

The application of simulation models and systems analysis in epidemiology: a review

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ABSTRACT

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A method for classifying epidemiologic process models is presented along with a brief history of epidemiologic modeling. Epidemiologic models are distinguished as being associative or process models. Associative models attempt to establish etiology by observing the associations of various risk factors with the occurrence of disease. Process models attempt to quantitatively describe the course of disease in a dynamic population. This begins with a hypothesis regarding the underlying structural processes involved. A process model can be classified further according to: (1) how it models the effect of chance; (2) application perspective; (3) the mathematical treatment of time; (4) the computational treatment of individuals; (5) the method for determining a solution.

The literature was reviewed for examples of applied epidemiologic process models. Examples are cited and classified according to the classification method proposed in this paper. Suggestions for appropriate applications of various models and further research are made.

INTRODUCTION

It long has been recognized that the occurrence of disease is a result of interactions between components of the famous agent–host–environment complex. The discipline of epidemiology has developed as a result of efforts to unravel the mysteries of this complex. A survey of current epidemiologic literature (Susser, 1985) shows most of the mathematical and quantitative work in epidemiology has resulted in what King and Soskoline (1988) have termed ‘associative models’. These are models that attempt to establish etiology by observing the associations of various risk factors with the occurrence of dis-

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ease. This approach has been very fruitful and has resulted in a variety of health recommendations, mostly referring to individual risk factors for chronic and non-infectious disease.

However, these associative models generally overlook the fact that interactions in this famous complex are dynamic and relationships change over time, as do the populations in which these interactions are occurring (Anderson and May, 1985; Catalano and Serxner, 1987). Efforts to address this issue of dynamic interactions in epidemiology have resulted in what are best termed as 'process models' (King and Soskoline, 1988). Associative models are equivalent to the classic statistical models. Process models attempt quantitatively to describe the course of disease in a population, so that state of the population (in terms of number infected, susceptible, etc.) can be expressed over time. This distinction of associative versus process seems to be similar to Thrusfield's (1986) designation of empirical versus explanatory models. This paper is focused on the process type of modeling. The objectives are: (1) to present a brief perspective on the development of epidemiologic process models; (2) to offer a method for classification of these process models; (3) to classify specific applied models.

HISTORY

Some of the earliest epidemiologists were process modelers (Susser, 1985). Early workers, such as William Farr in 1840, Brownlee, Greenwood, Kermack, and McKendrick, observed the consistent patterns of the occurrence of epidemics. They developed mathematical representations of these patterns with the hopes of predicting the course of epidemics *a priori*. One of the first and few 'successful' attempts at modeling was on a veterinary problem. In a letter to the London Times in 1865, W. Farr used an equation of second and third ratios to predict the outcome of a rinderpest epidemic in England. This success was not often repeated but it encouraged workers like Brownlee who persisted in the attempt to fit epidemic curves to variations of the normal curve (Fine, 1979). Bailey (1975) mentioned the work of Greenwood, Kermack and McKendrick along with Hamer, Soper and Ross, who developed versions of what would later be called mass-action models. Wade Hampton Frost (the first chair of epidemiology at the Johns Hopkins School of Hygiene and Public Health) was the originator of the Reed-Frost model of epidemics which still finds wide application today (Abbey, 1952; Ackerman et al., 1984).

Given the illustrious beginnings of early process modeling, one might well ask, why is this not an important part of epidemiology today? A further look at the history of epidemiology and process modeling might offer some possible explanation. As the early twentieth century progressed, epidemiology and process modeling were cooperative partners in addressing disease-control problems such as malaria and helminth infections in humans (particularly

schistosomiasis) (Fine et al., 1982; Hethcote and Yorke, 1984; Anderson and May, 1985; Dietz and Schenzle, 1985). Study of these reviews and others (Bailey, 1982; Koopman, 1987) shows mathematical model development occurring concurrently with data collection and disease-control policy recommendations. Nobel laureate Sir Ronald Ross derived the first threshold theorem from a differential equation model (Ross, 1911). This model determined that there was a threshold density of man and mosquitoes below which malaria would not be able to maintain itself. George MacDonald's (1956) conclusions (that control of adult mosquitoes by residual insecticides is more effective than larval control) is considered by some as 'the single most important insight into public health planning from modelling' (Dietz and Schenzle, 1985). MacDonald (1965) also published an important paper on the dynamics of schistosome infections and humans that has spawned a great deal of mathematical development in parasitology. This is thoroughly discussed by Anderson and May (1985).

In time, however, one can see a divergence between applied epidemiology and mathematical modeling (Bailey, 1975; Thrusfield, 1986). Bailey (1975) suggested that this point of divergence occurred around 1957. Susser (1985) inferred that the change began after World War II. During this period it is possible to perceive two responsible forces. First, epidemiologists began to be more concerned with chronic, non-infectious diseases (Susser, 1985; King and Soskoline, 1988) which tend to focus on individual risk factors versus population dynamics. These models find more use for associative (statistical) models than for process models. Secondly, the limiting assumptions of the early mathematical models (the mass action and chain binomial) began to impinge on their practical applicability. (These limiting assumptions will be discussed briefly later.) As a result, the models were not able to describe recurrent cycles of disease and fell out of use by many epidemiologists (King and Soskoline, 1988).

The net result of these phenomena can be expressed by the nursery rhyme bemoaning the fact that 'the dish (epidemiologist) ran away with the spoon (statistician)', and left the cow (mathematician) to more esoteric pursuits, such as 'jumping over the moon'. This observation has been echoed by the mathematicians themselves (Bailey, 1982; Bart et al., 1983). One leader in the field of measles and helminth modeling has noted: 'some of the mathematical literature has taken on a life of its own, free from data and full of elegant theorems in hopeful search of a disease' (May, 1982). The modeling literature that occurs after this time is largely theoretical (Wickwire, 1977; Mollison, 1977; Dietz and Schenzle, 1985; Isham, 1988) and difficult for the non-mathematician (Koopman, 1987; King and Soskoline, 1988).

Unfortunately, a great deal of this rich theory has been overlooked by most epidemiologists. This is particularly unfortunate for the veterinary epidemiologist, who often is dealing with disease in dynamic populations. It also

may be a fair assumption that he or she is often dealing with infectious disease or parasitic disease (with which almost all of the process-model development has dealt).

During this same post-war period and separate from epidemiology, the theory and practice of systems analysis began to develop (Chestnut, 1965). This methodology has enjoyed a very fruitful tenure with a wide variety of applications to industrial processing (Law and Kelton, 1982), management and social sciences (Sutherland, 1975), ecology and entomology (Kitching, 1983). Before the late 1970s, only a few apparent applications of this theory to epidemiology can be found (Waalder et al., 1962; Brogger, 1967; Waalder, 1968; ReVelle et al., 1969). The count is increased if one includes the few health-care management applications (Farrow et al., 1971; Bailey and Thompson, 1975).

In the late 1970s and early 1980s one can see signs that the once-separated fields of dynamic mathematics and epidemiology had begun to reunite (Nokes and Anderson, 1988). Epidemiology is bringing along the more fully developed field of statistics, and dynamic mathematical disease models have been enhanced by computer simulation. Simulation allows for relaxation of some of the assumptions, while decreasing the need for rigorous mathematics and closed-form analytical solutions. This approach can more effectively deal with non-linearities, time dependence and various forms of feedback (Habtemariam et al., 1982b; Angulo, 1987). The possibility that systems analysis would begin to contribute to epidemiology was suggested by Bailey (1982), Koopman (1987), and by some examples in the current literature (which will be discussed below). Koopman (1987) called for a science of transmission systems analysis which merges the mathematical theory of dynamic populations with simulation modelling (as in Ackerman et al., 1984). This science keeps a constant eye to statistical interpretation of real-world data, as in Haber et al. (1988). Stimulated by the current epidemic of human immunodeficiency virus (HIV) infections and the call for more population-based and economically oriented veterinary medicine, it is anticipated that this science of transmission systems analysis (or the systems approach) will gain an increased role in epidemiology.

CLASSIFICATION

Any new methodology or discipline seems to suffer from an ambiguity of terminology and lack of a unified classification scheme. This ambiguity seems to exist in epidemiologic process modeling. The result is an increase in the amount of words required to communicate the essential features of a model. Miscommunication and an overall decrease in the rate of new developments results. Based on the writings of various authors, a means of describing and hence classifying current process models is presented in this paper. We be-

lieve that all current models can be classified this way. We have also characterized specific applied models published since 1970 according to this classification scheme. Their apparent applications also are identified.

An effort has been made to include only papers that we considered to be applied and epidemiologic in nature. Applied papers are those attempting to answer a specific epidemiologic question, using data that are current enough to be useful (it was not necessary that the data were collected primarily for the model, as most models depend heavily on literature for estimates of many parameters). Some models were considered to be theoretical and were excluded, because we felt that the purpose of the data was only to evaluate behavior of the model—not to make control recommendations. Epidemiologic papers are those that relate to control of disease in animals or humans. Agricultural production models (Jenkins and Halter, 1963; Oltenacu et al., 1980, 1981) and statistical simulation models (Lemeshow et al., 1985; Suttmoller, 1986; Akhtar et al., 1988), along with econometric simulations (McCauley et al., 1977) generally were excluded. We did not attempt to evaluate the usefulness, quality, or validity of the specific models included.

Classification method

The classification of epidemiologic models might be achieved best by the application of six characteristics that would express most of a model's salient features (Fig. 1). These characteristics are: (1) the model's causal perspective; (2) how it models the effect of chance; (3) its application perspective; (4) its mathematical treatment of time; (5) its computational treatment of individuals; (6) its method for determining a solution. Each of these characteristics is dichotomous. This allows both for flexibility in model characterization and simplicity.

A model's causal perspective reflects the nature of the original hypotheses in which an investigator may have been interested. Associative models will infer causality without a knowledge of the pathways or processes leading to the observed phenomenon. Process models begin by defining hypothesized pathways and structural processes that may describe the system under investigation.

Following King and Soskoline's (1988) hierarchy, one can distinguish the characteristic of how a model relates to the effects of chance. A model can be described as being stochastic or deterministic. Stochastic models include elements of random variation and chance. If fully stochastic models are run repeatedly, the runs will lead to a distribution of epidemic sizes and durations (Ackerman et al., 1984). These fully stochastic models are exhibiting the minimum theorem of epidemics (McKendrick, 1926). Stochastic models of non-infectious disease will include the random effects of certain variables, but will not exhibit the threshold phenomenon. Stochastic models have the

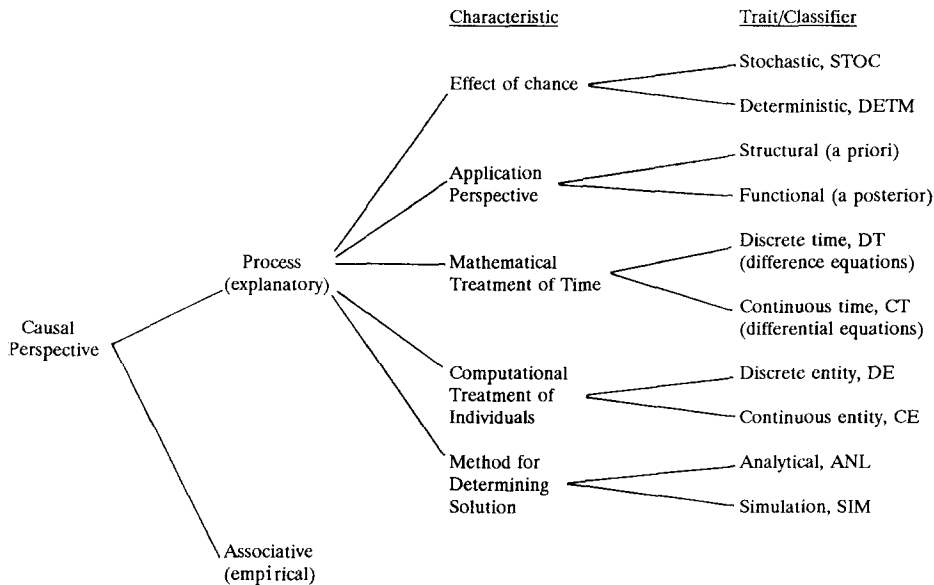


Fig. 1. Proposed classification method for process epidemiologic models.

advantage of reflecting the realistic aspects of chance and uncertainty in a model's behavior. The predictions can be expressed with confidence intervals and expected values, instead of just point estimates. Deterministic models give the same result every time they are run, and one can consistently determine the state of the model for any given set of initial starting values and parameters. Deterministic models are useful for determining the sensitivity of a system's behavior to changes in certain parameters.

The next level of classification is a model's application perspective. A model is either functional or structural (King and Soskoline, 1988). (This is similar to Fine's (1982) distinction of descriptive (a posteriori) versus a priori, or dynamic, models.) Structural models attempt to portray the underlying mechanism of the disease transmission process for the purpose of making a priori predictions or of exploring implications of assumptions. Most simulation models are of this type. Functional models, on the other hand, begin from the standpoint of modeling a process—but their goal is to quantitate observed phenomena (or to gain estimates of risk factors) with a statistical analysis of the process model. Functional models look backward in time; these functional models are not the focus of this paper.

The next characteristic of a model relates to its mathematical treatment of time. A model will be discrete-time or continuous-time. Discrete-time models divide time into units of equal duration and employ the algebra of finite-

difference equations. For example, the number of susceptibles at the next time period equals the number of susceptibles at this time period minus the number of new cases ($S_{t+1} = S_t - C_{t+1}$) (Fine, 1982). Continuous-time models treat time as a continuous variable and use differential equations to express instantaneous rates of change. For example, the rate of change of new infections (i.e. infection rate) might be a function of the number of susceptibles (S), cases (C) and some contact parameter (b); the number of cases at any given point in time ($dC/dt = S \times C \times b$) is just the integral of this rate (Bailey, 1975).

For the computational treatment of individuals, a model can be classified as discrete-entity or continuous-entity. Discrete-entity models track one individual at a time through the simulation model. This individual is exposed to infectious individuals and any other experiences (such as calving, death, etc.). The behavior of the system is the sum of the behavior of each individual. These types of models can get very complex, and this increases as the number of individuals in a population increases. This complexity has the disadvantage of increased computer and programmer time and decreased intuitive appeal (Ackerman et al., 1984). Continuous-entity models treat the number of individuals in any state as a real number; such models can be computed in either continuous or discrete time. Continuous-entity models (or macromodels; Ackerman et al., 1984) tend to deal with homogeneously mixing populations. The homogeneous-population assumption can be a disadvantage if one feels that interactions are not the same for each individual in the population. The advantage is that the size of the population being simulated will not affect the speed of computer processing for continuous-entity models. Any model defined in continuous time (i.e. with differential equations) is a continuous-entity model. (However, the distinction blurs when a differential-equation model is simulated on a digital computer, since time is discretized into very small units for numerical integration (Law and Kelton, 1982).)

In terms of how a model arrives at its solutions, one can classify a model as analytical versus simulation (Fine, 1982). Analytical models depend on mathematical manipulation alone to explore the relationships between variables; i.e. they seek a closed-form solution to the state of the system at some equilibrium. There are many of these types of epidemic models which are largely the domain of the mathematician (Bailey, 1982). The advantages are that they can be evaluated rigorously and stability criteria can be determined. The disadvantages are that much realism is often assumed away in order to produce a more tractable model, and analytic models are inaccessible to the non-mathematician. Simulation models depend on numerical substitution (according to model-defined rules) to find the expected outcome of a mathematical formulation (Fine, 1982; Ackerman et al., 1984). The example models presented below are mostly simulation models.

General model types

Three general types of models can be identified and described. Identification of a model's genera and specific classification will convey most of the important information on a model's technicalities. Types of models such as the mass-action model, the Reed–Frost model, Markov models, network models, matrix models, and systems models can be grouped into three genera: mass-action models, chain-binomial models, and systems models (Fig. 2).

Mass-action models refer to the phenomenon that infection is the result of the random and homogeneous mixing of infectious and susceptible individuals within a population (Fine, 1982). Mass-action models can be deterministic or stochastic (Bartlett, 1953); they can be discrete-time (Soper, 1929) or continuous-time (Bailey, 1955), but are always continuous-entity. Limiting assumptions are that they assume random and homogeneous mixing, and there is a linear relationship between the incidence rate and the number of cases (e.g. $C_{t+1}/S_t = C_t \times b$). This linear relationship makes it possible, in a small population, to erroneously calculate more cases than there are suscep-

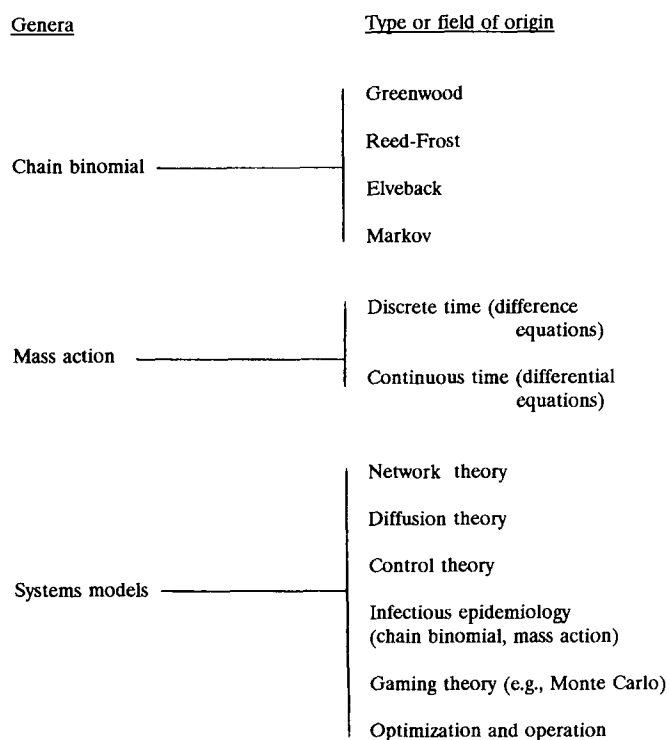


Fig. 2. Genera of epidemiologic process models.

tibles. Also, the epidemiologic meaning of the transmission coefficient (b) for mass-action models is not quite clear (Fine, 1982).

In order to overcome these limiting assumptions, the chain-binomial models were developed (Greenwood, 1946). In these models, new cases of disease occur in a series of stages. The number of cases at any stage will have a binomial distribution depending on the numbers of infectious and susceptible individuals at the previous stage (Bailey, 1975). These models are fully stochastic, discrete-time and continuous-entity. These models assume that the period of infectiousness is relatively short and of constant duration, and that there is a constant probability of infection in each serial interval (Fine, 1982).

There are at least four types of chain-binomial models: the Greenwood (Greenwood, 1946), Reed–Frost, Elveback, and Markov models (Table 1). Markov models or chains are sometimes used for simulations; these are mathematically equivalent to chain-binomial models with a finite state and discrete-time parameter (Dietz, 1967).

A special case of the chain binomial is the Reed–Frost model where the expected number of cases for the epidemic can be derived deterministically from the recursive formula shown in eqn. 1 (Ackerman et al., 1984). This model is discrete-time and continuous-entity. Mathematically, it is deterministic—but it can be made stochastic with computer simulation. It still suffers from the assumption of random mixing, and short, constant length of the infectious period.

$$C_{t+1} = S \times (1 - q^{C_t}) \quad (1)$$

where C is cases, S is susceptible, $q = 1 - p$, p is probability of effective contact.

A discrete-entity version of the Reed–Frost model often is referred to as the ‘Elveback’ type of model (Ackerman et al., 1984). In this model, one individual at a time is processed through a simulation model and randomly infected, with the probability of infection derived from the above equation. These models have the advantage of allowing for heterogeneity of contact and different infection probabilities for each individual. However, they soon become very complicated and computer intensive.

There exists a third genus of models that are not derived from any particular mathematical school of thought. These we might call ‘systems models’. These models use whatever mathematical or simulation techniques are necessary to describe the particular system of interest (i.e. whatever works). This may include differential equations (Thrusfield, 1986), Leslie matrices (Kitching, 1983), Monte Carlo theory, and network theory (Paton and Gettinby, 1983). Cohen (1977) calls them hybrid dynamic models when referring to the schistosomiasis models of Nasell (1976a, b) and others (Nasell and Hirsch, 1973). These models employ both Markov laws and differential equations. A variety of optimization techniques also can be included (Carpenter and Howitt, 1988). The mass-action models and chain-binomial

TABLE 1

Classification of applied epidemiologic structural process models

Chance	Time	State	Method	Genus	Reference	Application
STOC	DT	DE	SIM	CB	Barret, 1988	Heterosexual spread of HIV in early epidemic
STOC	CT	CE	SIM	Sys	Carpenter and Howitt, 1988	Determine optimal downtime and head placement for a broiler operation
DETM	DT	CE	SIM	Markov	Dijkhuizen, 1988	Evaluate economics on alternatives to vaccination for control of FMD
DETM	DT	DE	SIM	Sys	Oluokun and David-West, 1988	Evaluate factors controlling calf mortality in Nigeria, with economic effects
STOC	DT	DE	SIM	Sys	Sorensen, 1988	Evaluate economic effects on pneumonia levels in a dairy cattle herd
DETM	DT	DE	SIM	Markov	Tsevat et al., 1988	Prevention of tuberculosis with isoniazid
DETM	CT	CE	SIM	MA	Anderson et al., 1987	Impact of mass vaccination on incidences of mumps
DETM	DT	CE	SIM	RF	Carpenter et al., 1987	Economics of control of <i>Bruceella ovis</i>
STOC	DT	DE	SIM	Elve	Sattenspiel, 1987	Spread of hepatitis A in day care centers
DETM	CT	CE	SIM	MA	Anderson and May, 1986	Find important factors for future trends on HIV epidemic
DETM	CT	CE	SIM	MA	Anderson and Greenfell, 1986	Impact of vaccination strategies on CRS
STOC	DT	DE	SIM	Sys	Dijkhuizen et al., 1986	Economics of culling and reproductive failure
STOC	DT	CE	SIM	CB	Papoz et al., 1986	Predict rates of seroconversion to toxoplasmosis in a population
STOC	DT	DE	SIM	Sys	Shonkwiler and Thompson, 1986	Study outbreak of toxoplasmosis
DETM	DT	CE	SIM	Sys	Paton and Gettinby, 1985	Evaluate control strategies for <i>Ostertagia</i> in sheep
STOC	DT	DE	SIM	Sys	Kramer and Reynolds, 1981	Evaluate 28 control programs for gonorrhea
STOC	DT	DE	SIM	Sys	Meek and Morris, 1981	Evaluate control programs for ovine fascioliasis
DETM	DT	CE	SIM	Markov	Carpenter and Riemann, 1980	B/C for eradication of <i>Mycoplasma meleagridis</i>
DETM	DT	CE	SIM	?	Harris et al., 1980	Identify environmental variables important in the prevalence of hydatid disease
DETM	DT	CE	SIM	Sys	Knox, 1980	Predict effectiveness on alternative vaccination policies for CRS

Chance	Time	State	Method	Genus	Reference	Application
DETM	?	?	SIM	Sys	MacDonald and Bacon, 1980	Explore the effect of vaccination of foxes for rabies control
DETM	CT	CE	ANL	MA	Longini et al., 1978	Optimum influenza vaccine distribution among age groups
DETM	CT	CE	ANL	MA	Nasell, 1977	Test efficiency of sanitation for control of schistosomiasis
STOC	DT	DE	SIM	Elve	Elveback et al., 1976	Effect of vaccination for influenza A in school children
STOC	DT	DE	SIM	Sys	Hugh-Jones, 1976	Test effect of milk-lorry borne spread of FMD
DETM	DT	CE	SIM	Markov	Miller, 1976	Simulate spread of FMD across the USA
STOC	DT	DE	SIM	Elve	Roe and Morris, 1976	Brucellosis control in Australia
DETM	DT	CE	SIM	MA	Horwitz and Montgomery, 1974	Effect of underreporting an alternative vaccination program for measles in USA
DETM	CT	CE	SIM	Sys	Reynolds and Chan, 1974	Evaluate control programs for gonorrhea
DETM	DT	CE	SIM	MA	Dietz et al., 1974	Quantitate different interventions for malaria control
DETM	DT	CE	SIM	MA	Cvjetanovic et al., 1973	B/C analysis of sanitation versus vaccination for cholera
DETM	DT	CE	SIM	MA	Cvjetanovic et al., 1972	B/C analysis of different vaccination programs for tetanus
DETM	CT	CE	SIM	Sys	Longini et al., 1985	Predict global spread of Hong Kong influenza
STOC	DT	DE, CE	SIM	CB	Ackerman et al., 1984	Many applied and theoretical models of polio and influenza
DETM	DT	CE	SIM	Sys	Levy, 1984	Effect of measles vaccination program on number of susceptibles
DETM	CT	CE	ANL	MA	Anderson and May, 1983	Impact of different vaccination policies on incidence measles and CRS
DETM	CT	CE	ANL	MA	Hethcote, 1983	B/C analysis on vaccination strategies for measles and CRS
DETM	DT	CE	SIM	Sys	Smith, 1983	Alternative control strategies for <i>Babesia bovis</i>
DETM	DT	—	SIM	Sys	Habtemariam and Cho, 1983	Determine level of poultry inspection for any given farm at slaughter
STOC	DT	CE	ANL	Sys	Paton and Gettinby, 1983	Control of <i>Ostertagia</i> in sheep
DETM	CT	CE	SIM	MA	Croll et al., 1982	Effectiveness of mass treatment for eradication of <i>Ascaris lumbricoides</i>
DETM	DT	CE	SIM	Matrix	Cvjetanovic et al., 1982	Cost effectiveness analysis on vaccination programs, measles and polio in USA
DETM	DT	CE	SIM	Matrix	Habtemariam et al., 1982a	B/C analysis of control of trypanosomiasis

TABLE 1 (*continued*)

Chance	Time	State	Method	Genus	Reference	Application
STOC	CT	CE	SIM	Sys	Habtemariam et al., 1982b	Describe epidemic and endemic characteristics of trypanosomiasis
STOC	CT	CE	SIM	Sys	Habtemariam et al., 1982c	Disease and vector control of trypanosomiasis
DETM	CT	CE	ANL	MA	Hethcote et al., 1982	Evaluate six prevention methods for gonorrhea
DETM	CT	CE	ANL	MA	Dietz, 1981	Determine best method to compute cost for vaccination strategies of measles
DETM	CT	CE	SIM	MA	Cvjetanovic et al., 1971	B/C analysis of sanitation and mass vaccination for typhoid fever
STOC	DT	DE	SIM	Elve	Elveback et al., 1971	Effect of school closing and vaccination on spread of polio

STOC, stochastic; DETM, deterministic; DT, discrete-time; CT, continuous-time; DE, discrete-entity; CE, continuous-entity; SIM, simulation; ANL, analytical; ?, not enough information to classify; MA, mass-action; CB, chain-binomial; MC, Monte Carlo, chain-binomial; RF, Reed-Frost; Elve, Elveback type of chain-binomial; HIV, human immunodeficiency virus; FMD, foot and mouth disease; CRS, congenital rubella syndrome; B/C, benefit-cost analysis; Sys, systems model.

models often may be the essential building blocks of the systems models, but modifications are made in order to move away from many of the limiting assumptions, and in order to represent the complexities of the whole system.

The definition of systems analysis or the systems approach may seem to be as broad as the problems it attempts to solve. However, certain consistencies in the various definitions can be found. The essential features are that (1) it is a methodology for solving unstructured problems, (2) it begins with a defined set of needs, (3) it moves to a description of the whole system as it currently exists, (4) it generates alternatives for meeting the expressed needs, (5) it evaluates those alternatives with various modeling techniques, and (6) it designs and (7) implements the policies found most capable of meeting the needs (Checkland, 1981; Manetsch and Park, 1982). The two important attributes are that it 'overtly seeks to include all factors which are important in arriving at a "good" solution, and it makes use of quantitative models and often computer simulation in making rational decisions' (Manetsch and Park, 1982). Simply put, it is a holistic approach (Martin et al., 1987). Systems models offer the greatest potential for future use as they are not limited by the assumptions of basic infectious-disease models (Bailey, 1982; Koopman, 1987). They are also valuable tools for consideration of the economics of disease and disease control.

It is possible, in most cases, to apply the six classification criteria to systems models and thus aid in giving a better description of these techniques. This is

important because these models do not easily fit into clear classes. An advantage of the proposed classification scheme is its ability to describe the wide range of models in existence. For example, models that use queuing theory might be described as discrete-time, discrete-entity, stochastic-simulation models (Law and Kelton, 1982).

Classification of applied models

Shown in Table 1 are the publications that we identified as applied epidemiologic models published since 1970 and of the structural-process type.

Of the over 200 simulation and mathematical articles reviewed for this paper, only 49 were applied, epidemiologic, structural, process models. Of those, 19 seemed to represent enough complexity and holistic view to be classified as systems models. The majority of the systems-type models dealt with veterinary or zoonotic problems; this reflects the importance that this approach has for veterinary epidemiology.

DISCUSSION

Some other models of a very narrow, well-defined system also could have been considered as systems models. For example, Carpenter et al. (1987) present a Reed–Frost model where the system could be defined as only the sheep in the simulated herd; the only inputs are vaccination and price information. As one can see, the differentiation of systems models from the other model types is somewhat debatable. However, we believe it is still a useful distinction. This is particularly true if one considers the historical perspective from which the system-modeling approach is derived, as opposed to the mass-action and chain-binomial models. These latter two types of models are derived from the dynamics of interactions between individuals, with strict emphasis on the assumptions of infectious disease; by collecting the experiences of individuals, the models are able to describe a dynamic population. The systems models, on the other hand, begin from the top down in describing the behavior of an unstructured problem. A systems model will use any mathematical, computerized or symbolic means in order to describe the important phenomena. If a systems model ends up using a mass-action or chain-binomial model, it is to represent the behavior of that system best, although modifications are usually made to reduce (but perhaps not eliminate) the assumptions required. If assumptions are made it is because they are not considered to be important, or—lamentably—because the data are lacking. This is in contrast to the other model types which often make assumptions due to mathematical constraints of the base model, and then force a situation to fit.

Whether a model was applied or theoretical usually was clear. Many articles concluded by saying that the model could be applied to a specific problem,

implying that it had not been applied as yet. Some models were obviously theoretical, as they began with another author's model and made certain changes, testing the effects of those changes against an example dataset. There is a much smaller group of articles that seemed to have originated with the intent of making some epidemiologic conclusions; however, due to lack of data, the authors of these papers were forced to conclude that the models could be more valuable, given the appropriate data.

Further research

It is often the case that the modeling exercise brings to light important deficiencies in the available body of knowledge (Martin et al., 1987). The model can be used to demonstrate the importance of the missing data and direct-data collection efforts. Model building is an important means of generating and formalizing hypotheses.

Given the potential value of systems modeling and the relative paucity of work in this area it is reasonable to conclude that a great deal more work needs to be done. This work should be in the areas of model development and the application to specific veterinary problems (Riemann, 1988). It is likely that veterinary epidemiologists will be the leaders in this area as they commonly deal with populations and the unit of concern is often the herd. Much work will be related to the behavior of these populations within the context of the overall production system. Here, one can see the need for the systems approach to the interactions between the financial system, animal system, and crop system. The systems approach is more than a modeling technique—it is a point of view that is essential for the modern practitioner of veterinary preventive medicine, and its development should be encouraged. It has been recommended for inclusion in the educational curriculum of medical and public health practitioners (Nokes and Anderson, 1988).

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REFERENCES

- Abbey, H., 1952. An examination of the Reed–Frost theory of epidemics. *Hum. Biol.*, 24: 201–233.
- Ackerman, E., Elveback, L.R. and Fox, J.P., 1984. *Simulation of Infectious Disease Epidemics*. Charles C. Thomas, Springfield, IL.
- Akhtar, S., Gardner, I.A., Hird, D.W. and Holmes, J.C., 1988. Computer simulation to compare

- three sampling plans for health and production surveillance in California dairy herds. *Prev. Vet. Med.*, 6: 171–181.
- Anderson, R.M. and Greenfell, B.T., 1986. Quantitative investigations of different vaccination policies for the control of congenital rubella syndrome (CRS) in the United Kingdom. *J. Hyg.*, 96: 305–333.
- Anderson, R.M. and May, R.M., 1983. Vaccination against rubella and measles: quantitative investigations of different policies. *J. Hyg.*, 90: 259–325.
- Anderson, R.M. and May, R.M., 1985. Helminth infection of humans: math models, population dynamics and control. *Adv. Parasitol.*, 24: 1–9.
- Anderson, R.M. and May, R.M., 1986. The invasion, persistence and spread of infectious diseases within animal and plant communities. *Philos. Trans. R. Soc. London Ser. B*, 314: 533–570.
- Anderson, R.M., Crombie, J.A. and Grenfell, B.T., 1987. The epidemiology of mumps in the U.K.: a preliminary study of virus transmission, herd immunity, and the potential impact of immunization. *J. Hyg.*, 99: 65–84.
- Angulo, J.J., 1987. Interdisciplinary approach in epidemiological studies. II. Four geographic models of the flow of contagious disease. *Soc. Sci. Med.*, 24(1): 57–69.
- Bailey, N.T.J., 1955. Some problems in the statistical analysis of epidemic data. *J. R. Statist. Soc. Ser. B*, 17: 35–68.
- Bailey, N.T.J., 1975. *The Mathematical Theory of Infectious Diseases and its Applications*, 2nd edn. Charles Griffin, London.
- Bailey, N.T.J., 1982. *The Biomathematics of Malaria*. Charles Griffin, London, 210 pp.
- Bailey, N.T.J. and Thompson, M., 1975. *Systems Aspects of Health Planning*. World Health Organization, Geneva, 347 pp.
- Barrett, J.C., 1988. Monte Carlo simulation of the heterosexual selective spread of the human immunodeficiency virus. *J. Med. Virol.*, 26: 99–109.
- Bart, K.J., Orenstein, W.A., Hinman, A.R. and Amler, R.W., 1983. Measles and models. *Int. J. Epidemiol.*, 12: 263–266.
- Bartlett, M.S., 1953. Stochastic processes or the statistics of change. *Appl. Statist.*, 2: 44–64.
- Brogger, S., 1967. Systems analysis in tuberculosis control: a model. *Am. Rev. Resp. Dis.*, 95: 421–434.
- Carpenter, T.E. and Howitt, R.E., 1988. Dynamic programming approach to evaluating the economic impact of disease on production. *Acta Vet. Scand.*, 84: 356–359.
- Carpenter, T. and Riemann, H., 1979. Benefit-cost analysis of a disease eradication program in the United States: a case study of mycoplasma meleagridis in turkeys. In: *Proceedings Second International Symposium on Veterinary Epidemiology and Economics*, 7–11 May 1979, Canberra, Australia, pp. 458–462.
- Carpenter, T.E., Berry, S.L. and Glenn, J.S., 1987. Economics of *Brucella ovis* control in sheep: epidemiological simulation model. *J. Am. Vet. Med. Assoc.*, 190(8): 977–982.
- Catalano, R. and Serxner, S., 1987. Time series designs of potential interest to epidemiologists. *Am. J. Epidemiol.*, 126(4): 724–731.
- Checkland, P. (Editor), 1981. *Systems Thinking, Systems Practice*. John Wiley, New York.
- Chestnut, H., 1965. *Systems Engineering Tools*. John Wiley, New York, 646 pp.
- Cohen, J.E., 1977. Mathematical models of schistosomiasis. *Annu. Rev. Ecol. Syst.*, 8: 209–233.
- Croll, N.A., Anderson, R.M., Gyorkos, T.W. and Ghadirian, E., 1982. The population biology and control of *Ascaris lumbricoides* in a rural community in Iran. *Trans. R. Soc. Trop. Med. Hyg.*, 76: 187–197.
- Cvjetanovic, B., Grab, B. and Uemura, K., 1971. Epidemiological model of typhoid fever and its use in planning and evaluation of antityphoid immunization and sanitation programmes. *Bull. WHO*, 45: 53–75.
- Cvjetanovic, B., Grab, B., Uemura, K. and Bytchenko, B., 1972. Epidemiological model of

- tetanus and its use in the planning of immunization programmes. *Int. J. Epidemiol.*, 1: 125–137.
- Cvjetanovic, B., Uemura, K., Grab, B. and Sundaresan, T., 1973. Use of mathematical models in the evaluation of the effectiveness of preventive measures against some infectious diseases. In: *Uses of Epidemiology in Planning Health Services, Proceedings 6th International Meeting, International Epidemiological Association, 29 August to 3 September 1971, Pri-mosten, Yugoslavia, Vol. 2. International Epidemiological Association, London*, pp. 913–933.
- Cvjetanovic, B., Grab, B. and Dixon, H., 1982. Epidemiological models of poliomyelitis and measles and their application in the planning of immunization programmes. *Bull. WHO*, 60: 405–422.
- Dietz, K., 1967. Epidemics and rumours: a survey. *J. R. Statist. Soc. Ser. A.*, 130: 502–528.
- Dietz, K., 1981. The evaluation of rubella vaccination strategies. In: R.W. Hiorns and D. Cooke (Editors), *The Mathematical Theory of the Dynamics of Biological Populations, Vol. II. Academic Press, London*, pp. 81–98.
- Dietz, K. and Schenzle, D., 1985. Mathematical models for infectious disease statistics. In: A.C. Atkinson and S.E. Fienberg (Editors), *A Celebration of Statistics. The ISI Centenary Volume. Springer-Verlag, New York*, pp. 167–204.
- Dietz, K., Molineaux, L. and Thomas, A., 1974. A malaria model tested in the African savannah. *Bull. WHO*, 50: 347–357.
- Dijkhuizen, A.A., 1988. Epidemiological and economic evaluation of foot-and-mouth disease control strategies, using a Markov chain spreadsheet model. *Acta Vet. Scand.*, 84: 350–352.
- Dijkhuizen, A.A., Stelwagen, J. and Renkema, J.A., 1986. A stochastic model for the simulation of management decisions in dairy herds with special reference to production, reproduction, culling, and income. *Prev. Vet. Med.*, 4: 273–289.
- Elveback, L.R., Ackerman, E., Gatewood, L. and Fox, J.P., 1971. Stochastic two-agent epidemic simulation models for a community of families. *Am. J. Epidemiol.*, 93: 267–280.
- Elveback, L.R., Fox, J.P., Ackerman, E., Langworthy, A., Boyd, M. and Gatewood, L., 1976. An influenza simulation model for immunization studies. *Am. J. Epidemiol.*, 103: 152–165.
- Farrow, S.C., Fisher, D.J.H. and Johnson, D.B., 1971. Statistical approach to planning an integrated haemodialysis/transplantation programme. *Br. Med. J.*, 2: 671–676.
- Fine, P.E.M., 1979. John Brownlee and the measurement of infectiousness: an historical study in epidemic theory. *J. R. Statist. Soc. Ser. A*, 142: 347–362.
- Fine, P.E.M., 1982. Background paper. In: P. Selby (Editor), *Influenza Models—Prospects for Development and Use. MTP Press, Boston*, pp. 15–85.
- Fine, P.E.M., Aron, J.L., Berger, J., Bradley, D.J., Burger, H.J., Knox, E.G., Seeliger, H.P.R., Smith, C.E.G., Ulm, K.W. and Yekutieli, P., 1982. The control of infectious disease group report. In: R.M. Anderson and R.M. May (Editors), *Population Biology of Infectious Diseases. Springer-Verlag, Berlin*, pp. 121–147.
- Greenwood, M., 1946. The statistical study of infectious diseases. *J.R. Statist. Soc. Part II*, 109: 85–103.
- Haber, M., Longini, Jr., I.M. and Cotsonis, G.A., 1988. Models for the statistical analysis of infectious disease data. *Biometrics*, 44: 163–173.
- Habtemariam, T. and Cho, Y., 1983. A computer based decision-making model for poultry inspection. *J. Am. Vet. Med. Assoc.*, 183(12): 1440–1446.
- Habtemariam, T., Howitt, R.E., Ruppanner, R. and Riemann, H.P., 1982a. The benefit–cost analysis of alternative strategies for the control of bovine trypanosomiasis in Ethiopia. *Prev. Vet. Med.*, 1: 157–168.
- Habtemariam, T., Ruppanner, R., Riemann, H.P. and Theis, J.H., 1982b. An epidemiologic systems analysis model for African trypanosomiasis. *Prev. Vet. Med.*, 1: 125–136.
- Habtemariam, T., Ruppanner, R., Riemann, H.P. and Theis, J.H., 1982c. Evaluation of trypan-

- nosomiasis control alternatives used as epidemiologic simulation model. *Prev. Vet. Med.*, 1: 147–156.
- Harris, R.E., Revfeim, K.J.A. and Heath, D.D., 1980. A decision-oriented simulation for comparing hydatid control strategies. In: W.A. Geering, R.T. Roe and D.D. Heath (Editors), *Veterinary Epidemiology and Economics. Proceedings of the Second International Symposium*, 7–11 May 1979, Canberra. Australian Government Publishing Service, Canberra.
- Hethcote, H.W., 1983. Measles and rubella in the United States. *Am. J. Epidemiol.*, 117: 2–13.
- Hethcote, H.W. and Yorke, J.A., 1984. *Gonorrhea Transmission Dynamics and Control. Lecture Notes in Biomathematics* 56. Springer-Verlag, Berlin, 105 pp.
- Hethcote, H.W., Yorke, J.A. and Nold, A., 1982. Gonorrhea modeling: a comparison of control methods. *Math. Biosci.*, 58: 93–109.
- Horwitz, J.S. and Montgomery, D.C., 1974. A computer simulation model of a rubella epidemic. *Comp. Biol. Med.*, 4: 189–198.
- Hugh-Jones, M.E., 1976. A simulation spatial model of the spread of foot and mouth disease through the primary movement of milk. *J. Hyg.*, 77: 1–9.
- Isham, V., 1988. Mathematical modelling of the transmission dynamics of HIV infection and AIDS: a review. *J. R. Statist. Soc. Ser. A*, 151: 5–30.
- Jenkins, K.B. and Halter, A.N., 1963. A multi-stage stochastic replacement decision model: application to replacement of dairy cows. *Oregon Agric. Exp. Stn. Tech. Bull. No. 67*.
- King, M.E. and Siskind, C.L., 1988. Use of modeling in infectious disease epidemiology. *Am. J. Epidemiol.*, 128(5): 949–961.
- Kitching, R.L., 1983. *Systems Ecology. An Introduction to Ecological Modelling*. University of Queensland Press, St. Lucia, Qld.
- Knox, E.G., 1980. Strategy for rubella vaccination. *Int. J. Epidemiol.*, 9: 13–23.
- Koopman, J., 1987. Modeling problems in epidemiology: diagnosis and treatment or promoting a science of transmission system analyses. Paper presented to Los Alamos National Laboratory, 9 September 1987.
- Kramer, M.A. and Reynolds, G.H., 1981. Evaluation of a gonorrhea vaccine and gonorrhea control strategies based on computer simulation modeling. In: S. Busenberg and K.L. Cooke (Editors), *Differential Equations and Applications in Ecology, Epidemics and Population Problems*. Academic Press, New York, pp. 97–114.
- Law, A.M. and Kelton, W.D., 1982. *Simulation Modeling and Analysis*. McGraw-Hill, New York.
- Lemeshow, S., Tserkovnyi, A., Tulloch, J.L., Dowd, J.E., Lwanga, S.K. and Kejas, J., 1985. A computer simulation of the EPI survey strategy. *Int. J. Epidemiol.*, 14(3): 473–481.
- Levy, D.L., 1984. The future of measles in highly immunized populations. A modeling approach. *Am. J. Epidemiol.*, 120: 39–48.
- Longini, Jr., I.M., Ackerman, E. and Elveback, L.R., 1978. An optimization model for influenza A epidemics. *Math. Biosci.*, 38: 141–157.
- Longini, Jr., I.M., Fine, P.E.M. and Thacker, S.B., 1985. Predicting the global spread of new infectious agents. *Am. J. Epidemiol.*, 123: 383–391.
- McCauley, E.H., Aulaki, N.A., Sundquist, W.B., New, J.C. and Miller, W.M., 1977. A study of the potential economic impact of foot-and-mouth disease in the United States. *Proc. Annu. Meet. U.S. Anim. Health Assoc.*, 81: 284–296.
- MacDonald, G., 1956. Theory and eradication of malaria. *Bull. WHO*, 15: 369–387.
- MacDonald, G., 1965. The dynamics of helminth infections, with special reference to schistosomes. *Trans. R. Soc. Trop. Med. Hyg.*, 59: 489–506.
- MacDonald, D.W. and Bacon, P.J., 1980. To control rabies: vaccinate foxes. *New Sci.*, 87: 640–645.
- McKendrick, A.G., 1926. Applications to mathematics to medical problems. *Proc. Edin. Math. Soc.*, 44: 98–130.

- Manetsch, T.J. and Park, G.L., 1982. System Analysis and Simulation with Applications to Economic and Social Systems. Part I—Methodology, Modeling and Linear System Fundamentals, 4th duplicated edn. Department of Electrical Engineering and Systems Science, Michigan State University, E. Lansing, MI.
- Martin, S.W., Meek, A.H. and Willeberg, P., 1987. Veterinary Epidemiology. Principles and Methods. Iowa State University Press, Ames, IA.
- May, R.M., 1982. Introduction. In: R.M. Anderson and R.M. May (Editors), Population Biology of Infectious Disease. Dahlem Konferenzen. Springer-Verlag, Berlin, pp. 1–12.
- Meek, A.H. and Morris, R.S., 1981. A computer simulation model of bovine fascioliasis. *Agric. Syst.*, 7: 49–77.
- Miller, W.M., 1976. A state-transition model of epidemic foot-and-mouth disease. In: P.R. Ellis, A.P.M. Shaw and A.J. Stephens (Editors), New Techniques in Veterinary Epidemiology and Economics, Proceedings of an International Symposium, July 1976, University of Reading. International Society of Veterinary Epidemiology and Economics, Reading, UK, pp. 51–67.
- Mollison, D., 1977. Spatial contact models for ecological and epidemic spread. *J. R. Statist. Soc. Ser. B*, 39: 283–326.
- Nasell, I., 1976a. A hybrid model of schistosomiasis with snail latency. *Theor. Popul. Biol.*, 10: 47–69.
- Nasell, I., 1976b. On eradication of schistosomiasis. *Theor. Popul. Biol.*, 10: 133–143.
- Nasell, I., 1977. On transmission and control of schistosomiasis, with comments on Macdonald's model. *Theor. Popul. Biol.*, 12: 335–365.
- Nasell, I. and Hirsch, W.M., 1973. The transmission dynamics of schistosomiasis. *Commun. Pure Appl. Math.*, 26: 395–477.
- Nokes, D.J. and Anderson, R.M., 1988. The use of mathematical models in the epidemiological study of infectious diseases and in the design of mass immunisation programmes. *Epidemiol. Infect.*, 101: 1–20.
- Oltenu, P.A., Milligan, R.A., Rounsaville, T.R. and Foote, R.H., 1980. Modelling reproduction in a herd of dairy cattle. *Agric. Syst.*, 5: 193–205.
- Oltenu, P.A., Rounsaville, T.R., Milligan, R.A. and Foote, R.H., 1981. Systems analysis for designing reproductive management programs to increase production and profit in dairy herds. *J. Dairy Sci.*, 64: 2096–2104.
- Oluokun, S.B. and David-West, K.B., 1988. Analytical models of the national herd: factors controlling calf-mortality and their effects on the rural economy. *Acta Vet. Scand.*, 84: 419–422.
- Papoz, L., Simondon, F., Saurin, W. and Sarmini, H., 1986. A simple model relevant to toxoplasmosis applied to epidemiologic results in France. *Am. J. Epidemiol.*, 123: 154–161.
- Paton, G. and Gettinby, G., 1983. The control of a parasitic nematode population in sheep represented by a discrete time network with stochastic inputs. *Proc. R. Irish Acad.*, 83B: 267–280.
- Paton, G. and Gettinby, G., 1985. Comparing control strategies for parasitic gastroenteritis in lambs grazed on previously contaminated pasture: a network modelling approach. *Prev. Vet. Med.*, 3: 301–310.
- ReVelle, C., Feldmann, F. and Lynn, W., 1969. An optimization model of tuberculosis epidemiology. *Manage. Sci.*, 16: B190–B211.
- Reynolds, G.H. and Chan, Y.K., 1974. A control model for gonorrhea. *Bull. Inst. Int. Statist.*, 46(2): 264–279.
- Riemann, H.P., 1988. The future of veterinary epidemiology and economics. *Acta Vet. Scand.*, 84: 85–88.
- Roe, R.T. and Morris, R.S., 1976. The integration of epidemiological and economic analysis in the planning of the Australian brucellosis eradication programme. In: P.R. Ellis, A.P.M. Shaw and A.J. Stephens (Editors), New Techniques in Veterinary Epidemiology and Economics,

- Proceedings of an International Symposium, July 1976, University of Reading. International Society of Veterinary Epidemiology and Economics, Reading, UK, pp. 75–88.
- Ross, R., 1911. The Prevention of Malaria, 2nd edn. Murray, London.
- Sattenspiel, L., 1987. Epidemics in nonrandomly mixing populations: a simulation. *Am. J. Phys. Anthropol.*, 73: 251–265.
- Shonkwiler, R. and Thompson, M., 1986. A validation study of a simulation model for common source epidemics. *Int. J. Biomed. Comput.*, 19: 175–194.
- Smith, R.D., 1983. *Babesia bovis*: computer simulation of the relationship between the tick vector, parasite, and bovine host. *Exp. Parasitol.*, 56: 27–40.
- Soper, H.E., 1929. Interpretation of periodicity in disease-prevalence. *J.R. Statist. Soc.*, 92: 34–73.
- Sorensen, J.T., 1988. Examining the impact of different health levels and management strategies on dairy heifer production through computer simulation. *Acta Vet. Scand.*, 84: 496–498.
- Susser, M., 1985. Epidemiology in the United States after World War II: the evolution of technique. *Epidemiol. Rev.*, 7: 147–177.
- Sutherland, J.W., 1975. Systems. Analysis, Administration, and Architecture. Van Nostrand Reinhold, New York.
- Sutmoller, P., 1986. Computer simulation of foot-and-mouth disease vaccine potency tests. *Prev. Vet. Med.*, 4: 329–339.
- Thrusfield, M., 1986. Veterinary Epidemiology. Butterworths, London, 280 pp.
- Tsevat, J., Taylor, W.C., Wong, J.B. and Pauker, S.G., 1988. Isoniazid for the tuberculin reactor: take it or leave it. *Am. Rev. Resp. Dis.*, 137: 215–220.
- Waller, H.T., 1968. A dynamic model for the epidemiology of tuberculosis. *Am. Rev. Resp. Dis.*, 98: 591–600.
- Waller, H.T., Geser, A. and Andersen, S., 1962. The use of mathematical models in the study of the epidemiology of tuberculosis. *Am. J. Publ. Health*, 52: 1002–1013.
- Wickwire, K., 1977. Mathematical models for the control of pests and infectious diseases: a survey. *Theor. Popul. Biol.*, 11: 182–238.