larly in the groups. Since the primary purpose of this study is to isolate the effects of treatment on survival, a method of analysis which would correct the observed survival experience for the effects of these covariates is necessary.

The thesis presented here is divided into two parts. The first portion deals with the development and testing of a mathematical model [which considers covariables] to predict survival in this diabetic population. The second portion is concerned with analyzing these data to determine the comparative effects of severe antihypoglycemic therapies on survival.

Dissimilarities in the distribution of potentially confounding variables are not unusual in observatonal studes. If the sze of the study population is large then analysis of survival is possible by subclassifying individuals on the basis of risk level and appyling the traditional life table methods described by Chiang (*1*), Elveback (*2*) or Cutler and Ederer (*3*) or by methods of relative survival discussed by Ederer et al. (*4*) within each risk category. Often, however, the size of the study population is not large enough for this to be a feasible approach. In such cases, it is desirable to have an appropriate mathematical model which considers the effect on survival both of the confounding variables and the specific treatments.

Most often, models of the exponential form, i.e. where

$$(1.1)\quad P(T)=Pr(\text{surviving to time } T)=e^{\alpha\lambda T}$$

(λ is known as the force of mortality) are postulated as the appropriate formulation for describing survival over time. Recently the form of the exponent in (1.1) has been modified (*5*, *6*, *7*) to include covariables.

For example,

$$(1.2a)\quad P_i(T)=Pr\ (\text{ith person survives to time } T)=e^{-\lambda_i T}$$

where

$$(1.2b)\quad \lambda_i=1/(a+bx_i)$$

or

$$(1.2c)\quad \lambda_i=e^{(a+bx_i)}$$

and x_i is the value of the covariate for the ith person. Generally such models include only one covariable and even in such simple cases, iteration is necessary to estimate the parameters in the exponent. Mantel and Myers (*8*) have recently extended the model to the case of three covariates and discuss the problems in covergence encountered in the iterative process. Further discussion of these covariate approaches may be found in Chapter II.

In each of the cases discussed above, the model is used to predict the survival experience of persons acutely ill with cancer. In only one case (of 34 total individuals) is there any attempt to test goodness of fit. Work done by Drolette (*9*) suggests that simple exponential models are not sufficient to describe the observed survival experience of a chronically ill population.

In chapter II an exponential model is postulated which considers the effects of four covariates plus three treatments on survival in the Joslin Clinc data. It is the purpose of this paper to generate the maximum liklihood equations necessary to estimate the parameters of this model; to compare the problems in convergence observed here with those encountered by Mantel and Myers and to investigate methods of handling them; and, finally, to evaluate the ability of this exponential model to describe the observed surviva experience of lthe popuation both in terms of the overall fit to the data and as compared to two simpler forms of the exponential.

The results of this investigaton show that estimation o fthe parameters is difficult and requires some unuual (though common sensical) manipulations to ensure convergence; and that although this model does make it possible to delineate individuals on the basis of risk, it does not adequately reproduce the observed survival experience of this population.

In the discussion, several alternatives to the exponential formuation are considered athough the best one (if any) is not readily aparent. It is suggested that the ability of the exponential to describe survival in other chronically ill populations be investigated as well as the alternative models.

The purpose of Chapter III is to present data about the relationship of three anti-diabetic treatments on survival in a population of diabetics. The three treatments considered are: insulin, tolbutamide (both given to control the level of blood glucose) and control by diet alone. It is of particular interest to determine if individuals treated with tolbutamide are more likely to die from cardiovascular causes than persons treated by either of the other two regimens.

As was mentioned previously, patients are not randomly assigned to treatment groups and, therefore, treatment is intimately linked to the severity of the