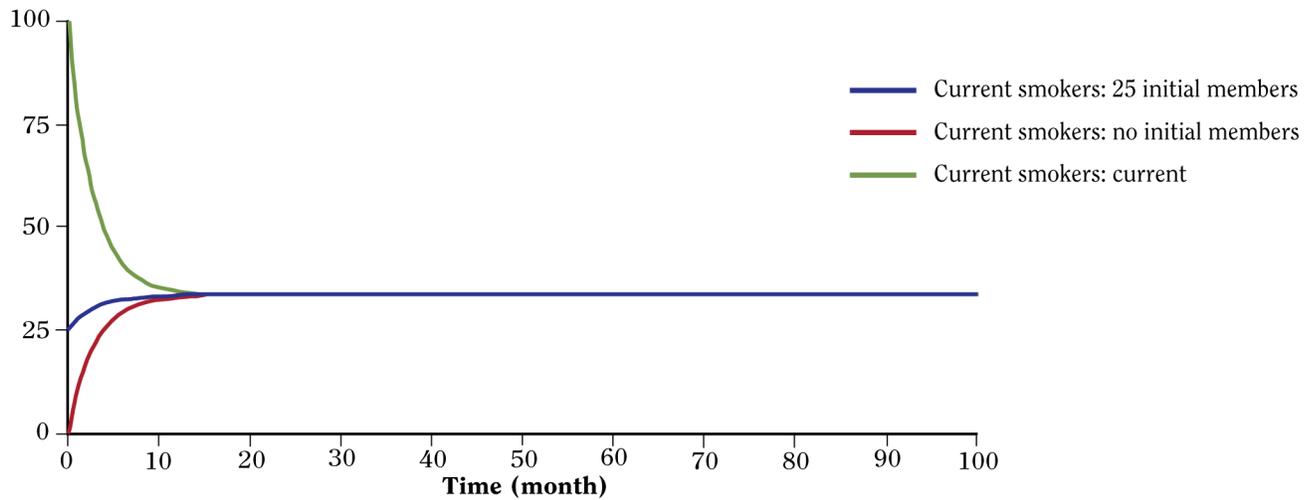
in Figure 15.1.3, this scenario leads to a self-regulating, stable situation in which a higher value of the stock leads to a higher outflow (and thus a higher rate of outflow), and a lower value of the stock results in a smaller outflow (and hence a slower rate of outflow). At the equilibrium value of the stock itself, the flows will be in perfect balance, and the stock will rest unchanging. Figure 15.1.3 shows the resultant behavior for a system such as this.

Some balancing feedbacks are associated with longer delays in perception and/or response. In the context of tobacco, such a response or target might be staffing levels for a quitline or regulatory guidelines or policy initiatives in place to counter tobacco activities. For such feedbacks, the push-back arising from the balancing feedback loop at a given time is dictated by a disturbance experienced some time ago and not by the disturbance impinging at the current time. In this case, the system's response and action often lead to oscillations in system output, as the

system will frequently overshoot the target level when approaching equilibrium (Figure 15.1.4). Such oscillations stem from certain familiar experiences from daily life. Oscillations occur when an individual compensates for a course deviation by overshooting his/her correction and ends up deviating in the opposite direction (similar to the fluctuations one experiences when trying to walk on a balance beam). Bearing in mind that it could apply to many particular situations, Figure 15.1.4 displays a generic system structure for such a system. This system attempts to regulate the change of the response variable so that it matches a perceived target. However, in a key difference from the balancing feedbacks depicted in Figures 15.1.1 and 15.1.2, the perception of the discrepancy between the current situation and the target is delayed. Even when trying to match a fixed target, the behavior for the regulated quantity (response) exhibits damped oscillations (Figure 15.1.5).

**Figure 15.1.4   Generic system structure for feedback with delayed perception of discrepancy**
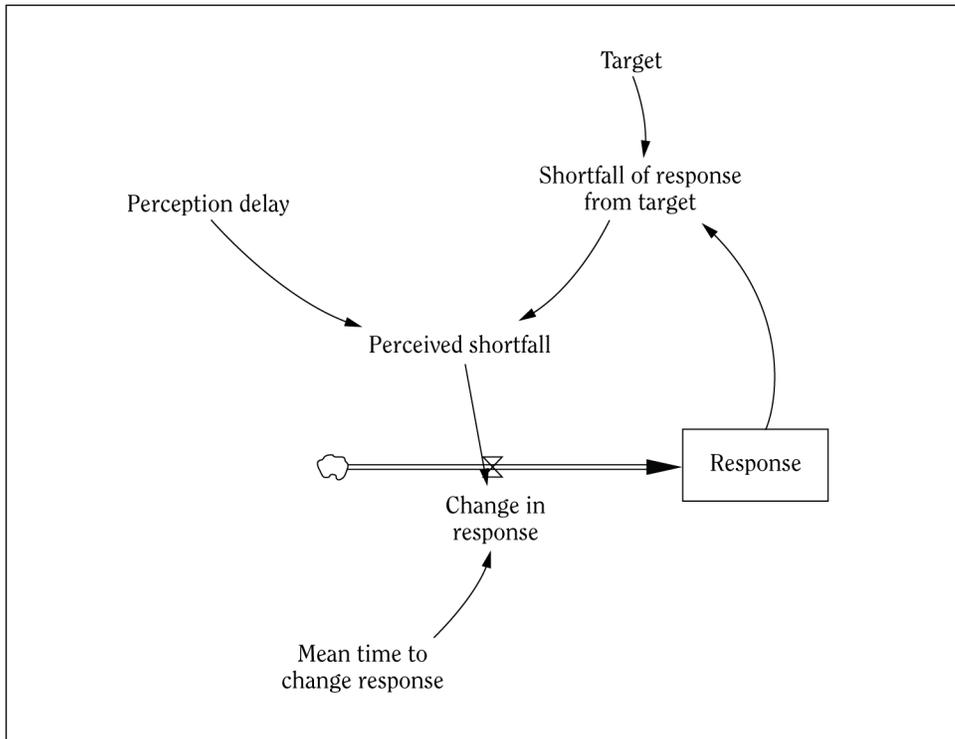
Figure 15.1.5   Level of response mustered to a constant target in which the presence of a perception delay leads to an overshoot
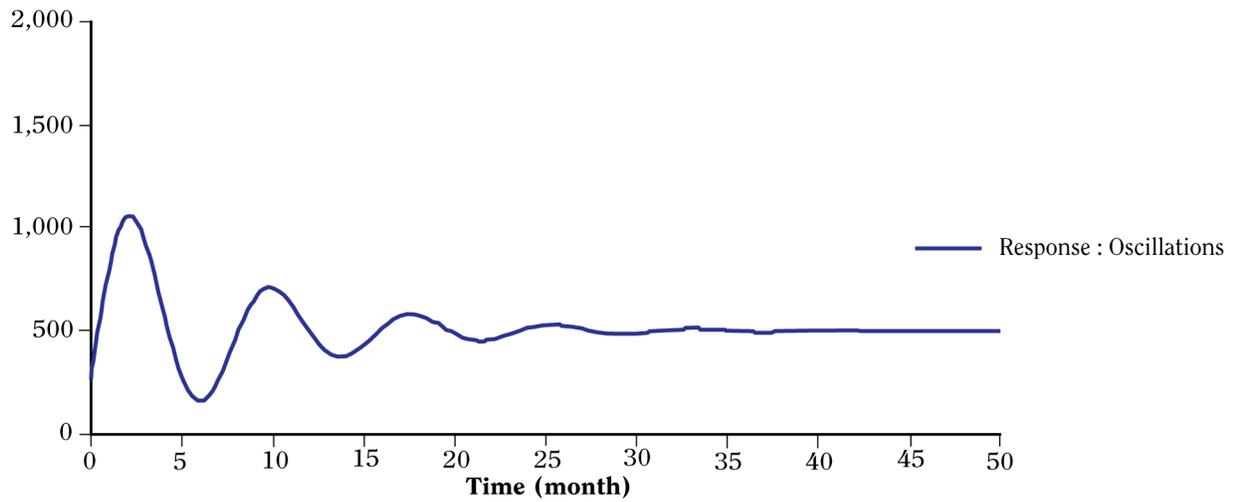
Although balancing feedbacks frequently lead to stability and resistance to change, reinforcing feedbacks generally trigger rapid and accelerating change (e.g., the rise and replacements of fads or the rapid spread of infectious disease outbreaks or rumors). Figure 15.1.6 presents a diagram of a simple reinforcing feedback loop. The loop consists of a stock (population) and a flow (births), in which the number of people born per year is given by a birth rate times the value of the stock. If birth is the only flow associated with the stock, then any birth rate greater than zero will yield ever-accelerating growth of the stock: A value of the stock at a given time will yield births that flow into that stock, yielding a yet higher stock and an elevated number of births per year (Figure 15.1.7).

Heterogeneity

In system dynamics models, stocks capture accumulations of things that are hypothesized to be relatively similar, at least from the perspective of the model's purpose. The contents of such stocks are assumed to be well-mixed, interchangeable, and relatively homogenous in terms of criterion of concern to the model. Population heterogeneity significantly shapes the effects of health interventions (Shepard and Zeckhauser 1980). Behavioral patterns of tobacco use differ markedly across age groups and ethnic and gender categories (Giovino 2002). Recognizing underlying heterogeneity of this sort may permit more judicious targeting of tobacco intervention strategies and can offer information about unintended side effects of tobacco control policies.

Parameter Estimates

Direct Parameter Estimates

System dynamics models typically contain a variety of parameter values. Although a model's structure (i.e., the arrangement of stocks and flows and their associated relationships) captures a dynamic hypothesis about how the world works, the parameters of the model specify particular assumptions that tailor the hypothesis to a particular context.

The particular set of parameters associated with a model depends on the purpose of the model. In the context of tobacco, for example, common parameters may be associated with the natural history of health conditions (e.g., rate of development of cardiovascular disease or oncological progression), risks of morbidity and mortality for classes of individuals, a level of smoking undertaken, and behavior change hazards. Notably, however, a quantity represented merely as an exogenous parameter in one model (e.g., an age-specific rate of smoking initiation) may in fact be treated endogenously in another model (e.g., a model in which the rate of smoking initiation is driven endogenously by the effects of peer pressure or depends on the prevalence of smoking).

Figure 15.1.6   Example of a simple reinforcing (or positive) feedback loop
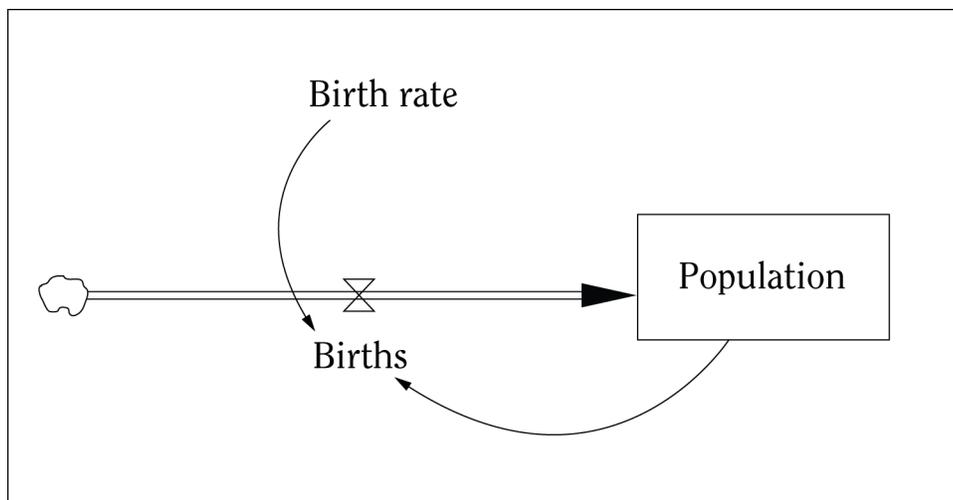
Figure 15.1.7   Dynamics of the "population" stock for different initial values of the population
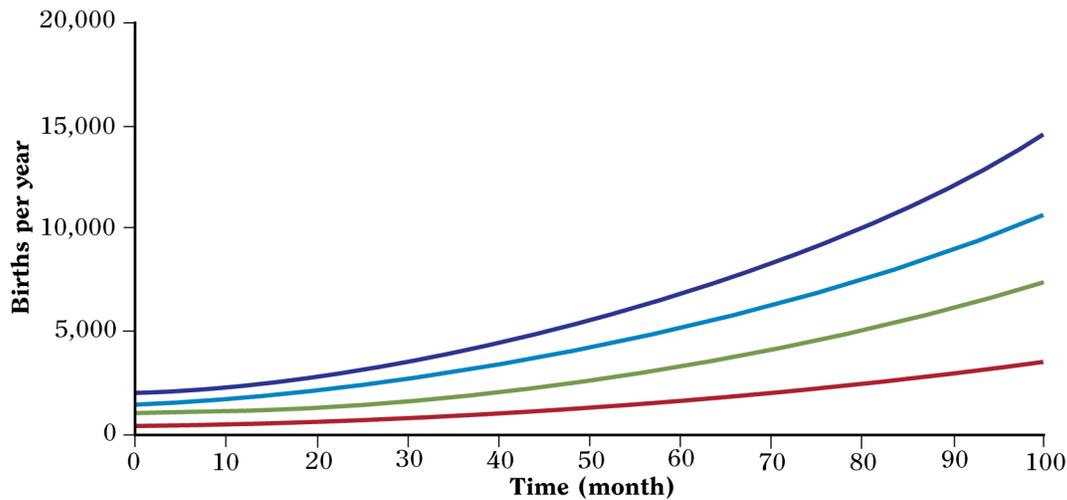
Parameters of models are generally drawn from a variety of sources. In some cases, modelers can use biostatistical techniques to estimate the parameters from the primary data that are available. In other cases, parameters can be taken from secondary sources, such as published estimates, in particular sources in the literature; the results of externally or internally conducted meta-analyses; estimates from other models; findings from surveys findings; or judgments from experts.

Calibration

Despite the ability to perform a sensitivity analysis, direct data may not be available on certain parameters of a model or aspects of a model state. However, data may be available on some (and sometimes many) aspects of system behavior that are proximally or distally related to such parameters. For example, a modeler may seek to build a model that includes representation of the illegal (black) tobacco market, but he or she may not be able to obtain direct data on the diversion of tobacco crops to this market or on the level of consumption of such illegal products. The modeler can then look to historic data on such factors as contraband seizures or results of surveys suggestive of levels of use of illegal tobacco products or that give estimates of overall tobacco use inconsistent with recorded tobacco sales data. Although such types of data do not allow direct estimates of the parameter values of interest, the fact that the observed phenomena are influenced by those parameters often means that they implicitly provide information on, and constraints about, the underlying values of the parameters that shape them.

In such circumstances, a process known as "calibration" can be leveraged to estimate the parameters of a model. This process not only helps with estimating the values of parameters, but it frequently can provide insight on the need to refine the model and can help to identify research priorities. Modelers use the calibration process to adjust the parameters of a model for which few data are available; this allows the output of the resulting model to better match the observed patterns from historical data. In certain cases, this process yields a good fit to the historical data. The derived values of the parameter are not guaranteed to be correct, but they serve as a plausible assignment of values for the parameters—one that is consistent with what has been observed in the system.

A process known as "cross-calibration" can further increase the level of confidence in a model. In this process, the model is first calibrated to only a subset of the known data; the remaining data are set aside for later use. Greater confidence in the model is achieved if it can predict the remaining data, despite not having been calibrated to match that data.

Scenarios

Model Experimentation

In most cases, a baseline scenario is created to serve as a reference case (sometimes referred to as the "status quo scenario"). Output of other (alternative) scenarios can then be compared with this reference scenario. The baseline scenario could depict some default situation but is generally not particularly privileged. Alternative scenarios

are typically run by modifying some element of the model (reflecting the desire to examine the impact of different assumptions or to represent some intervention), simulating that model, and comparing the results of that model to the baseline scenario. Results of interest from the model could include the trajectory of any model variable, such as the accumulated number of tobacco-related deaths or life-years lived, the quality-adjusted life-years lived, or the accumulated costs. For some types of analyses (e.g., cost-effectiveness analysis), either the model itself or the modeler must compute one or more differences of a given alternative scenario from the baseline.

Capturing Intervention Impacts

An important use of system dynamics and compartmental models in tobacco control is to investigate the effects of common interventions (e.g., policies, such as price increases or smokefree laws; cessation treatment policies and programs; program interventions, such as mass media campaigns) that are used alone or in combination with proposed new interventions (e.g., warning labels on tobacco packages, changes in tobacco product toxicity). Interventions can be simulated as model scenarios at different levels of detail. The simplest way of representing model interventions starts by positing that a given intervention will change particular parameters of a model by certain values. This assumption could be based on published sources of data on intervention impacts (e.g., measuring increases in the rates of cessation that result from the availability of quitlines or increases in the excise tax, or measuring decreases in the rates of smoking initiation after exposure to peer education programs), or it could be based on a more theoretical framework that seeks to examine the possible impacts of a broad set of possible intervention effects, without focusing on the exact mechanisms by which such effects are realized. For example, a baseline scenario could represent a business-as-usual (i.e., status quo) case in which observed patterns in changes of tobacco behavior remain similar to what is currently observed. Next, modelers could establish alternative scenarios to examine the impacts of decreasing the rates of smoking initiation in population subgroups by a certain proportional amount (e.g., 10%). Modelers could then compare the effects of each of these scenarios on the outcomes of interest. On the other hand, modelers could systematically examine the impacts of changing the rates of smoking initiation, cessation, and relapse in population subgroups and then examine the impacts of concern (Tengs et al. 2001b).

In other cases, modelers may decide to make a more detailed representation of an intervention. This could be undertaken by adding to the model the additional stocks and flows that are necessary to capture the effect of the intervention over time. For example, a broader simulation model of cessation treatment explored the effects on population smoking prevalence of implementing a comprehensive tobacco control strategy with four components: (1) price increases through cigarette tax increases, (2) smokefree indoor air laws, (3) mass media/educational policies, and (4) boosting evidence-based and promising cessation treatment policies (Levy et al. 2010d). The goal of the model was to examine the relative effectiveness of the four policies and their combined contribution to meeting the *Healthy People 2010* goal of 12% smoking prevalence. In another example, modelers wanted to represent the impact of a school-based antitobacco education program that involved a nationwide, multitiered training effort for teachers and other staff (Tengs et al. 2001a). A program of this sort yields textured dynamics in terms of its health effects (e.g., impacts on rates of smoking initiation) and teacher training. Following the initiation of a program of this sort, the first priority might be to train the program instructors and, as the instructors become available, to initiate training of the classroom teachers. Given this multistage training approach and the time required for training each teacher, many years could go by until large numbers of students are being exposed to the classroom-based program. Figure 15.1.8 shows one way of seeking to extend the model displayed in Figure 15.1.1, so as to capture the dynamics of teacher training and associated factors. Such a model could readily be extended to represent additional factors, such as intervention costs.

Sensitivity Analyses

Modelers perform a sensitivity analysis to examine the impact on model results of making alternative assumptions about a model. Such an analysis is accomplished by reflecting the changed assumptions in the model, and then simulating one or more model scenarios. In most cases, the changed assumptions are reflected in a model by altering the specific values that are associated with the parameters of the model. In some cases, the behavior of a particular variable in the model over time will be highly sensitive to the value of a particular parameter and, in other cases, the behavior of a variable may be insensitive to the value of a parameter. Practitioners of system dynamics models commonly look at (1) how soon these differences appear and (2) the magnitude and direction of the eventual differences. In other cases, representing the changed assumptions in the model may necessitate changes to the structure of the model (e.g., adding new stocks, disaggregating an existing stock into several stocks, eliminating flows, and providing additional pathways for movement from one stock to another).

Figure 15.1.8   Model from Figure 15.1.1, extended to incorporate the structure required to capture intervention dynamics
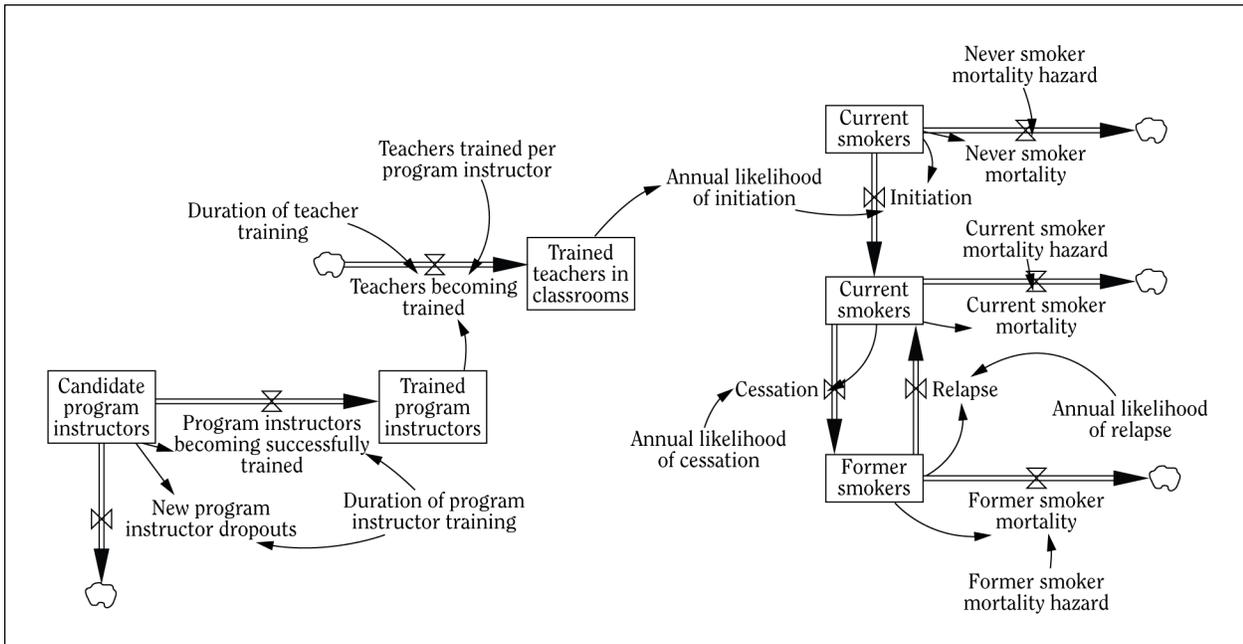
In a process known as "structural sensitivity analysis," modelers can examine the impact of these changes on particular variables over time.

In addition to examining the impact of changing model assumptions on the trajectories of particular model variables over time, modelers can also examine the impact of the changed assumptions on the model's reported trade-offs between interventions. In some cases, changing model assumptions may widen a disparity between the impacts of two interventions that were first recognized by simulating the baseline scenario. In other cases, alternative assumptions may reverse the relative desirability of each intervention, causing an intervention that was viewed as most competitive during the baseline scenario to be eclipsed in desirability by another intervention.

Modelers can also perform a sensitivity analysis to investigate interventions. In this manner, the proximal effects of an intervention are represented by imposing changes on the parameters of a model (e.g., the smoking cessation rate for a certain age group or the assumed impact of peer pressure on rates of smoking initiation for other age groups). In some cases, structural cases may be added to a model. For example, assume that modelers created a model to capture the dynamic impacts of the interaction between human papillomavirus (HPV) infection and tobacco use, but they were further interested in examining the impact of interventions, such as targeting HPV vaccination at smokers. Modelers could then incorporate a smoking vaccinated stock into the model. Such a stock would represent smokers who had received an HPV vaccine to lower their tobacco-induced risk of cervical cancer and risk of transmission. Modelers could run the scenario to examine the impact of these changes on the outputs of the model.

Agent-Based Models

Agent-based models offer a powerful way to model complex social interactions. The individual agents follow plausible adaptive rules for interacting with each other and with the (possibly changing) environment, and can be at any level or multiple levels of aggregation (Hammond 2008). In terms of policy impact, agent-based models are accessible to decision makers because they are rule-based and have highly visual outputs (Mann et al. 2008). Agent-based models are also user-friendly and interactive, which facilitates interdisciplinary model development and allows for less restrictive assumptions about individuals and system-level behavior. The results of an agent-based model are emergent, in the sense that agent-based models can highlight macro-level outcomes or patterns that emerge from micro-level actions and interactions among individuals.

Agent-based models are relatively new techniques that have quickly become useful in public health areas where behavior plays an important role in evaluating health policies, understanding behaviors and behavior changes (Cooley et al. 2008; Epstein et al. 2009), and filling a gap in existing research by integrating possible interacting scenarios in a formal way.

More traditional methods, such as regression and system dynamics models, do not always provide clear answers to questions about tobacco initiation, use, and cessation. Some questions might look at local behavior in a specific environment, group of individuals, or even separate individuals, while others might address the issue of how heterogeneity and local interactions influence collective behavior (Cooley et al. 2008). Other questions may explore self-organization and propagation of ideas and behaviors on networks, such as QuitNet and other social networks, which could change over time. In addition, theoretical questions may allow for the translation of local behavior into a global, self-organizing phenomenon (Epstein et al. 2010).

Luke and Stamatakis (2012) reviewed the potential utility of using network analysis to study tobacco control issues. They proposed that high-level, aggregate models (including system dynamic models) like those described above can be useful in forecasting long-term population trends, but may be less useful due to their aggregate structures at identifying important mechanisms or relational structures that could be very important in producing changes in tobacco use behaviors. Luke and colleagues (2011) further noted that agent-based modeling was only starting to be used to evaluate tobacco control issues. The researchers commented that agent-based models could be very useful in the evaluation of the dynamic impact of changes in tobacco retailer densities due to attrition, increased licensing feeds, or buffer zones around schools.

Implications

Agent-based models can be an important tool for decision makers because such models can uncover details that could be masked by other approaches. Agent-based models can be used to forecast the outcomes of future interventions and to avoid policy resistance before the intervention is implemented. Because agent-based models can incorporate a high level of individual detail, they can consider a broad range of factors, from environmental propensity to genetic propensity to get addicted and be successful in treatment. Despite being relatively new, agent-based models are developing fast, and with the help of novel data collection techniques and advances in computer science, they have the potential to be an effective tool in tobacco control.

Main Challenges and Future Developments

Two critical issues restrain the broader use of agent-based models: (1) the availability of the appropriate data for populating the model and (2) the additional uncertainty associated with the stochastic nature of communication and decision making among the agents.

Data Collection Approaches and Data Use in Agent-Based Models

Epidemiological and policy studies have long depended on survey data that are aimed at providing reliable, representative evidence about an entire population. Surveillance data systems have been used to track incidence and abnormalities at the population level. Recent and still evolving developments of data collection—such as ethnographic studies (Hoffer et al. 2009), ecological momentary assessments (Minami et al. 2011), and dynamic social networks (e.g., QuitNet, Facebook, Framingham Study, cell phone networks)—provide a basis for developing agent-based models (Christakis and Fowler 2008; Cobb et al. 2011).

Another emerging and fast-growing area of data collection comes from virtual social networks, such as Quitnet and Facebook (Cobb and Graham 2012). These networks can potentially provide invaluable data about human interaction, health and behavior, spread of information, innovation, and beliefs (Cobb et al. 2010, 2011). The use of new media (e.g., text messaging) opens avenues to reach younger adults that are otherwise underutilized in existing smoking cessation services (Bock et al. 2004; Boudreaux et al. 2010; Cobb 2010). Finally, virtual communities, such as Second Life, can provide novel vehicles in data collection and interventions that have not been studied sufficiently (Cook et al. 2009; Murphy et al. 2010). At the same time, the concerns of privacy and misuse of personal data impose a significant barrier to quickly implementing modeling techniques that use this data.

Agent-based models can use new technologies through three approaches. The first approach pertains to studies of tobacco-using trajectories that use ecological momentary assessments or ethnographic or other detailed behavior data. Understanding drug-using trajectories can help to identify mechanisms that lead to the initiation and persistent use of particular drugs and to the identification of individuals who are at the greatest risk (Epstein et al. 2007; Hoffer et al. 2009; Bobashev et al. 2010). For example, Bobashev and colleagues (2010) showed that an agent-based model can simulate potential longitudinal trajectories for individuals in a cross-sectional sample, thereby identifying those who are most likely to contract HIV. Similarly, an agent-based model that uses youth

characteristics in a particular school or neighborhood might be able to identify individuals who are most likely to start smoking, which could lead to the development of focused interventions. In the same way, an agent-based model might be used to evaluate potential scenarios for other focused interventions that are aimed at different stages of tobacco use.

The second approach uses network data and extends static network analysis into a dynamic context. For example, several studies have shown that social networks play a critical role in accepting specific behaviors, such as substance use and even obesity (Christakis and Fowler 2007), and in smoking cessation (Christakis and Fowler 2008; Cobb et al. 2011). Data from social networks can be problematic because it is almost always incomplete. In fact, it is sometimes difficult to define what constitutes a network, what kind of relationships should be included as connections, and how different network roles can impact the network structure (Davis and Carley 2008). Agent-based models allow social networks to be simulated based on known samples and the dynamics of connections to be incorporated, and they simulate how positive messages are spread through the networks. The most advanced models of this kind have been developed in the areas of infectious diseases, where the spread of the diseases and preventive public messages have been studied extensively (e.g., Modeling of Infectious Disease Agents Study [MIDAS] models), and national security, where the spread of radical ideas among populations and subgroups have been studied extensively (Carley et al. 2011). Cobb and colleagues (2011) studied data from Quitnet network, Facebook, Framingham Study, and AddHealth to examine the potential development of agent-based models that could guide public health interventions. The role of networks has been shown to amplify some messages (i.e., information passed to one person can influence several people). Other messages tend to die early without being spread among the network community. Agent-based models can allow various scenarios to be studied and could be used to identify key individuals, such as "super-spreaders" or "bridges," for spreading messages (Borgatti and Li 2009; Christakis and Fowler 2007).

The third approach applies agent-based models at the national level, incorporating higher levels of heterogeneity, including spatial (Kirchner et al. 2012). A number of models have been created to project smoking patterns in the future (e.g., SimSmoke, University of Michigan Tobacco Prevalence and Health Effects Model, and Smoking-Attributable Mortality, Morbidity, and Economic Costs [SAMMEC]). These models deal with different levels of granularity, which is appropriate to forecast an increase or decrease in population-level trends. When the goal is complete cessation, however, the modeling can shift its scale to more local areas and subpopulations where the risk of smoking initiation is high and/or the rate of cessation is low. These subpopulations could be localized in terms of specific geographic areas (and be dependent on local antitobacco laws) or represent specific demographics. In addition, tobacco use can be associated strongly with other types of substance use. For example, Bobashev and colleagues (2010) showed that tobacco initiation is associated strongly with alcohol initiation for certain age groups. Such associations could suggest that a joint tobacco–alcohol intervention might have a stronger effect on the initiation of both substances than just one intervention that focuses on tobacco. Thus, increased heterogeneity can be captured by estimating and applying distributions to the population of agents. Estimating these distributions is challenging in multivariate spaces, especially joint distributions.

Agent-based models have an advantage of being able to incorporate multivariate data directly from surveyed subjects. This advantage bypasses the estimation of distributions step, and simulated model outcomes could be related to the multivariate sets of input parameters. To populate detailed spatial agent-based models, synthetic populations can be used, such as those developed at RTI International within the framework of the MIDAS cooperative agreement (Wheaton et al. 2009). The synthetic population is a collection of agents that represent the population of a county, state, and potentially the entire United States. The statistical characteristics of the agents—such as demography, household size, education level, work place environment, and travel pattern—are equivalent to the ones of the real population at the block group or county level; however, the characteristics of each agent are drawn from the corresponding multivariate distribution. Thus, the synthetic population preserves local features of the underlying population but does not violate the privacy of individuals who actually reside in the area. Agent-based models can link behavioral patterns to characteristics of an agent and consider such characteristics as local laws, smoking prevalence, and geographic location.

Finally, agent-based models can be used in data collected in virtual communities, such as Second Life, where surveys and interventions could be conducted (Cook et al. 2009; Murphy et al. 2010). The impact of these data collection methods in virtual worlds has not been studied sufficiently, but they might have an effect because real people are responding behind virtual characters.

Examples of Simulation Models Used in Tobacco Control

Table 15.1.1 summarizes the main types of simulation models used in tobacco control research. This section expands on a subset of aggregate and agent-based simulation models that has been used for tobacco control. The selection of these examples is not based upon an extensive or systematic review of the scientific literature. The selection is based upon background work done by NIH Office of Behavioral and Social Sciences Research (OBSSR) in preparation for a January 2013 meeting (Tobacco Policy Modeling Workshop, January 17-18, 2013) to identify the best available examples of existing aggregate and agent-based simulation models. In this selection of tobacco policy models, the NIH OBSSR built upon its experience in setting up Envision, a network of computational modeling teams focused on policy interventions to combat obesity.

Examples of Aggregate (Compartmental) Simulation Models

Aggregate simulation models have been developed using a compartmental or a system dynamics approach. These models have been developed specifically to estimate the likely path of future smoking rates or to evaluate the impact of tobacco policies. This section briefly describes several of these models: SimSmoke; University of Michigan Tobacco Prevalence and Health Effects Model; Tobacco Policy Model (TPM); Benefits of Smoking Cessation Outcome (BENESCO) model; and Smoking-Attributable Morbidity, Mortality, and Economic Costs (SAMMEC) model. This section also describes the Cancer Strategy Analysis and Validation Effect (CANSAVE) model, which was developed to describe the natural history of cancer, not specifically tobacco-related cancer, and has been used to simulate the impact of smoking cessation strategies.

SimSmoke

SimSmoke is a tobacco control policy model that assesses the impact of tobacco policies on future smoking prevalence and smoking-attributable mortality. Originally developed for the overall United States, the model has been extended to individual states and to several other countries. The population in the model is dynamic, changing through births, deaths, and migration following a discrete, first-order Markov process.

As depicted in Figure 15.1.9 (Levy 2008), SimSmoke categorizes the population into never smokers, ever smokers, ex-smokers, and current smokers. The proportion of the population in each of these categories changes over time because of tobacco initiation, cessation and relapse, and births and deaths.

Figure 15.1.9 Example of the SimSmoke simulation model
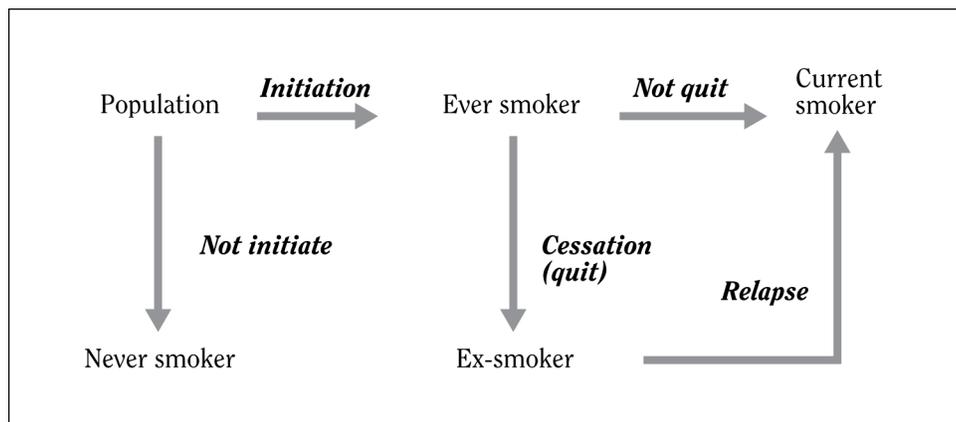
Source: Levy 2008.

Data for use in SimSmoke are taken from the Tobacco Use Supplement of the Current Population Survey, Teenage Attitudes and Practices Survey, Community Intervention Trial for Smoking Cessation (from the NCI), U.S. Census, the American Cancer Society's Cancer Prevention Study (CPS) II, and state- and country-specific data where appropriate. Policies are added to the model through modules that have been developed for different types of tobacco control policies. Figure 15.1.10 (Levy 2008) presents the basic approach to policy analysis embedded in SimSmoke.

SimSmoke includes separate modules for tobacco taxes and price increases, indoor air laws, mass media and educational campaigns, youth access laws, and cessation strategies. Policies can be evaluated independently or in combination. SimSmoke has been validated against historical data (Figure 15.1.11). The model has been used to assess the impact of tobacco control policies on rates of smoking and related deaths for the United States and to examine the attainability of smoking-related goals set forth by *Healthy People 2010* (Levy et al. 2010d).

For example, simulation models for smoking among adults, 18 years of age and older, have examined the impact of boosting tobacco control policies (taxes, indoor air), mass media, and the components of cessation interventions and their delivery systems, based on a review and quantification of the available scientific evidence that provided estimates of the degree to which each component of policy and cessation programs would contribute to reducing prevalence at the population level (Abrams et al. 2010). This review of the evidence base served as the starting point for parameter estimates and transitional probabilities.

A series of simulations suggested that boosting quit attempts, treatment use, and treatment effectiveness by 100% above 2008 base levels (e.g., annual quit rate among counseled smokers who make a quit attempt without using any evidence-based treatment assistance estimated to be 8%) would lead to moderate-to-dramatic reductions in prevalence by as early as 2020, to levels between 6.3% and 11.5% (Levy et al. 2010a,b). Building on the model of cessation treatments (Levy et al. 2010b), a broader simulation model was used to explore the effects on population smoking prevalence of implementing a comprehensive tobacco control strategy with four components: (1) price increases through cigarette tax increases, (2) smoke-free indoor air laws, (3) mass media/educational policies, and (4) evidence-based and promising cessation treatment policies (Levy et al. 2010d). The goal of the model was to examine the relative effectiveness of the four policies and their combined contribution to meeting the *Healthy People 2010* goal of 12% smoking prevalence (Figure 15.1.12).

The study showed that implementing all four policies at the same time would increase the population quit rate by 296% to meet the *Healthy People 2010* goal by 2013 (Levy et al. 2010c). Even with these aggressive efforts over a short period, however, the 40% reduction

Figure 15.1.10   SimSmoke's basic approach to policy analysis
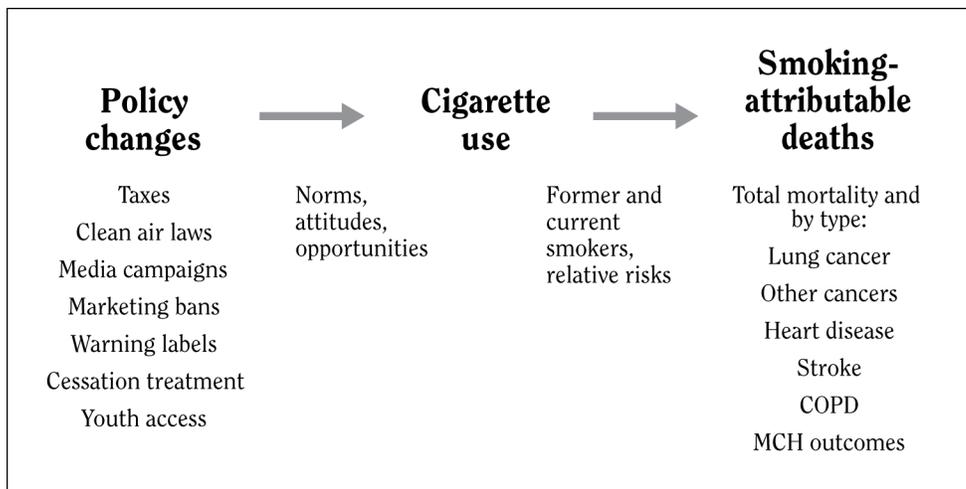
Source: Levy 2008.
Note: **MCH** = maternal and child health.

Figure 15.1.11 Validation of SimSmoke against historical data
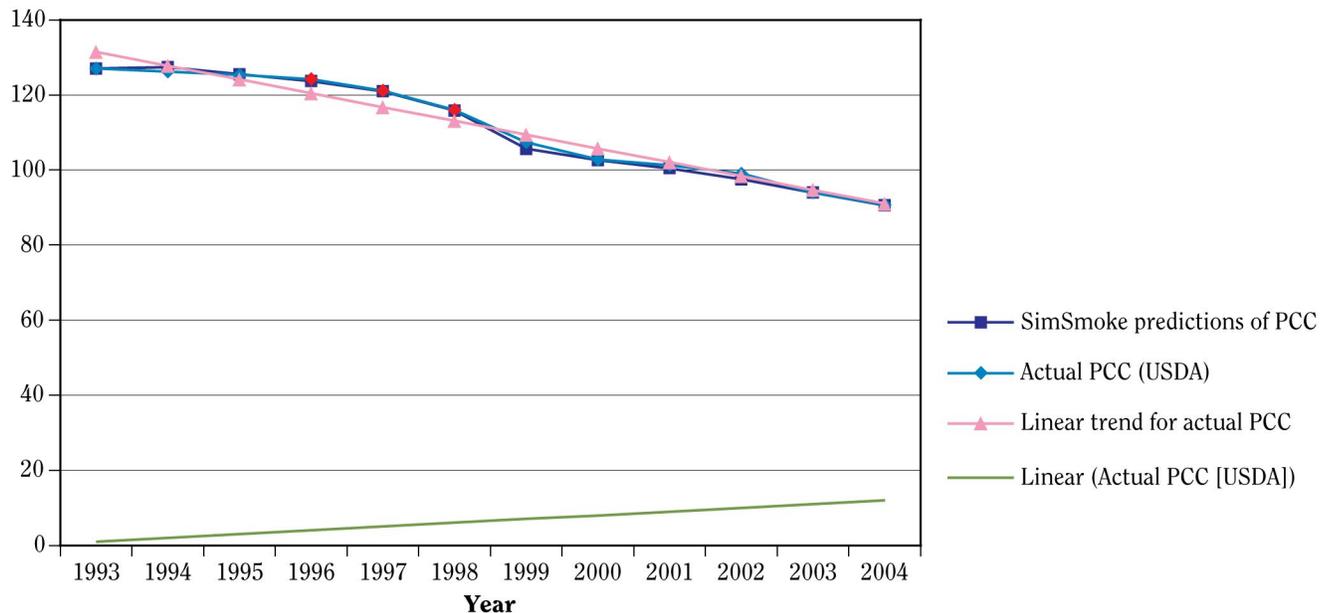
Note: **PCC** = per capita consumption; **USDA** = U.S. Department of Agriculture.

in national smoking prevalence moves the needle from 20.1% in 2008 to the estimated 12% in 2013 and does not end the tobacco epidemic.

The set of simulation models also illustrates the potential population impact of "systems integration" of intervention and policy elements, as recommended in Appendix A of Bonnie and colleagues (2007) and in the U.S. Department of Health and Human Services (USDHHS) strategic plan (USDHHS 2010). The HHS strategic plan stated that based on the above set of simulation models by Levy and colleagues, "The most current and authoritative model of the effect of comprehensive tobacco control measures concludes that, with all of these interventions implemented simultaneously, the Healthy People objective of reducing the adult smoking rate to 12% can be reached by 2020" (USDHHS 2010, p. 19).

In another and completely independent model, Mendez and Warner (2008) examined what the national prevalence rate would be if the comprehensive California intervention was extrapolated to the entire nation (Figure 15.1.13). Their model included the impact of both youth prevention programs, policy and taxation, and other elements in the comprehensive approach taken in California. They also used evidence-based parameter estimates and transition probabilities based on actual historical trends in California. These two very different models both suggest that under more ideal conditions the status quo prevalence rate of about 17% by 2020 could be dropped to about 13–14% with comprehensive policy approaches.

These models provide excellent examples of gap analysis between the status quo and what may be done if what is known is put into practice and policy under ideal conditions.

Simulations have also been conducted to determine the impact of policies directed at youth access on smoking prevalence, smoking-related mortality, and smoking levels. The use of SimSmoke has been extended to other countries, including Argentina (Ferrante et al. 2007), Vietnam (Levy et al. 2006), Korea (Levy et al. 2010a), Thailand (Levy et al. 2008), and Taiwan (Levy et al. 2005c). Levy and Friend (2002a,b) used SimSmoke to examine the effects of mandating access to tobacco cessation treatment through financial coverage. SimSmoke has also been used to examine the impact of various quit attempts, treatment use, and treatment effectiveness scenarios on the prevalence of smoking (Levy et al. 2010c). Although the original SimSmoke model was designed to be prospective in its simulations, it has also been used to evaluate past trends in smoking and the role that various tobacco policies might have played in determining observed smoking rates (Levy et al. 2005a).

Figure 15.1.12 Effects of a 100% reduction in the quit attempt rate, treatment use, and treatment effectiveness on smoking prevalence, 2008–2020
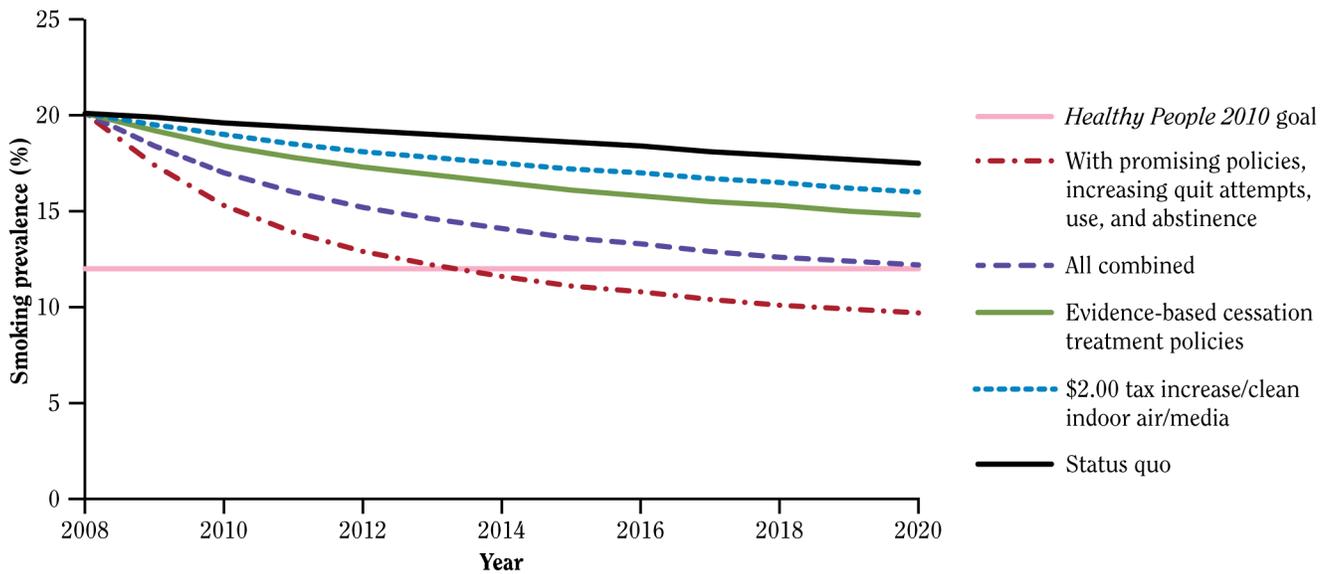
Source: Levy et al. 2010c.

Figure 15.1.13 Project of U.S. adult smoking prevalence rates under status quo scenario and California rate scenarios, 2005–2020
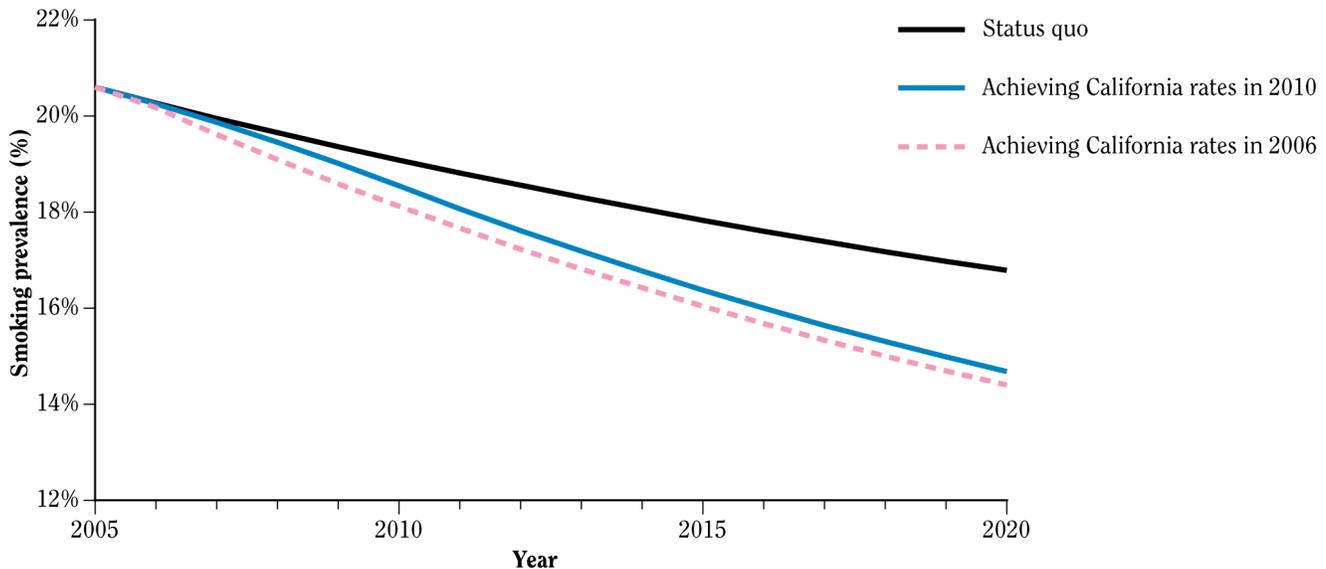
Source: Adapted from Mendez and Warner 2008 with permission of The Sheridan Press, © 2008.
Note: The bottom two lines depict corresponding scenarios assuming that the United States as a whole achieves California's 2005 rates (20% initiation rate and 3.33% cessation rate). The dotted line reflects the assumption that such rates are attained instantaneously (in 2006), whereas the solid line reflects the more plausible scenario that such rates will be achieved gradually (by 2020). The status quo initiation rate is 25%, and the cessation rate is 2.59%

University of Michigan Tobacco Prevalence and Health Effects Model

Mendez and colleagues (1998) initially developed a dynamic simulation compartmental model to forecast future smoking prevalence and differential mortality by smoking status (Figure 15.1.14). The model was later expanded to evaluate tobacco control policies. In this model, the prevalence of smoking is computed over time by tracking the inflow of new smokers and the outflow of smokers, the latter being the result of death or smoking cessation as the population ages. Sizes of birth cohorts, rates of initiation, and rates of age-specific deaths are input into the model using data from the National Health Interview Survey and the U.S. Statistical Abstracts.

The model uses historical data to estimate parameters of rates of smoking cessation. The model assumes that there is no initiation of smoking after 18 years of age, and it ignores migration. Given an initial date and a time horizon for the analysis, for each subsequent year and for each year of age (0–110), the model tracks the population of current, former, and never smokers. The model allows for a comparison of the impact of different policies (through different rates of smoking initiation and cessation) on future smoking prevalence and mortality by using different mortality rates for current, former, and never smokers. The model uses data from the CPS II to estimate relative risks for current and former smokers. The model tracks former smokers by age and number of years since quitting (0–30).

Mendez and Warner (2004) and Warner and Mendez (2012) validated the model by comparing prevalence predictions (Mendez et al. 1998) to the observed prevalence of smoking, concluding that the observed rates closely fit the model's projections. Figure 15.1.15 compares observed and predicted values for smoking prevalence among U.S. adults. The model has been used for diverse purposes. Mendez and Warner (2000) used the model to argue that the smoking prevalence goal (12%) set forth in *Healthy People 2010* was not feasible in the given time frame. Warner and colleagues (2004) used the model to evaluate the cost-effectiveness of smoking cessation programs in managed care organizations. Mendez and Warner (2008) employed the model to recommend targets for the prevalence of smoking for *Healthy People 2020*. Based on global data from the World Health Organization's Infobase database, Mendez and colleagues (2013) calibrated the model to evaluate the impact of smoking control policies on global trends in smoking. Figure 15.1.16 shows

Figure 15.1.14 Basic structure of the University of Michigan Tobacco Prevalence and Health Effects Model
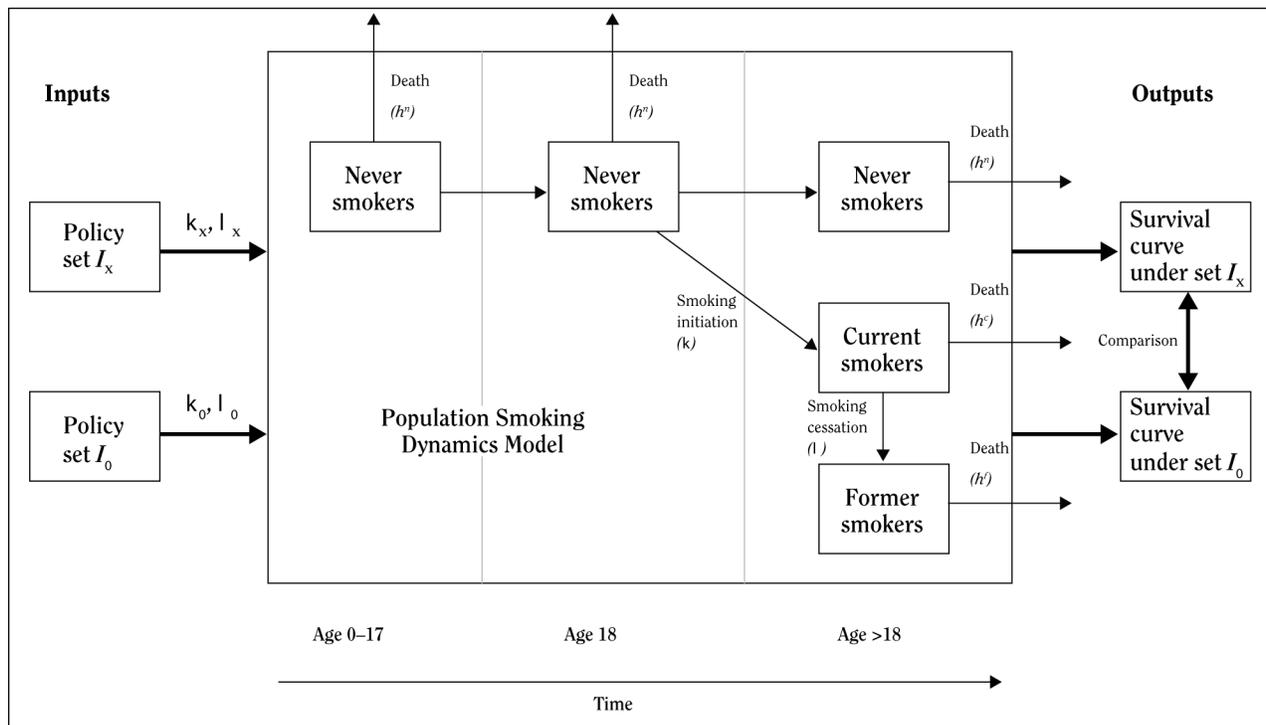
Figure 15.1.15 Comparison between observed and predicted values of the prevalence of smoking among U.S. adults, University of Michigan Tobacco Prevalence and Health Effects Model
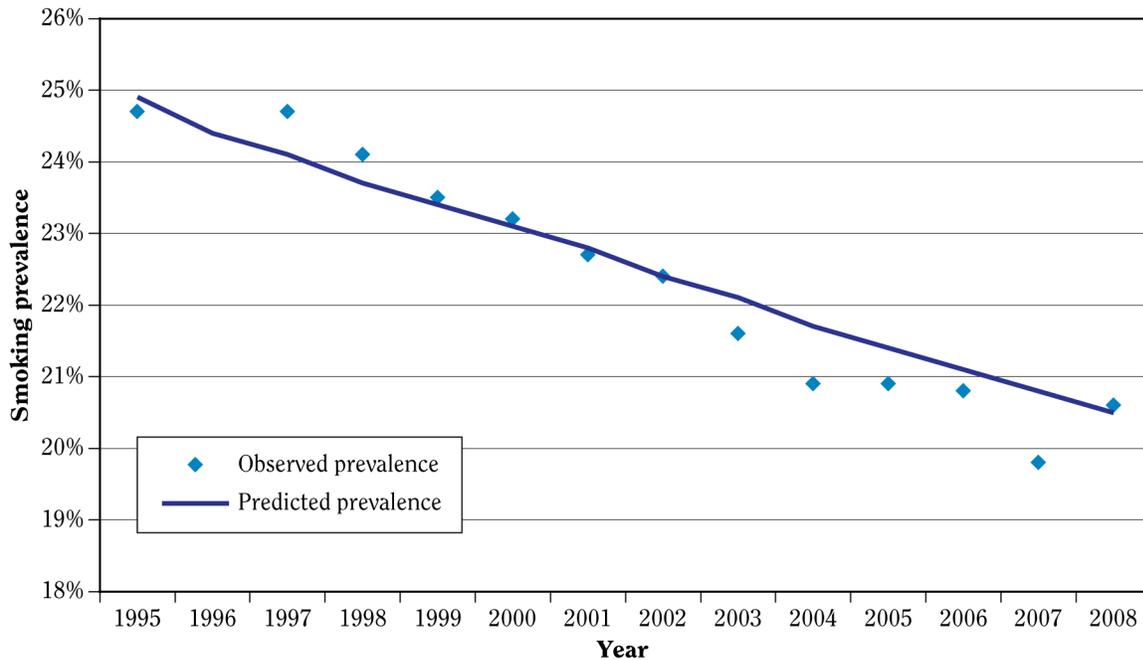
Source: Warner and Mendez 2010. Reprinted with permission from Oxford University Press, © 2010.

predictions from the model that consider different scenarios of rates of smoking initiation and cessation for U.S. adults.

Additional details on the Mendez and Warner model specifications are provided in Appendix K of Bonnie and colleagues (2007). Status quo initiation rates were set at 25%, which is consistent with the observed prevalence within the 18- to 24-year-old group. The status quo for cessation rates was based on previous estimates (Mendez et al. 1998): 0.21% (18–30 years of age), 2.15% (31–50 years of age), and 5.97% (51 years of age and older). Initiation and cessation rates for California and Kentucky were based on data from 2000 to 2003 from the Behavioral Risk Factor Surveillance System.

Tobacco Policy Model

TPM is a computer simulation model that was developed to calculate the public health gains or losses associated with changes in the prevalence of smoking and the pattern of cigarette use (Tengs et al. 2001b). In the model, the population is divided into age and gender cohorts and by smoking status (current, former, and never smokers). The model incorporates population transitions—such as births, deaths, aging, net migration and changes in smoking status in the form of smoking initiation, cessation, and relapse. Transition probabilities vary by age, gender, smoking status, and year. Outcomes are typically measured in quality-adjusted life years.

Population data are extracted from several sources: U.S. Bureau of the Census; Behavioral Risk Factor Surveillance Survey; National School-Based Youth Risk Behavior Survey; National Health Interview Survey, Health Promotion and Disease Prevention Supplement; National Health and Nutrition Examination Survey; Current Populations Survey's Tobacco Use Supplement; and the Teenage Attitude and Practice Survey. The model incorporates health-related quality of life derived from the Quality of Well Being Scale.

Simulations using the TPM have evaluated the impact of specific tobacco-control policies—such as reduced nicotine content in cigarettes on health (Tengs et al. 2004, 2005), the impact of a school-based antitobacco education program on population health (Tengs et al. 2001b), and the effect of increasing taxes on the use of cigarettes (Ahmad 2005a,b,c; Ahmad and Franz 2008). Using TPM in cost-effectiveness analyses, several studies have examined youth access policies (Ahmad 2005a,b,c; Ahmad and Billimek 2007). Tengs and colleagues (2001b)

Figure 15.1.16 Predicted rates of smoking initiation and cessation for U.S. adults, University of Michigan Tobacco Prevalence and Health Effects Model
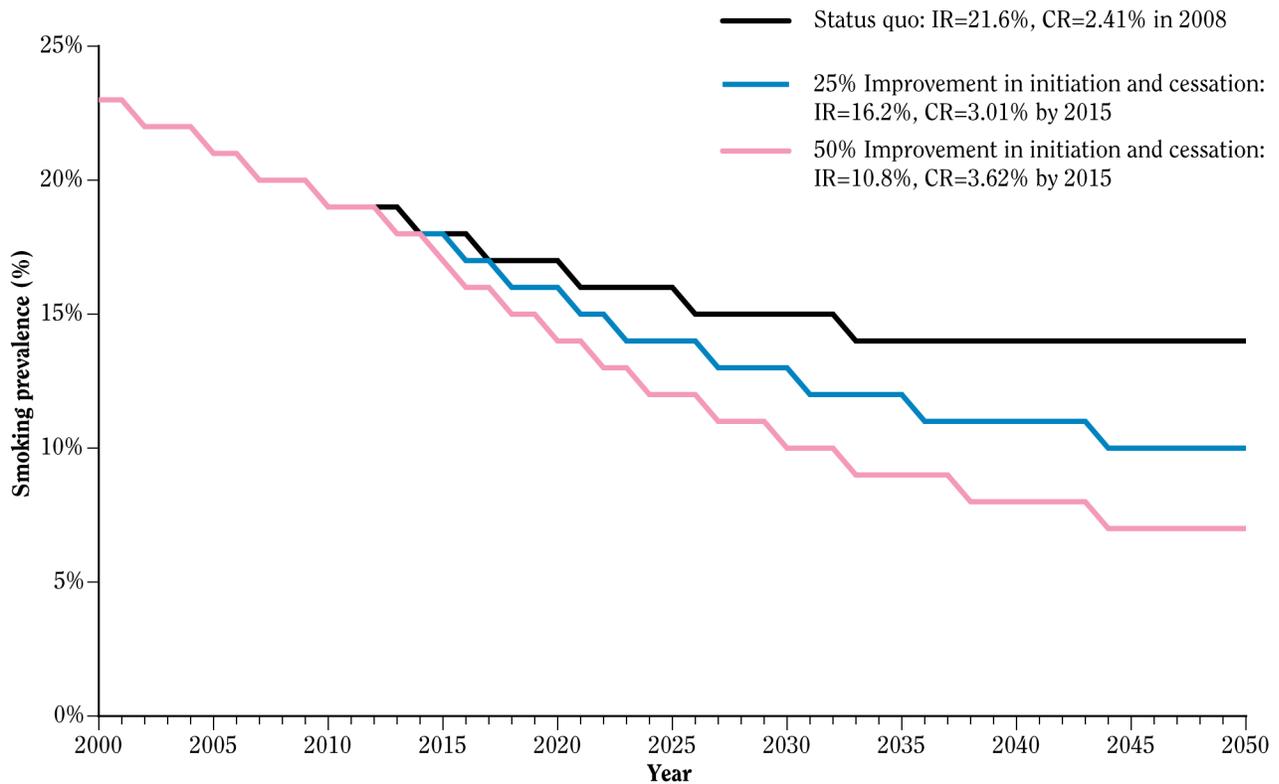
Source: Warner and Mendez 2010. Reprinted with permission from Oxford University Press, © 2010.
Note: **CR** = cessation rate; **IR** = initiation rate.

assessed the impact of varying levels of reduced rates of smoking initiation, increased rates of smoking cessation, and reduced rates of smoking relapse on health gains among U.S. adults.

Benefits of Smoking Cessation Outcome

BENESCO is a simulation model designed to predict smoking-related morbidity and mortality, and it calculates the cost-effectiveness of smoking cessation interventions (Orme et al. 2001). Individuals are classified into different compartments or states as smokers, recent quitters, and long-term quitters. Nonsmokers are not included in the model. Transition probabilities between states are determined by smoking status and morbidity status from the previous year. Figure 15.1.17 depicts the BENESCO model (Orme et al. 2001).

Annemans and colleagues (2009) used the BENESCO model to determine the cost-effectiveness of various cessation interventions in Belgium. Bolin and colleagues used the model to evaluate the cost-utility

of cessation interventions in Sweden (Bolin et al. 2008, 2009). Howard and colleagues (2008) conducted a simulation using BENESCO of a hypothetical cohort of U.S. adult smokers to determine the cost-utility associated with smoking cessation strategies. Knight and colleagues (2010) used BENESCO to estimate the cost-effectiveness of extended smoking cessation treatment compared with other strategies.

Smoking-Attributable Morbidity, Mortality, and Economic Costs

SAMMEC (see Chapter 12 for a comprehensive discussion) is designed to estimate the overall disease impact of smoking on adults 35 years of age and older and the health expenditures of adults 18 years of age and older. SAMMEC estimates health and health-related economic impacts of smoking, including smoking-attributable deaths, years of potential life lost, costs of health care, and productivity losses. SAMMEC divides the population into stocks of smokers and nonsmokers and applies an

Figure 15.1.17 Effect of cessation aid on smoking habit, Benefits of Smoking Cessation Outcome (BENESCO)
model
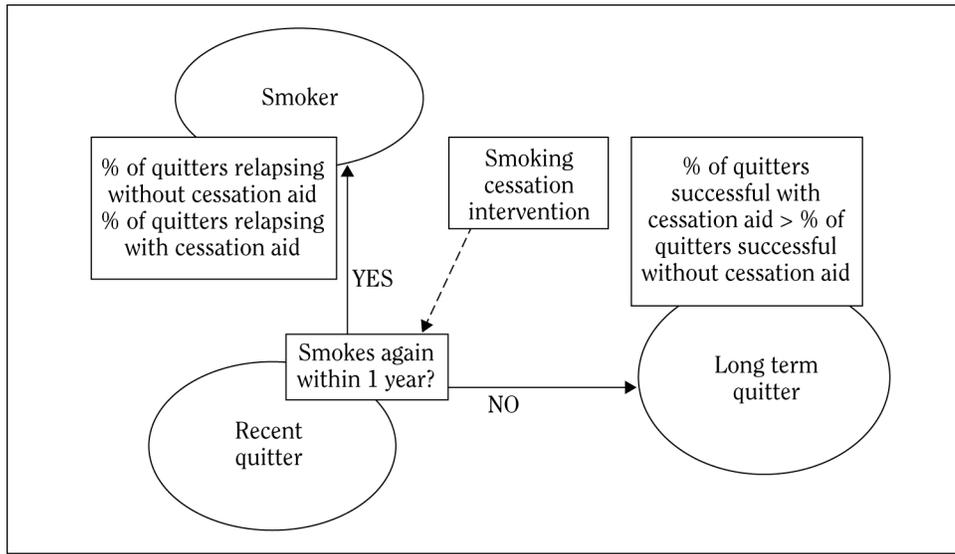
Source: Orme et al. 2001. Reprinted with permission from BMJ Publishing Group, Ltd., © 2001.

attributable-fraction formula—the proportion of cases of a disease or death that can be linked to cigarette smoking (Shultz et al. 1991). Emery and colleagues (2001) used SAMMEC to evaluate the impact of tobacco tax on the health of Latinos in California. The study estimated the elasticity of cigarette prices among smokers and the effects of a range of increases in cigarette taxes. Kaplan and colleagues (2001) estimated the impact of tax increases of $0.50 and $1.00 on the prevalence of smoking, population mortality and morbidity, and quality-adjusted life years of the population of California.

Cancer Strategy Analysis and Validation Effect

CANSAVE is a compartmental Markov model that is used for describing the natural history of cancer. Transition probabilities are estimated from preclinical to clinical, clinical to recovery, and clinical to death. Rates of lung cancer are calculated as a function of age and the effective years of smoking for smokers and as a function of age for nonsmokers. Effects are generated for current smokers, former smokers, and never smokers separately and then added to obtain the total number of lung cancer deaths by age and year. Yamaguchi and colleagues (1991, 1992, 1994) used CANSAVE to assess the impact of antismoking measures and screening in Japan. Figure 15.1.18 shows the main constructs of CANSAVE (Yamaguchi et al. 1994).

Cancer Intervention and Surveillance Modeling Network (CISNET)

CISNET (http://cisnet.cancer.gov) is a consortium of investigators funded by NCI that uses mathematical modeling to study the impact of cancer control interventions (e.g., prevention, screening, and treatment) on population trends in cancer incidence and mortality for several sites, including lung (Feuer et al. 2012). Five academic groups were funded under the NCI CISNET mechanism—Fred Hutchinson Cancer Research Center, Erasmus Medical Center, Pacific Institute for Research and Evaluation, Rice University/MD Anderson Cancer Center, Yale University—and one affiliated group at Massachusetts General Hospital. The consortium of investigators have met semiannually to compare their individual modeling approaches and to examine differences in a systematic fashion. The six CISNET microsimulation lung cancer models were developed independently to model the natural history of lung cancer (McMahon et al. 2012). As part of the research consortium, a set of common population inputs were adopted and a common set of outcomes were then selected (Figure 15.1.19).

As shown in Figure 15.1.19, each model used common shared components along with model-specific components to investigate the contribution of tobacco control efforts in the United States since 1964 on reducing lung

Figure 15.1.18 Main constructs of the Cancer Strategy Analysis and Validation Effect (CANSAVE) model, a Markovian stochastic model of the natural history of lung cancer
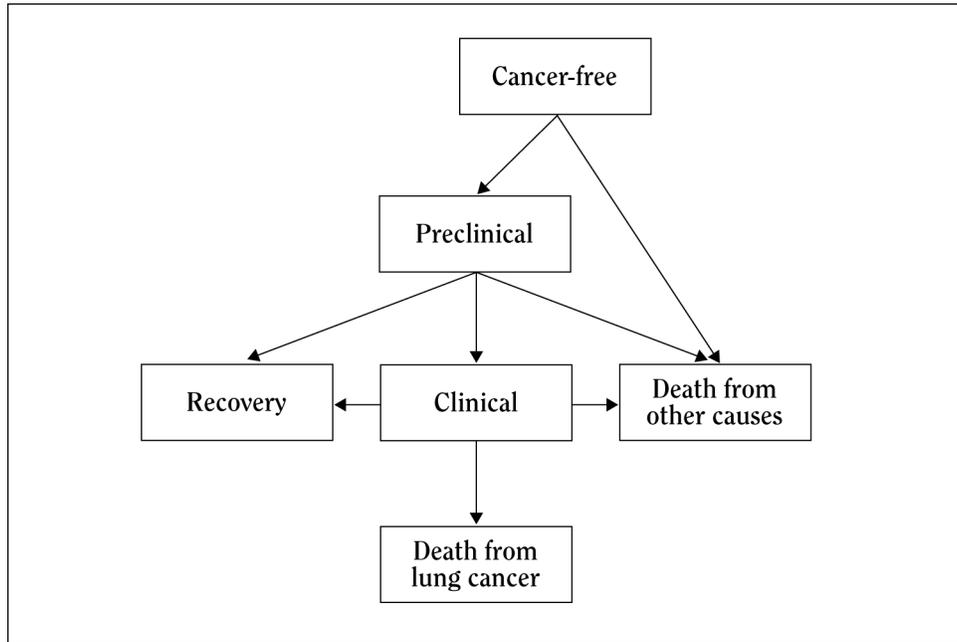
Source: Yamaguchi et al. 1994. Reprinted with permission from Environmental Health Perspectives.

Figure 15.1.19 Schematic of CISNET lung models, illustrating key events in a life history
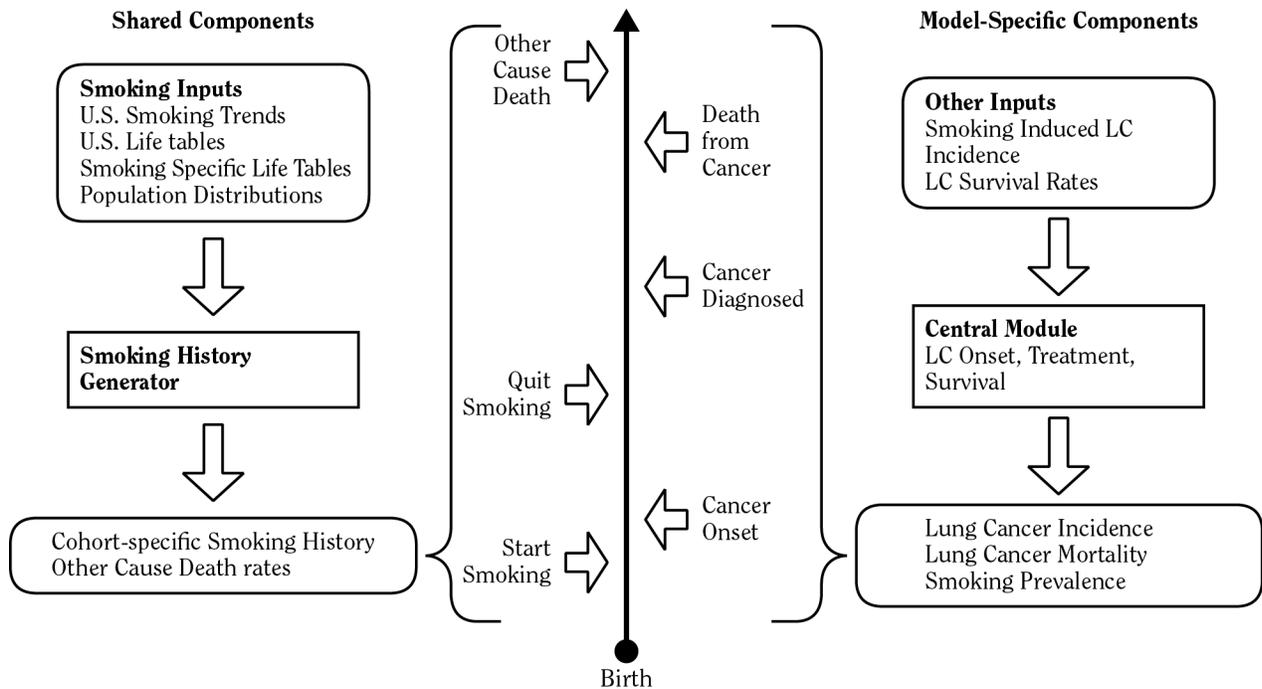
Source: McMahon et al. 2012. Reprinted with permission from John Wiley and Sons, © 2012.
Note: Key events in a life history, from birth to death, are indicated by the arrow (middle). Smoking histories and other-cause death rates are shared components (left side). Cancer events are predicted by each of the six models (right side). **LC** = lung cancer.

cancer deaths from 1975–2000. A key component of the inputs was three scenarios of the smoking histories of birth cohorts in the United States. An updated version of the output of the Smoking History Generator for the "actual" case scenario is shown in Figures 13.9 and 13.15 in Chapter 13 (Holford et al. in press). Descriptions of the Smoking History Generator methods are provided in Chapter 13 and in recent publications (Anderson et al. 2012; Holford and Clark 2012; Jeon et al. 2012; Rosenberg et al. 2012). Based on assumptions about tobacco control (i.e., no tobacco control since 1955 vs. all smoking ceased following the publication of the 1964 Surgeon General's report), the worst-case and best-case scenarios were generated. The smoking histories in birth cohorts included detailed data about smoking behaviors, such as smoking intensity and duration, and among ex-smokers, duration of quitting.

Table 15.1.2 shows the main differences and similarities across the six CISNET models. All models had the capacity to vary inputs from the Smoking History Generator, as well as estimates of disease risks. However, the six models also had significant differences in which aspects of the cancer control spectrum received emphasis (e.g., screening, tobacco control policies, variations in mortality risk) and how the biological relationship between smoking and lung cancer was included—for example, several models used the same two-stage clonal expansion stochastic model but calibrated the parameter estimates to different cohorts and end-points.

Moolgavkar and colleagues (2012) reported the collective results from the six models, evaluating the impact of the three scenarios of smoking histories since 1955 (i.e., actual-case, worst-case, best-case) on U.S. lung cancer deaths during the interval of 1975–2000. Compared to the worst-case scenario (no tobacco control since 1955) versus the actual case (declines in rates of smoking initiation and smoking intensity and increases in smoking cessation), approximately 795,851 lung cancer deaths were averted from 1975–2000 in the United States: 552,574 among men and 243,277 among women. However, the models estimated that this was only about 38% of the deaths that could have been averted between 1991–2000 compared to the scenario that all smoking ceased following the release of the 1964 Surgeon General's report. From 1975–2000, the models estimated that approximately 2,504,042 lung cancer deaths could have been averted if tobacco control efforts following the release of the 1964 Surgeon General's report were completely effective in eliminating smoking behavior as of 1965 (Figure 15.1.20).

As would be expected, the six models yielded a range of results. In comparing the actual- and worst-case sce-

narios, the high estimate for lung cancer deaths averted was 658,529 for men and the low estimate was 454,517. For women, the range of estimates was 333,976 and 201,788. McMahon and colleagues (2012) analyzed the factors related to this variation in estimates, and Holford and Levy (2012) evaluated the adequacy of the carcinogenesis models in estimating populations trends in lung cancer mortality in the United States. These more detailed analyses of the performance of individual models provide important insights for similar models that are being developed and applied.

The models used for the analysis by Moolgavkar and colleagues (2012) were expanded to consider all deaths rather than just lung cancer deaths, and the time period considered was lengthened from 1975–2000 in the earlier models to 1964–2012 (Holdford et al. 2014). In this expanded data set the relationship between tobacco control since 1964 and the number of early deaths avoided, life-years saved, and life expectancy gained in the United States were estimated. Similar to the earlier model, smoking histories prior to 1964 were used to estimate likely future patterns of smoking in the absence of tobacco control with these estimated patterns serving as the counterfactual scenarios in the models. In the counterfactual scenarios, an upper bound and lower bound were estimated. For men, the upper bound was set at 80% smoking prevalence at 30 years of age, based upon the observed history of the 1920 birth cohort of men. The actual prevalence of smoking among men in 1964 was set as the primary counterfactual smoking prevalence, and a decline to 60% in birth cohorts at 30 years of age was defined as the lower bound. For women, the upper bound counterfactual assumed that smoking prevalence rates in birth cohorts would continue to rise up to 70% at 30 years of age, 10% below the maximum for men. A more conservative increase up to 60% prevalence at 30 years of age was defined as the primary counterfactual, and a decline to 50% peak prevalence in birth cohort at 30 years of age was defined as the lower bound for women.

For estimating all-cause mortality rates by birth cohorts, the methodology developed by Rosenberg and colleagues (2012) was used to develop cohort life tables by smoking status. Using these life tables, the differences between mortality rates for both current or former smokers and never smokers were used to estimate avoidable increases in death rates related to exposure to cigarette smoking. These differences were calculated by single year, calendar year, smoking status, and gender, and then summed over the appropriate age range for each calendar year (1964–2012) yielding total premature deaths.

Table 15.1.2 Key differences and similarities across models

Abbreviation	E	F	M	P	R	Y
Institution	Erasmus MC	FHCRC	MGH-HMS	PIRE	Rice–M.D. Anderson	Yale
Model name	MISCAN lung	TSCE	Lung Cancer Policy Model	SBC Model	Rice Lung Cancer Model	Yale Lung Model
Original purpose[a]	Screening evaluation	Analysis of epidemiological data	Screening evaluation	Policy evaluation	Mortality risk due to smoking	Population trends and lung cancer
Unit of analysis/smoking histories	Microsimulation/ Individual	Microsimulation/ Individual	Microsimulation/ Individual	Macro-level/Group	Microsimulation/ Individual	Macro-level/Group
Simulation of populations or trials/cohorts	Both	Both	Both	Populations	Both	Populations
Central dose response model[a]	TSCE	TSCE	Probabilistic/logistic regressions	TSCE	TSCE	TSCE
Parameter source(s)[b]	NHS (F incidence), HPFS (M incidence), SEER (survival)	NHS (F mortality), HPFS (M mortality)	SEER (incidence, stage, size, type, survival)	CPS II (mortality)	MDA CCS (smoking histories), NHS (F mortality), CPS II (M mortality)	NHS (F mortality), HPFS (M mortality)
Natural history model features						
Histologic cell types	3 (SQ, AD + LC, SC)	No	5 (SQ, AD, LC, SC, OT)	No	No	No
Modeling of metastases	Implicit	Implicit	Explicit	Implicit	Implicit	Implicit
Tumor growth	No	NA	Gompertz	NA	NA	NA
Calibration of U.S. lung cancer mortality trends	NA	PC	PC	P[c]	NA	APC
Scope of cancer controls[a]						
Prevention	Yes	Yes	Yes	Yes	Yes	Yes
Screening	Yes	No	Yes	No	No	No
Treatment	Yes	No	Yes	No	No	No

Source: McMahon et al. 2012. Reprinted with permission from John Wiley and Sons, © 2012.

Notes: Additional details about how parameters were estimated, profiles of the models, and supporting references for the models are available at http://www.cancer.cisnet.gov/profiles and McMahon and colleagues (2012). **AD** = adenocarcinoma; **APC** = age, period, and cohort terms; **CPS** = Cancer Prevention Study; **FHCRC** = Fred Hutchinson Cancer Research Center; **HPFS (M)** = Health Professionals Follow-up Study (Males); **LC** = large cell carcinoma; **MC** = Medical Center; **MDA CCS** = M.D. Anderson case control study; **MGH-HMS** = Massachusetts General Hospital-Harvard Medical School; **MISCAN** = Microsimulation Screening Analysis; **NA** = not applicable; **NHS (F)** = Nurses' Health Study (Females); **N/SCLC** = nonsmall cell and small cell lung cancer; **OT** = other cell types; **P** =period terms only; **PC** = period and cohort terms; **PIRE** = Pacific Institute for Research and Evaluation; **SC** = small cell carcinoma; **SEER** = Surveillance, Epidemiology, and End Results; **SQ** = squamous cell carcinoma; **TSCE** = two-stage clonal expansion.

[a]Descriptions refer to model versions used for analyses by McMahon and colleagues (2012)and do not reflect earlier published versions or subsequent extensions of individual models.

[b]See McMahon and colleagues (2012) for details on how sources were used (as inputs or as calibration targets).

[c]See McMahon and colleagues (2012) for description of regression model.

Figure 15.1.20 Lung cancer death rates and counts for men and women, 30–84 years of age, as observed and modeled for tobacco control scenarios, 1975–2000

A. Death rates, men
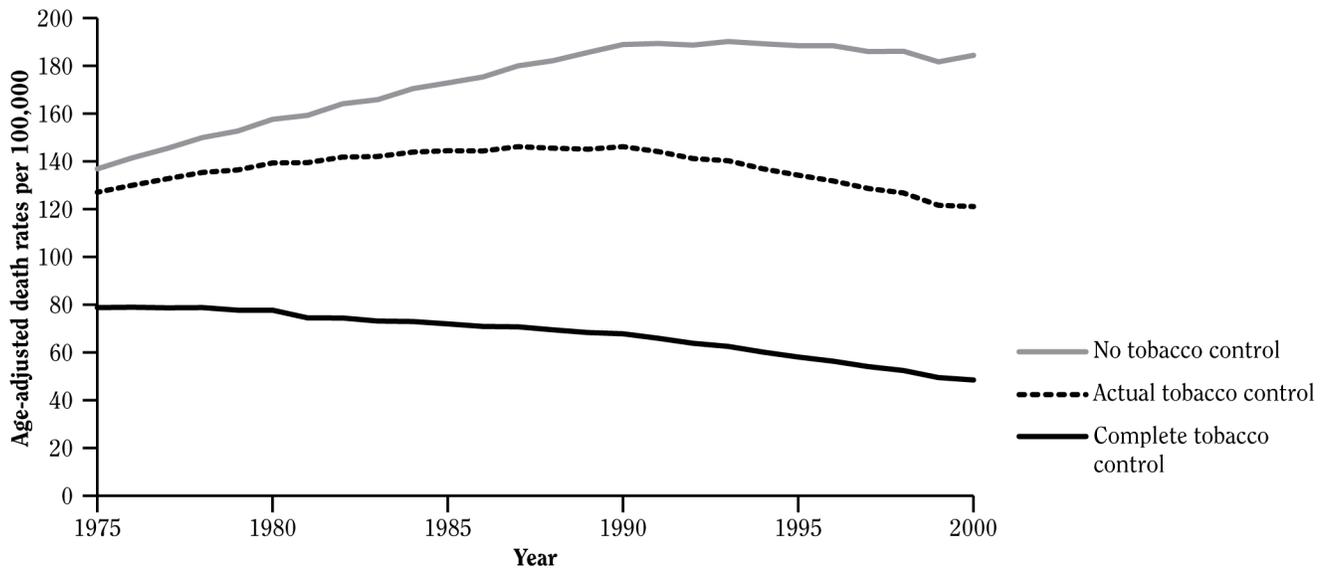
B. Death counts, men
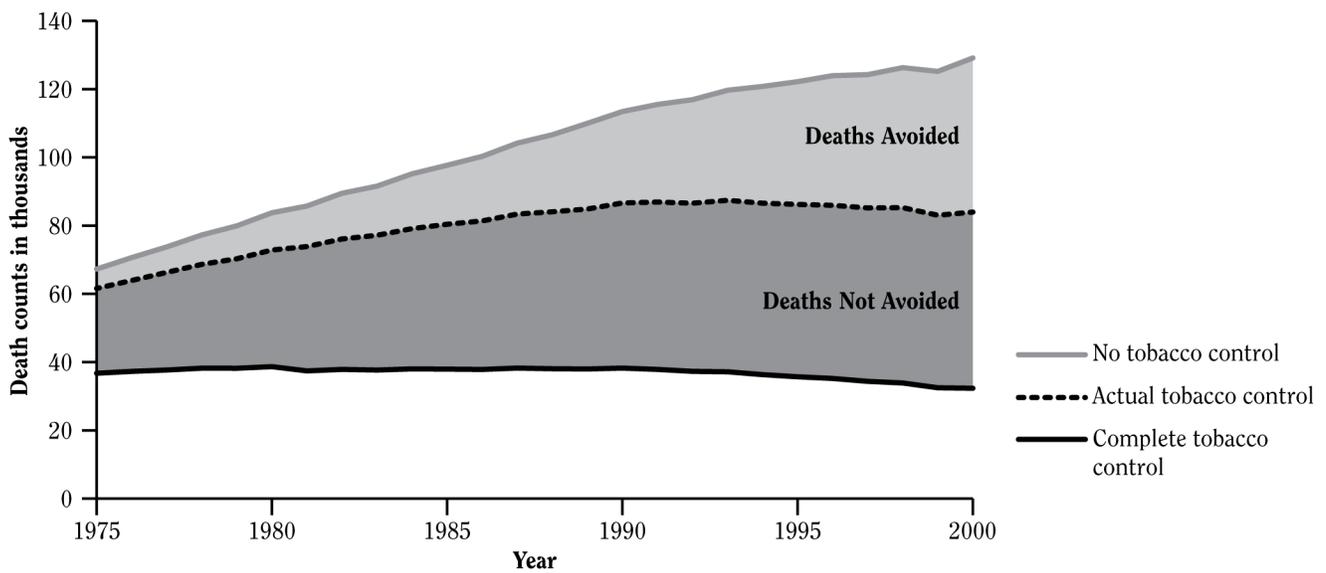
Figure 15.1.20 Continued

C. Death rates, women
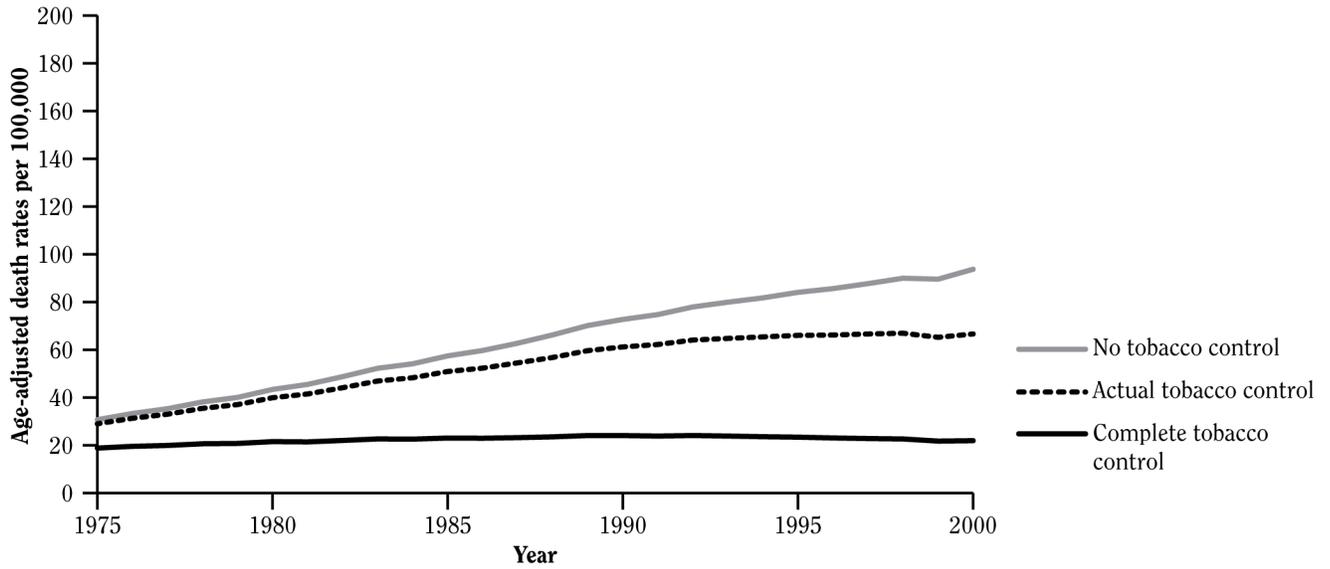
D. Death counts, women
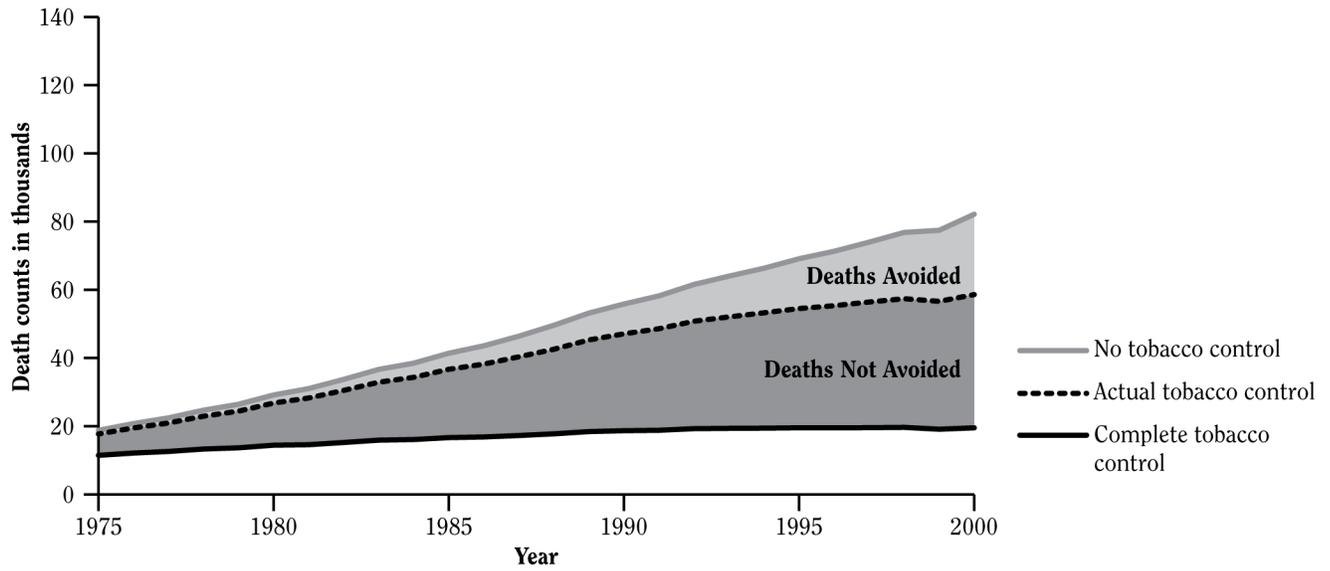
Source: Moolgavkar et al. 2012. Reprinted with permission from Oxford University Press, © 2012.

The differences between the actual and the no tobacco control scenarios provided a measure of mortality reduction related to tobacco control. These estimated data were patterns of death by age, years of life lost, and impact on life expectancy.

Table 15.1.3 shows the estimated number of premature deaths related to smoking in the United States over the period 1964–2012, compared with the estimated numbers of deaths under the counterfactual scenarios. The model estimated that between 1964–2012 there were a total of 17.7 million smoking-attributable deaths. In comparison with the counterfactual scenarios without tobacco control, reductions in smoking since 1964 resulted in an estimated 8.0 million (lower bound-upper bound scenario range from 7.4 to 8.3 million) premature smoking-attributable deaths averted due to tobacco control.

Table 15.1.4 shows the estimated number of years of life lost due to premature death and years saved in comparison to counterfactual scenarios. The model estimated that a 157 million (lower bound-upper bound scenario range from 139 to 165 million) gain in life years was associated with tobacco control since 1964. When these estimated years of life gained were considered for the whole population, the estimated trend in life expectancy at age 40 was computed. Figure 15.1.21 shows these trends. For men, life expectancy at 40 years of age was estimated to have been increased by 7.8 years. The model estimated that without tobacco control, life expectancy for men would have increased 5.5 years. For women, the increase in life expectancy was 5.4 years, and estimated to have been only 3.8 years without tobacco control. Thus, tobacco control was estimated to have contributed 30% of the life gain since 1964 for men and 29% for women.

The model results from Holford and colleagues (2014) can be compared with the estimates presented in Chapter 12, Table 12.15, for smoking-attributable mortality from 1965–2014. As shown in Table 12.15, the estimated total premature deaths caused by smoking and exposure to secondhand smoke from 1965–2014 is 20,830,000. The modeling by Holford and colleagues (2014) estimated the number of smoking-attributable deaths from 1965–2012 as 17.7 million. However, the time period for this estimate was 49 years versus the 50 years estimated in Table 12.15. Also, the estimate in Table 12.15 includes deaths attributable to exposure to secondhand smoke (2,457,000), residential fires (86,000), and conditions related to pregnancy and birth due to smoking by the mother (108,000).

Examples of Agent-Based Simulation Models

RTI International developed an agent-based model designed to estimate future smoking-attributable mortality. The model is based on the estimated smoking-attributable deaths from 1995–1999 and projects mortality for 2030–2059. Figure 15.1.22 shows the different states into which a single individual can transition in the model from RTI International (Mann et al. 2008). The model also provides a framework for quantitatively investigating policy-related questions (e.g., how many lives can be saved if rates of smoking cessation double) and thus allows evaluation of the effects of changes in smoking behaviors on mortality. Although the model is useful and provides insight on policy issues, several limitations (e.g., letting the agents interact with each other through established social networks) could be improved through further development.

The Concurrent Technologies Corporation (CTC) developed the prototype of an agent-based model to address smoking by teenagers (CTC 2010). The model integrates effects of multiple interventions using statistics from many peer-reviewed studies. The agents, using simple decision rules, display emergent complex behavior. Using large-scale experimental design techniques that it created and validated, the research team at CTC used the model to evaluate potential interventions, describing different investment strategies to abate teenage smoking.

Because this new approach models human decisions and multilevel interactions, this model may provide some unexpected results. The model more accurately reflects the results of individuals' decisions about their behavior (e.g., the decision to smoke or quit smoking). Individuals make decisions in the context of multiple roles and influences in their lives. CTC's model looks at how people make decisions in the context of these multiple roles, allowing for impact by, for example, community and societal factors and government influences.

Examples of Other Models

Elketroussi and Fan (1992) built a model of smoking cessation and relapse using individual level data from smokers who participated in the Multiple Risk Factors

Table 15.1.3   Estimated smoking attributable deaths (×1,000) avoided by tobacco control

A. All ages

	Gender	Actual number	Primary counterfactual		Lower limit		Upper limit	
			Number	Saved (%)	Number	Saved (%)	Number	Saved (%)
1964–1973	Men	2,512	2,867	355 (12)	2,867	355 (12)	2,867	355 (12)
1974–1983	Men	2,711	3,377	665 (20)	3,374	663 (20)	3,380	668 (20)
1984–1993	Men	2,903	3,930	1,027 (26)	3,897	994 (25)	3,953	1,050 (27)
1994–2003	Men	2,744	4,257	1,514 (36)	4,119	1,375 (33)	4,328	1,584 (37)
2004–2012	Men	2,271	4,028	1,758 (44)	3,729	1,458 (39)	4,150	1,879 (45)
Total	Men	13,141	18,460	5,319 (29)	17,986	4,845 (27)	18,678	5,537 (30)
1964–1973	Women	497	526	29 (5)	526	29 (5)	526	29 (5)
1974–1983	Women	834	980	146 (15)	979	146 (15)	980	146 (15)
1984–1993	Women	1,148	1,590	442 (28)	1,584	436 (28)	1,591	442 (28)
1994–2003	Women	1,155	2,064	909 (44)	2,028	873 (43)	2,074	918 (44)
2004–2012	Women	895	2,050	1,155 (56)	1,935	1,040 (54)	2,101	1,206 (57)
Total	Women	4,529	7,210	2,681 (37)	7,053	2,524 (36)	7,271	2,742 (38)
1964–1973	Both	3,009	3,393	384 (11)	3,393	384 (11)	3,393	384 (11)
1974–1983	Both	3,545	4,357	811 (19)	4,353	808 (19)	4,359	814 (19)
1984–1993	Both	4,052	5,520	1,469 (27)	5,481	1,430 (26)	5,544	1,492 (27)
1994–2003	Both	3,899	6,322	2,423 (38)	6,147	2,248 (37)	6,402	2,503 (39)
2004–2012	Both	3,166	6,079	2,913 (48)	5,664	2,498 (44)	6,251	3,086 (49)
Total	Both	17,670	25,670	8,000 (31)	25,039	7,368 (29)	25,950	8,279 (32)

B. Younger than 65 years of age

	Gender	Actual number	Primary counterfactual		Lower limit		Upper limit	
			Number	Saved (%)	Number	Saved (%)	Number	Saved (%)
1964–1973	Men	1,335	1,593	258 (16)	1,593	258 (16)	1,593	258 (16)
1974–1983	Men	1,214	1,615	400 (25)	1,612	398 (25)	1,618	403 (25)
1984–1993	Men	1,041	1,613	572 (35)	1,580	539 (34)	1,636	595 (36)
1994–2003	Men	835	1,773	938 (53)	1,636	801 (49)	1,842	1,007 (55)
2004–2012	Men	738	1,975	1,236 (63)	1,708	970 (57)	2,069	1,331 (64)
Total	Men	5,164	8,569	3,405 (40)	8,129	2,965 (36)	8,758	3,594 (41)
1964–1973	Women	284	306	22 (7)	306	22 (7)	306	22 (7)
1974–1983	Women	366	443	78 (18)	443	77 (17)	443	78 (18)
1984–1993	Women	347	504	156 (31)	498	151 (30)	504	157 (31)
1994–2003	Women	248	548	300 (55)	513	264 (52)	558	309 (55)
2004–2012	Women	198	649	451 (69)	555	357 (64)	699	500 (72)
Total	Women	1,443	2,450	1,007 (41)	2,315	871 (38)	2,510	1,067 (42)
1964–1973	Both	1,619	1,900	281 (15)	1,900	281 (15)	1,900	281 (15)
1974–1983	Both	1,580	2,058	478 (23)	2,055	475 (23)	2,061	481 (23)
1984–1993	Both	1,389	2,117	728 (34)	2,078	689 (33)	2,141	752 (35)
1994–2003	Both	1,083	2,321	1,238 (53)	2149	1,065 (50)	2,400	1,316 (55)
2004–2012	Both	936	2,624	1,687 (64)	2,263	1,327 (59)	2,768	1,831 (66)
Total	Both	6,607	11,019	4,412 (40)	10,444	3,837 (37)	11,268	4,661 (41)

Source: Holford et al. 2014. Reprinted with permission from American Medical Association. All rights reserved, © 2014.

Table 15.1.4   Years of life lost (×1,000) by tobacco control and gender

A. All ages

	Gender	Actual number	Primary counterfactual		Lower limit		Upper limit	
			Number	Saved (%)	Number	Saved (%)	Number	Saved (%)
1964–1973	Men	40,585	47,579	6,994 (15)	47,579	6,994 (15)	47,579	6,994 (15)
1974–1983	Men	40,625	52,565	11,939 (23)	52,466	11,841 (23)	52,661	12,035 (23)
1984–1993	Men	40,640	59,639	18,999 (32)	58,535	17,895 (31)	60,375	19,735 (33)
1994–2003	Men	37,446	69,866	32,419 (46)	65,676	28,230 (43)	71,838	34,392 (48)
2004–2012	Men	32,287	73,132	40,845 (56)	65,013	32,725 (50)	76,085	43,797 (58)
Total	Men	191,584	302,781	111,197 (37)	289,269	97,685 (34)	308,537	116,953 (38)
1964–1973	Women	8,970	9,609	640 (7)	9,609	640 (7)	9,609	640 (7)
1974–1983	Women	13,591	16,305	2,715 (17)	16,293	2,702 (17)	16,305	2,715 (17)
1984–1993	Women	16,852	24,166	7,314 (30)	23,964	7,112 (30)	24,191	7,339 (30)
1994–2003	Women	15,266	30,193	14,927 (49)	29,133	13,867 (48)	30,496	15,230 (50)
2004–2012	Women	11,717	32,103	20,386 (64)	29,166	17,449 (60)	33,585	21,868 (65)
Total	Women	66,396	112,377	45,981 (41)	108,164	41,769 (39)	114,187	47,791 (42)
1964–1973	Both	49,555	57,188	7,633 (13)	57,188	7,633 (13)	57,188	7,633 (13)
1974–1983	Both	54,216	68,870	14,654 (21)	68,759	14,543 (21)	68,966	14,750 (21)
1984–1993	Both	57,493	83,805	26,313 (31)	82,499	25,007 (30)	84,566	27,073 (32)
1994–2003	Both	52,712	100,059	47,347 (47)	94,809	42,096 (44)	102,334	49,622 (48)
2004–2012	Both	44,004	105,235	61,231 (58)	94,178	50,174 (53)	109,670	65,666 (60)
Total	Both	257,980	415,157	157,178 (38)	397,433	139,454 (35)	422,724	164,744 (39)

B. Younger than 65 years of age

|	Gender	Actual number	Primary counterfactual		Lower limit		Upper limit	
			Number	Saved (%)	Number	Saved (%)	Number	Saved (%)
1964–1973	Men	12,095	14,589	2,494 (17)	14,589	2,494 (17)	14,589	2,494 (17)
1974–1983	Men	9,876	13,391	3,515 (26)	13,333	3,457 (26)	13,447	3,572 (27)
1984–1993	Men	8,343	13,733	5,390 (39)	13,146	4,802 (37)	14,115	5,772 (41)
1994–2003	Men	7,007	17,282	10,275 (59)	15,386	8,379 (54)	18,089	11,082 (61)
2004–2012	Men	5,792	18,232	12,440 (68)	15,272	9,480 (62)	19,124	13,332 (70)
Total	Men	43,113	77,227	34,114 (44)	71,726	28,613 (40)	79,364	36,251 (46)
1964–1973	Women	2,751	2,973	222 (7)	2,973	222 (7)	2,973	222 (7)
1974–1983	Women	2,827	3,427	600 (17)	3,420	593 (17)	3,427	600 (17)
1984–1993	Women	2,270	3,429	1,159 (34)	3,332	1,062 (32)	3,442	1,172 (34)
1994–2003	Women	1,359	3,694	2,336 (63)	3,319	1,961 (59)	3,819	2,460 (64)
2004–2012	Women	1,115	4,314	3,199 (74)	3,627	2,512 (69)	4,783	3,668 (77)
Total	Women	10,323	17,838	7,515 (42)	16,672	6,349 (38)	18,444	8,121 (44)
1964–1973	Both	14,847	17,563	2,716 (15)	17,563	2,716 (15)	17,563	2,716 (15)
1974–1983	Both	12,703	16,818	4,114 (24)	16,753	4,050 (24)	16,874	4,171 (25)
1984–1993	Both	10,613	17,162	6,549 (38)	16,478	5,864 (36)	17,557	6,943 (40)
1994–2003	Both	8,366	20,976	12,611 (60)	18,705	10,339 (55)	21,908	13,542 (62)
2004–2012	Both	6,907	22,546	15,639 (69)	18,900	11,993 (63)	23,907	17,000 (71)
Total	Both	53,436	95,065	41,629 (44)	88,398	34,962 (40)	97,808	44,372 (45)

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Figure 15.1.21 Life expectancy at age 40 years by gender
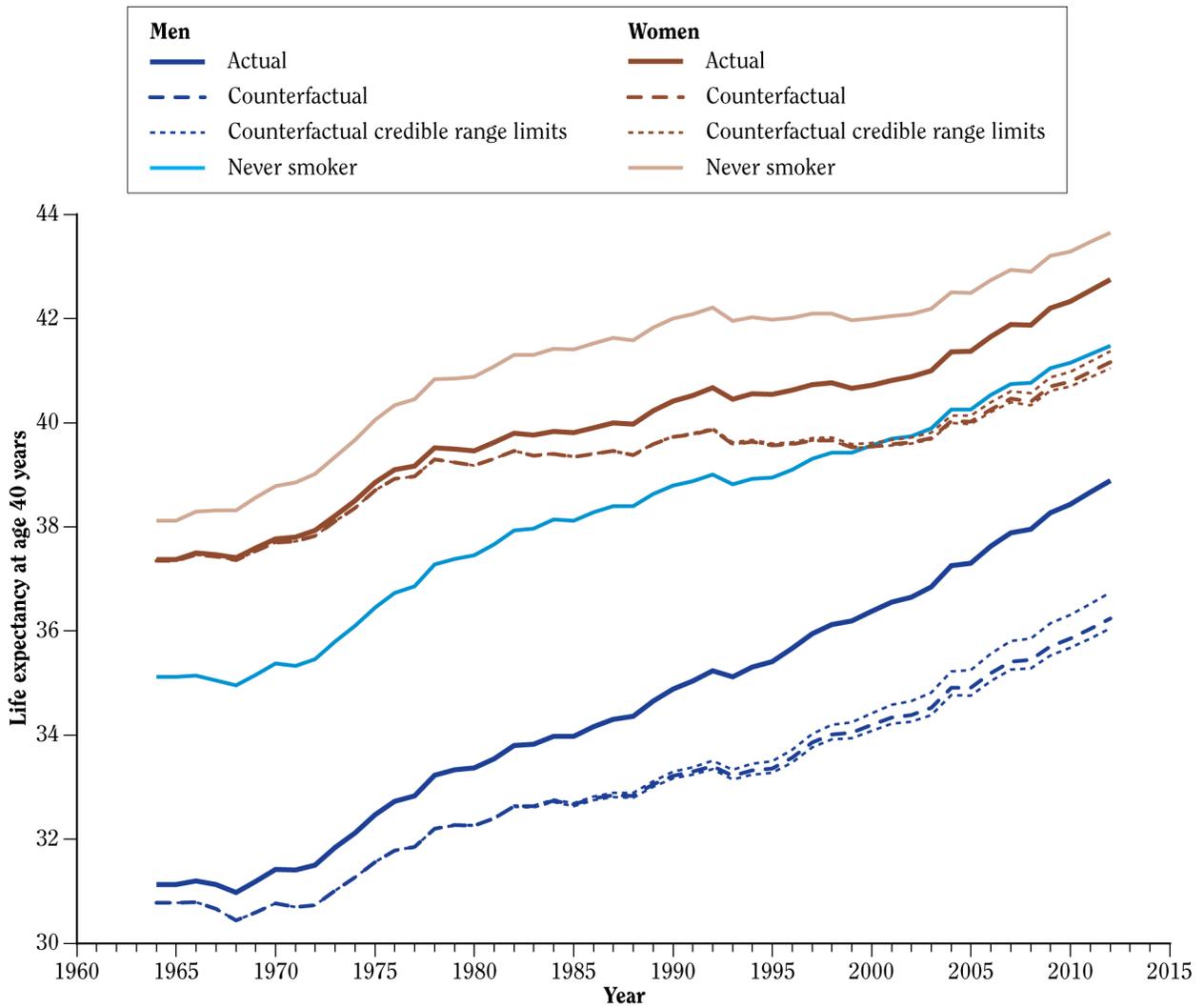
Source: Holford et al. 2014. Reprinted with permission from American Medical Association. All rights reserved, © 2014.

Figure 15.1.22 Individual transition diagram of agent-based model from RTI International, in which an individual has state variables, such as disease status, in each state
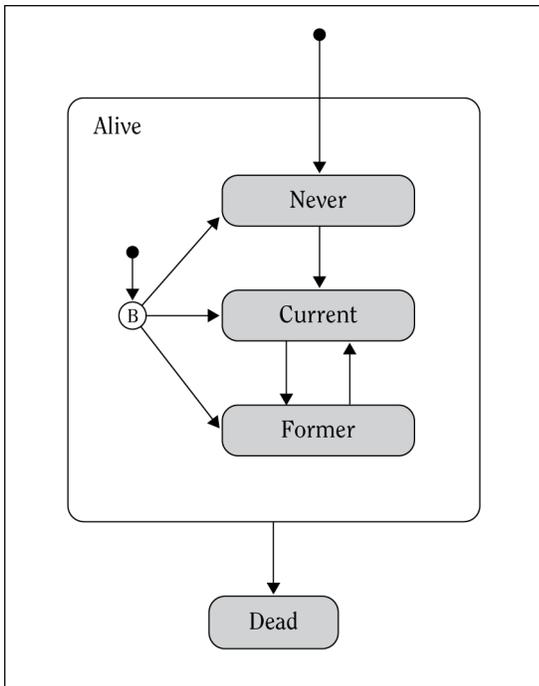
Source: Mann et al. 2008.

Intervention Trial. The model incorporated individual attributes (e.g., craving, self-efficacy, and motivation) in describing any changes in smoking behavior. For each individual, the amount of change is a result of that individual's trajectory. Using an agent-based approach, Song (2006) and Axtell (2006) incorporated the effects of peers in a student's social network to assess an individual's probability of smoking.

Other simulation models have been used to predict quality-adjusted life years (Kaplan et al. 2001; Tengs et al. 2004, 2005; Ahmad 2005a,b,c); cost savings for medical or health care (Ahmad and Franz 2008); the effects of a smoking ban on the risk of acute myocardial infarction (Richiardi et al. 2009); and complex interactions of multiple risk factors (including smoking and exposure to secondhand smoke), context, and capacity on reducing cardiovascular disease at the local level (Homer et al. 2008).

Table 15.1.5 summarizes the models that are discussed in this section.

Table 15.1.5 Summary of models

Name of model	Type of model	Purpose
SimSmoke	Aggregate, compartmental	Policy and scenario analysis
University of Michigan Tobacco Prevalence and Health Effects Model	Aggregate, compartmental	Policy and scenario analysis
Tobacco Policy Model	Aggregate, compartmental	Policy and scenario analysis
BENESCO	Aggregate, compartmental	Cost-effectiveness of smoking cessation interventions
SAMMEC	Aggregate, compartmental	Estimation of health-related economic impact of smoking
CANSAVE	Aggregate, compartmental	Description of lung cancer progression and evaluation of screening policies
RTI Model	Agent-based	Smoking-related mortality and policy evaluation
CTC Model	Agent-based	Evaluation of strategies to combat teenage smoking

Note: **BENESCO** = Benefits of Smoking Cessation Outcome; **CANSAVE** = Cancer Strategy Analysis and Validation Effect; **CTC** = Concurrent Technologies Corporation; **SAMMEC** = Smoking-Attributable Morbidity, Mortality, and Economic Costs.

Recommendations for the Future Use of Modeling and Simulation

Informing Policy

Simulation models are an essential tool in the tobacco-control arsenal. They provide a view of the future impact of tobacco-control policies given the best knowledge of present effects. The tobacco epidemic is extremely complex and amenable to a variety of interventions. These interventions may interact with each other and may have a combined effect that is not anticipated. Simulation models provide a representation of reality, making it possible to examine the likely effects of policies before their actual impact can be observed. Simulation models can also warn about potentially unfavorable interactions among policies that have already been implemented. Models can be used to project the consequences of proposed solutions and visualize how proposed solutions will interact in a single environment. For example, the individual decision to smoke depends in part on the environment in which the individual is immersed. Young people start smoking in large part because of peer pressure, and having friends who smoke is a determinant of whether an individual continues to smoke (USDHHS 2012). Simulation models can be used to understand how smoking behavior is modulated by, and propagated through, social networks and how social networks might be used to curb smoking.

Consequently, as the tobacco problem continues to change (e.g., with an increasing diversity of products), simulation modeling will become even more useful for informing policy decisions and crafting interventions. Policymakers and intervention specialists cannot directly observe the counterfactual (i.e., what would have happened if policies and interventions had taken a different course), but simulation modeling can help to identify the tradeoffs associated with policy and intervention decisions regarding the underlying system.

Designing Adaptive Policies

In many complex systems, including those of tobacco control, interventions designed to alter such systems in a desired way are often met with compensatory measures (e.g., the response by the tobacco industry to an effective policy action). Policy resistance (Sterman 2000)—referring to the intended effects of a system intervention being delayed, defeated, or diluted by the response to the intervention itself—may result. Policy resistance is common and has been observed in tobacco control (e.g., light cigarettes were intended to reduce harm but people smoked them in a compensatory fashion and harm was not reduced) (Hatsukami et al. 2006). Therefore, policymakers may have to look toward adaptive policies—that is, policies that are flexible enough to change as the conditions on which they are based also change. Simulation models present an ideal platform to explore such dynamically adaptive policies.

Developing Biobehavioral Models

Tobacco use is addictive. The 2012 Surgeon General's report reviewed how the onset and maintenance of addiction involves the interplay between numerous factors, including genetic, physiological, psychological, social, and economic, among others (USDHHS 2012). Models need to be developed to incorporate advancing biological understanding, coming from new lines of investigation, such as functional imaging and genetics. Models must be capable of bridging scales of analysis to help researchers understand how these factors interact and evolve over time to result in tobacco use and related behaviors. The span of time covered needs to extend from childhood all the way to older ages, when cessation is critical for limiting the burden of tobacco-caused disease and morbidity. Further longitudinal data are needed to support models that cover the lifespan. As noted in the 2012 Surgeon General's report (USDHHS 2012), a limited amount of cohort data are available to study smoking trajectories from adolescence to adulthood. Available evidence indicates that adolescent smoking patterns follow different trajectories from experimentation to addiction; however, the study of how genetic, physiological, psychological, social, and economic factors interact in these trajectories could provide important insights into prevention policies and programs.

Using Models for Target Setting

Many organizations set goals for addressing public health needs. These goals, including those for tobacco control, are not always realistic or achievable (Mendez and Warner 2000; Levy et al. 2005a,b,c). Furthermore,

some goals are written broadly and do not acknowledge the possibility of significant differences in what subgroups of a population can achieve, based on where they start. *Healthy People 2020* included modeling as a target setting method but it was not used to develop all of the targets. Nonetheless, targets have been set for tobacco control by diverse organizations, including USDHHS. Models can provide useful guidance on setting aspirational but achievable targets and test packages of policies for their likely success in meeting various targets.

Engaging Stakeholders

Community-based research has demonstrated the benefits of working directly with affected constituencies when conducting research on problems that affect the community and when developing potential solutions. Many modeling methodologies have a strong history of including stakeholders in all facets of the modeling process. Doing so can enhance buy-in and strengthen the implementation of policies and their impact. In addition, policymakers often have particular questions in which they are interested. When models are developed without engagement of policymakers, the models may not adequately address the specific questions or the results may not be well-suited to the questions. Therefore, the modeling process should engage stakeholders (including policymakers and community leaders, where possible) early and often, beginning with identifying the questions to be modeled. Moreover, by engaging in the process throughout, stakeholders are much more likely to have a solid understanding of the model's capabilities and limitations and of assumptions made. Lessons can be learned from those who have been successful in convincing policymakers of the utility of models (Ferencik and Minyard 2011; Glasser et al. 2011).

Establishing Standards of Good Practice for Modeling

For the purpose of tobacco control, as in other applications, standards of good practice are necessary for model documentation, transparency, verification, validation, reporting, sharing, and interoperability. Standards should also be developed for base case scenarios for tobacco control modeling. Establishing such a referent set will allow different models and modeling approaches to reference the same base case and will facilitate comparisons of policy impact across models. Standards for model reporting may also be developed to help stakeholders understand and interpret results of the model. In addition, standards for education and training should be developed for tobacco-control researchers who want to collaborate with modelers and use modeling in their work. These standards of good practice will be instrumental for facilitating interactions between community leaders, policymakers, and others who will use and potentially benefit from decisions made based on the results of modeling.

Summary

This Appendix examines how simulation modeling is used in tobacco control research and policy development. Currently, two main types of simulation models are used: aggregate or compartmental models and individual-based (particularly agent-based) models.

Aggregate models follow the dynamic path of homogeneous entities or groups of interest, such as the number of smokers in the population. System dynamics models are a specific type of aggregate model that emphasize complex and often nonlinear interactions and feedback effects among the elements of the system being modeled. Agent-based models, the main type of individual model in use for tobacco control purposes, follow individuals, incorporating their unique characteristics and complex interactions within their specific environments and social networks.

This review showed that models are gaining increasing prominence in the field of tobacco control. Models have been used for various purposes, ranging from estimating the future path of smoking prevalence and consumption to estimating the health effects of past, current, and future use of tobacco in the population and to evaluating the potential impact of tobacco control policies on tobacco use and health effects. Models will be a critical tool for setting strategies intended to further reduce tobacco use, particularly as approaches are tailored to reduce smoking in population groups with high rates of prevalence and to further lower overall prevalence.

Conclusions

1. Models are a useful tool for selecting, evaluating, and refining tobacco-control strategies. They can be used to assess the consequences of past interventions and to project the consequences of various policy options to guide decision making.

2. Models are available that can reflect the complexities of the tobacco epidemic and the dynamic consequences of tobacco control.

3. Models have already proved useful in tobacco control and best practices have been developed for their application.

4. Based upon the preliminary results of models reviewed, evidence suggests that in the next phase of tobacco control, as efforts are made to push prevalence rates to ever lower levels, models will be a key tool for designing strategies to address groups with high rates of prevalence and to hasten the end of the tobacco epidemic.

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