# Working Paper

THE EXPECTED NUMBER OF TRANSITIONS FROM ONE STATE TO ANOTHER: A MEDICO-DEMOGRAPHIC MODEL

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FOREWORD

The principal aim of health care research at IIASA has been to develop a family of submodels of national health care systems for use by health service planners. The modeling work is proceeding along the lines proposed in the Institute's current Research Plan. It involves the construction of linked submodels dealing with population, disease prevalence, resource need, resource allocation, and resource supply.

In this paper Anatoli Yashin focuses on the changing health status of a population as revealed by a multistate analysis of transitions between various states of illness and the healthy state. The mathematical apparatus that he outlines yields useful indices of the frequencies of demands for health care services.

Recent related publications in the Health Care Systems Task are listed at the end of this paper.

Andrei Rogers
Chairman
Human Settlements
and Services Area

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## ABSTRACT

Medico-demographic models are used to describe the dynamic properties of a population's health status. In these models the human population is represented as a number of interacting social groups of individuals whose dynamic properties are birth, aging, death, and the transition of an individual from one state to another. The probability of these transitions plays a central role in the analysis of a population's health status.

This paper concentrates on the expected number of transitions between states of selected groups of individuals and other variables from both discrete and continuous time models using the Markovian assumption. Correlation properties of the variables generated by the transition properties are also investigated.

The derived formulas and properties may help the health care decision maker to estimate the expected frequency of hospitalization and the expected number of visits to physicians during a selected time interval. It also gives a reasonable basis for calculating health care resource demands within the limits of the assumptions used. Forecasting transition probabilities helps in detecting possible future problems that may arise in a health care system.

CONTENTS

# THE EXPECTED NUMBER OF TRANSITIONS FROM ONE STATE TO ANOTHER: A MEDICO-DEMOGRAPHIC MODEL

## 1. INTRODUCTION

Health care systems are special regulators of the health status of a population. Although these systems may vary throughout the world, they all carry out identical primary functions and pursue identical goals: the availability of medical experience and knowledge to individuals requiring health care.

Throughout the centuries of human evolution, disease has appeared in different forms. At the beginning of civilization, epidemic diseases were the main danger for human beings. Step by step, the spectrum of diseases has changed over time, until now cardiovascular disease and cancer are the main causes of mortality in developed countries. In response to these disease transformations, local health care systems continually change their structures and redefine the emphasis of their programs. New problems are continually being generated by the rapid change of environment and the social-economic conditions of life in different countries. Are the health care systems ready to meet these problems? One of the main purposes of health care system modeling is to give a correct answer to this question. Another purpose is to help health care decision makers solve the management problems that arise from these new conditions.

The decision maker who learns to use these models as an aid in policy planning is more informed and therefore able to make a wiser decision.

The ability to adapt is an immanent property of natural biological living systems. When these systems start to lose this property, the process of deterioration, which comes from aging, begins to take place and ends with either death or renewal. Within this biological framework, one can say that social and organizational systems have one remarkable property: their aging and adaptation processes are controllable. Returning to the health care systems, we can formulate the problem of controlling the adaptation processes to new conditions and use the modeling approach for this purpose.

The methodology used in health care modeling addresses the peculiarities of the system that distinguish it from other socio-economic systems (Venedictov 1976, Yashin and Shigan 1978, Shigan et al. 1979, Shigan and Kitsul 1980). Some of these peculiarities are:

-- The heterogeneity of the human population from the medical point of view
-- The changing of the heterogeneity characteristics over time
-- The important role of the human factor at different levels of control
-- Uncertainties in the links between health care subsystems and the environment
-- The absence of a unique formal criterion of managing health care systems
-- The variety of the sources of information used for decision making (biological, physiological, medical, demographic, etc.)

For this reason, models in health care often have a probabilistic description, are oriented to a multicriterion optimization, contain behavioral aspects, and use formal and informal procedures to check their validity (Yashin and Shigan 1978).

The dynamic properties of a population's medical heterogeneity are described with the help of medico-demographic models. The methodology of designing such models presupposes that the population under investigation may be divided into a finite number of social groups. If we let N denote the number of these groups, we may numerate them by 1,2,...,N and relate each of them to social, medical, and spatial factors, which are common to the majority of people. Two sets of social groups are relevant for selection in medico-demographic models. One of them characterizes the population's medical status and corresponds to unhealthy groups with different kinds of illnesses. For example, the people who have tuberculosis may be considered as one group; another group may contain the people with cancer. A more detailed consideration would include the different stages of the diseases. "Vaccinated", "initial stage", "intermediate stage", "active form" are examples of such divisions. (Begun et al. 1980, Waaler and Piot 1969).

Another set of groups characterizes the healthy portion of the population. The structure of this part arises as a result of the difference in probabilities of falling into illness in different social, professional, ethnic or spatial groups. These groups identify the different chances of becoming ill and may be called risk groups. In special cases researchers introduce some auxiliary groups such as "latent ill" in screening models (Petrovski et al. 1978) or "susceptible" in epidemic disease models (Waaler and Piot 1969). The dynamic properties of the medico-demography model reflect birth, aging, and death processes as well as the transitions of individuals from one group to another (e.g., transitions from the state of being healthy to being ill, from ill to death, a change in social status, a change in residence, etc.)

The central part of our research will be the model of individual transitions. One of the generally accepted properties used in describing individual transitions between states is the Markovian property. It implies that the individual's behavior is modeled by the Markovian type of stochastic process with a finite number of states in discrete or continuous time. Using a Markov model, one may derive useful characteristics such as the number of individuals in different groups, their specific sex and age distributions, their expected period of stay in the group, and the group from which they came. These characteristics are also important for the estimation of the influence of the health care acitivity on external economic subsystems. The mathematical description of the medico-demographic model is close to that used in the investigations of multiregional migration (Rogers 1975) and manpower dynamics (Bartholomew 1973). The main distinction is to be found in the internal structure of transition coefficients, the spectrum of output variables, and the peculiarities of the available information that is used for the estimation of unknown parameters.

In this paper we consider the properties of the special class of random variables generated by the sampling path of such a Markov process. Among them are the expected number of transitions from one state to another during the selected time interval, the number of departures from various states during the selected time interval, and the number of entries into various states during the selected time interval. Expressions for average values of these variables and also the structure of their covariance matrix are of interest in this model. In the case of a constant intensity matrix in continuous time, some of the properties of the expected number of events may be found in Albert (1962).

## 2. THE EXPECTED NUMBER OF EVENTS IN THE DISCRETE TIME MARKOV PROCESS MODEL

The transitions of individuals from one state or group to another generate a sequence of random events whose statistical properties are interesting for the researchers of multistate population dynamics. One such sequence may be represented by the transitions between two selected groups. The average number of these transitions during the given time interval is often an important frequency characteristic, useful for many social, economic, and medical applications. The expected number of transitions that a person makes from one region to another during a selected time interval reflects the migration inclinations of individuals, a factor that influences the economic status of the regions. The frequency of changing professional status reflects employment situations. The properties of the expected numbers of transitions are important characteristics of marriage-divorce processes in multistate demographic models. They are also useful in the investigations of childbearing, abortions, criminal behavior, and road accidents. They may characterize the frequency of transitions between the different branches of an economy, the quantity of breakages and repairs of technical equipment, the elimination of technological processes, and so on.

In the medical field many transitions can be analyzed and projected through a Markov process model, thus providing us with information concerning not only changes but also the effects these changes have on society. In the simplest case of one group being healthy and another ill, such a model can predict the expected number of people who will fall ill during a selected time interval as well as define the expected duration of time spent in this state and the expected load on the medical service system. The average number of transitions between stages of a particular disease characterizes the peculiarities of the evolution of that illness, the properties of the applied drugs, and the peculiarities of the curing procedure.

All the examples mentioned above can be expressed in a similar way mathematically. Assume that the behavior of "standard" individuals is described by the discrete time finite state Markov chain $y(t)$, with the transition probabilities matrix $\underset{\sim}{P} = [P_{ij}(t)]$ $i,j = \overline{1,N}$, $t = 0,1,2,\ldots$. The initial distribution is given as $P_i(0)$, $i = \overline{1,N}$. The duration of process $y(t)$ in state $j$ is interpreted as an individual staying in group $j$.

Denote by $N_{ij}(t)$ the number of transitions from $i$ to $j$ that are made by individual during the time interval $[0,t]$. The point of our interest is the expression for E $N_{ij}(t)=\overline{N}_{ij}(t)$, which is the expected number of transitions from i to j during the time interval [0,t]. The symbol E denotes the operator of the mathematical expectation and $\overline{N}_j(t)$ will represent the expected number of entries to state j during the time interval [0,t]. Besides the expected number of transitions between two selected groups, some other characteristics are also important for users of medico-demographic models. Among them are the expected number entering a selected state, the expected total number of deaths for all reasons, the average number of hospitalizations during the year, the expected number of road accidents, etc., are all examples of useful output variables of this model.

Other important output variables of medico-demographic models are the expected numbers of departures from selected states. The average number of departures from the state of being healthy during a selected time interval characterizes the general morbidity of a region. The expected number of departures from the initial stage of a degenerative disease during a selected time interval depicts the speed of disease development and may also reflect the efficiency of the cure. We will denote the expected number of departures from the state i by the symbol $\overline{N}^i(t)$. Some generalizations of these variables include the expected number of transitions between two different sets of social groups, the expected number entering selected social groups or average number of departures from such groups during some time interval. These generalizations are necessary for the aggregation of the data in order to design a general strategy for a population's health system.

If A and B are the given sets of groups, we will denote by $\overline{N}_{AB}(t)$, $\overline{N}_B(t)$, and $\overline{N}^A(t)$ as the corresponding expected number of transitions between sets A and B, the expected number entering set B, and the expected number departing from set A, respectively. The convenient expressions for these variables are given in the following theorem.

THEOREM 1. *Let $y(t)$ be the discrete time Markov process with finite number of states $N$ and a one-step transition probability matrix $[P_{ij}^{(k)}]$ $i,j = \overline{1,N}$, $k=1,2,\ldots$. The following expressions are true for the expected number of events which were introduced above.*

$$\bar{N}_{ij}(t) = \sum_{k=1}^{t} P_i(k-1)P_{ij}(k), \quad i,j=\overline{1,N}, \quad i\neq j \tag{1}$$

$$\bar{N}_j(t) = \sum_{i\neq j} \sum_{k=1}^{t} P_i(k-1)P_{ij}(k), \quad j=\overline{1,N} \tag{2}$$

$$\bar{N}^i(t) = \sum_{j\neq i} \sum_{k=1}^{t} P_i(k-1)P_{ij}(k), \quad i=\overline{1,N} \tag{3}$$

$$\bar{N}_{AB}(t) = \sum_{i\in A} \sum_{j\in B} \sum_{k=1}^{t} P_i(k-1)P_{ij}(k) \tag{4}$$

$$\bar{N}_B(t) = \sum_{j\in B} \sum_{i\notin B} \sum_{k=1}^{t} P_i(k-1)P_{ij}(k) \tag{5}$$

$$\bar{N}^A(t) = \sum_{i\in A} \sum_{j\notin A} \sum_{k=1}^{t} P_i(k-1)P_{ij}(k) \tag{6}$$

*The probabilities $P_i(k)$, $k=1,2,\ldots$, may be calculated from the discrete time Kolmogorov equations*

$$P_i(k) = \sum_{m=1}^{N} P_m(k-1)P_{mi}(k), \quad P_i(0), \quad i=\overline{1,N} \tag{7}$$

The proof of these formulas is given in Appendix A.

## 3. THE EXPECTED NUMBER OF EVENTS IN THE CONTINUOUS TIME FINITE STATE MARKOV PROCESS MODEL

Attempts to make the model of individual behavior more realistic leads to generalizations of the previous Markov chain scheme. One reason for this is the fact that individual transitions may occur at arbitrary time moments in a selected time interval. This circumstance compels one to replace the discrete time scheme with the more realistic continuous time model. Thus in this section the individual's transition behavior will be described by the continuous time Markov process which will be denoted by $y(t)$. The method of investigating these transitions in continuous time will be based on the previous results, which were obtained for the discrete time case, and on the use of some limited operations (see Appendix B).

Let $q_{ij}(t)$, $i,j=\overline{1,N}$ be the transition intensities of the continuous time Markov process $y(t)$, $q_{ij}(t) > 0$, $i \neq j$, $q_{jj}(t) = -\sum_{i} q_{ji}(t)$. We will use the same notation for the expected number of events, as in the discrete time case. The following theorem gives us the expression for these variables.

THEOREM 2. *Let $y(t)$ be the continuous time Markov process with a finite number of states $N$ and a transition intensity matrix $[q_{ij}(t)]$, $i,j=\overline{1,N}$, $t>0$. The following expressions are true for the expected number of events generated by $y(t)$:*

$$\overline{N}_{ij}(t) = \int_0^t P_i(s)q_{ij}(s)ds \tag{8}$$

$$\overline{N}_j(t) = \sum_{i\neq j} \int_0^t P_i(s)q_{ij}(s)ds \tag{9}$$

$$\overline{N}^i(t) = \sum_{j\neq i} \int_0^t P_i(s)q_{ij}(s)ds \tag{10}$$

$$\overline{N}_{AB}(t) = \sum_{i\in A} \sum_{j\in B} \int_0^t P_i(s)q_{ij}(s)ds, \qquad A\cap B = \phi \tag{11}$$

$$\overline{N}_B(t) = \sum_{i \notin B} \sum_{j \in B} \int_0^t P_i(s) q_{ij}(s) ds \quad (12)$$

$$\overline{N}^A(t) = \sum_{i \in A} \sum_{j \notin A} \int_0^t P_i(s) q_{ij}(s) ds \quad (13)$$

where $P_i(s)$, $i=\overline{1,N}$ satisfies the Kolmogorov forward equations:

$$P_i(t) = \int_0^t \sum_{k=1}^{N} P_k(s) q_{ki}(s) ds + P_i(0) \quad (14)$$

In application one sometimes needs to know the expected number of transitions which occur during the time interval $[x,t]$, where $x > 0$. Denote this value by $\overline{N}_{ij}(x,t)$. It is not difficult to see that with the help of similar calculations we can find

$$\overline{N}_{ij}(x,t) = \int_x^t P_i(s) q_{ij}(s) ds$$

Sometimes one may have some additional information about the state of the process $y(t)$ at the initial time moment or at time moment $x > 0$. So denoting by $\overline{N}_{ij}(x,t,k)$ the expected number of events which occur during time interval $[x,t]$ given $y(0)=k$ and by $\overline{N}^k_{ij}(x,t)$ the expected number of events which occur during the same time interval given $y(x)=k$ and using the calculation as before, we get

$$\overline{N}_{ij}(x,t,k) = \int_x^t P_{ki}(s) q_{ij}(s) ds$$

$$\overline{N}^k_{ij}(x,t) = \int_x^t P_{ki}(x,s) q_{ij}(s) ds$$

where $P_{ki}(s)$ and $P_{ki}(x,s)$ are the solutions of the Kolmogorov equations

$$P_{ki}(s) = \delta_{ki} + \sum_{z=1}^{N} \int_0^s P_{kz}(u) q_{zi}(u) du$$

$$P_{ki}(x,s) = \delta_{ki} + \sum_{z=1}^{N} \int_x^s P_{kz}(x,u) q_{zi}(u) du$$

## 4. THE PROPERTIES OF THE SECOND MOMENTS OF RANDOM PROCESSES GENERATED BY THE SEQUENCE OF EVENTS -- DISCRETE TIME CASE

The expected number of events gives a good but often insufficient characterization of the point processes $N_i(t)$, $N_{ij}(t)$, $N_j(t)$, $i,j=\overline{1,N}$, $t=0,1,2,\ldots,$. In applications, the properties which are connected with the behavior of the second moments of some processes generated by the given sequence of events are also useful. For example, the knowledge of the correlation characteristics between two processes generated by the two sequences of transitions between one couple of groups and another couple of groups correspondingly may be useful for the estimation of the medical demands in medico-demographic models when the information about some transitions is incomplete. The change in variance of the random number of transitions over time characterizes the accuracy of the forecast; the establishment of the independency properties between some of such processes simplifies the further investigations, and so on.

In order to give a precise formulation of the results connected with the second moment properties, we introduce the processes $\mu_{ij}(t)$ with the help of equalities

$$\mu_{ij}(t) = N_{ij}(t) - \sum_{s=1}^{t} I_i(s-1)P_{ij}(s), \quad i,j=\overline{1,N}, \quad t=0,1,2,\ldots,. \tag{15}$$

As is shown in Appendix A the variables

$$I_i(s-1)P_{ij}(s), \quad i,j=\overline{1,N}, \quad s=0,1,2,\ldots,.$$

coincide with the conditional mathematical expectations of the random variables $\Delta N_{ij}(s)$ given the history of the process $y(t)$ up to time $s-1$. So the processes $\mu_{ij}(t)$ may be considered as a sequence of random numbers of transitions between i and j which are bounded by the conditional mathematical expectations. The remarkable property of the processes $\mu_{ij}(t)$ is formulated in the following theorem.

THEOREM 3. *Let the processes* $\mu_{ij}(t)$ *and* $\mu_{km}(t)$ *be generated by the transitions of the process* $y(t)$ *from the state* $i$ *to state* $j$ *and from the state* $k$ *to state* $m$ *respectively. Then the expression for the mathematical expectation of the product* $\mu_{ij}(t)\cdot\mu_{km}(t)$, $i,j=\overline{1,N}$, $k,m=\overline{1,N}$, $i\neq j, k\neq m, t=0,1,2,\ldots,$ *is given by the following equality*

$$E[\mu_{ij}(t)\mu_{km}(t)] = \delta_{ij,km} \sum_{s=1}^{t} P_i(s-1)P_{ij}(s)[1-P_{ij}(s)],$$

$$i,j=\overline{1,N}, \quad t=0,1,2,\ldots \tag{16}$$

where $$\delta_{ij,km} = \begin{cases} 1, & \text{if } i=k,\ j=m \\ 0, & \text{if } i=k, \text{ or } j\neq m \end{cases}$$

is the Kronecker's symbol and $P_i(s)$ satisfies the Kolmogorov equation (7).

*Corollary 1.* From the equality (16) one can see immediately that the processes $\mu_{ij}(t)$ and $\mu_{km}(t)$ are uncorrelated if $i\neq k$ or $m\neq j$.

*Corollary 2.* The expression for the variance of the process $\mu_{ij}(t)$ also follows from the formula (16) when $i=k$, $j=m$. It is

$$E\mu^2_{ij}(t) = \sum_{s=1}^{t} P_i(s-1)P_{ij}(s)[1-P_{ij}(s)], \quad i,j=\overline{1,N}, \quad t=0,1,2,\ldots,. \tag{17}$$

The proof of this theorem is shown in Appendix C.

## 5. THE PROPERTIES OF THE SECOND MOMENTS OF RANDOM PROCESSES GENERATED BY THE SEQUENCE OF EVENTS -- CONTINUOUS TIME CASE

The continuous time case also has similar properties of the second moment of the analogous processes. As before, we will denote by $\mu_{ij}(t)$ the bounded processes defined by the equalities:

$$\mu_{ij}(t) = N_{ij}(t) - \int_0^t I[y(s=i)]q_{ij}(s)ds , \quad i,j=\overline{1,N}, t \geq 0 \qquad (18)$$

The remarkable property of these processes is the subject of the following theorem.

THEOREM 4. *Let the processes* $\mu_{ij}(t)$ *and* $\mu_{km}(t)$ *be generated by the transitions of the processes* $y(t)$ *from the state* $i$ *to state* $j$ *and from the state* $k$ *to state* $m$, *respectively. Then the expression for the mathematical expectation of the product* $\mu_{ij}(t)\mu_{km}(t)$, $i,j=\overline{1,N}$, $k,m=\overline{1,N}$, $i\neq j$, $k\neq m$, $t\geq 0$ *is given by the following equality*

$$E[\mu_{ij}(t)\mu_{km}(t)] = \delta_{ij,km} \int_0^t P_i(s)q_{ij}(s)ds, \; k,j=\overline{1,N}, \; t\geq 0 \qquad (19)$$

*Corollary 1.* If $k\neq 1$ or $m\neq j$ the processes $\mu_{ij}(t)$ and $\mu_{km}(t)$ are uncorrelated.

*Corollary 2.* The variance of the process $\mu_{ij}(t)$ is given by the formula

$$E\mu^2_{ij}(t) = \int_0^t P_i(s)q_{ij}(s)ds \qquad (20)$$

The proofs of the both corollaries is straightforward. The proof of theorem 4 is shown in Appendix D.

## 6. FURTHER GENERALIZATION OF THE TRANSITION MODEL

A number of specialists in the field of demography, sociology, and medical demography (e.g., Rogers 1981) assert that the Markov process model does not satisfactorily describe the regularities in an individual's transitions between different groups. This is because in the Markov process model one does not use the past history of the process, which can fundamentally influence the future behavior of the individual's real life. The next step in making the transition model closer to reality is the relaxation of the Markovian property using the more complicated process simulating the individual's transitions between a finite number of states. Semi-Markov processes are often used as the natural generalization of the Markovian scheme. The main distinction between these two kinds of processes lies in the type of distributions for the time interval that the individual stays in some selected states. In the Markovian case, this distribution is exponential. In the semi-Markovian case, it may be an arbitrary distribution concentrated on the positive half of the real line. Not using the Markovian property complicates the calculations of the output variables of the medico-demographic model and leads to the use of the more sophisticated techniques of martingale theory which is also suitable for the investigation of more complex situations.

The methodology of martingale theory has been developed intensively during the last decade. It also has many applications. The more popular examples of martingales are the likelihood ratio process, stochastic integrals, the sum of zero-mean random variables, and the risk function in stochastic optimal control problems. The notion of martingales $X(t)$ is indistinguishable from the nondecreasing right-continuous family of $\sigma$-algebras $(F_t)$, $t \geq 0$. The martingale $X(t)$ is measurable with respect to $F_t$ for any current time moment $t \geq 0$. Sometimes it is said that martingale $X(t)$ is adapted with respect to $(F_t)$, $t \geq 0$. The properties that distinguish martingales from other stochastic processes, adapted with respect to flow $(F_t)$, $t \geq 0$, are as follows:

(1) $E\ |X(t)| < \infty, \qquad t \geq 0$

(2) $E\ \left(X(t) \mid F_s\right) = X(s), \ s \leq t$

In our consideration the flows of $\sigma$-algebras are generated by the histories of the stochastic processes given on some basic probabiltiy space $(\Omega, F, P)$. Every point process $N_{ij}(t)$ has its own predictable $(F_t)$-adapted process $A(t)$ called "compensator" (Liptser and Shirjaev 1978). The main property of this compensator is that the processes $\mu_{ij}(t)$ $i \neq j$, $t \geq 0$, $i,j = \overline{1,N}$ defined by the equalities $\mu_{ij}(t) = N_{ij}(t) - A_{ij}(t)$ are $(F_t)$ - adapted martingales. In the case of Markovian processes, the compensators $A_{ij}(s)$ were

$$\sum_{s=1}^{t} I_i(s) P_{ij}(s) \qquad \text{and} \qquad \int_0^t I_i(s) q_{ij}(s) ds$$

respectively, for the cases of discrete and continuous time.

The martingale properties of the processes $\mu_{ij}(t)$ allow one to establish the following general relation between expected number of transitions from i to j and the corresponding compensators. This relation follows from the second condition in the definition of martingales and is as follows:

$$E\ N_{ij}(t) = E\ A_{ij}(t)$$

The next step in developing formal description methods for non-Markovian random jumping processes is the probabilistic representation of the compensators $A_{ij}(t)$, that is the representation $A_{ij}(t)$ in terms of probabilistic distributions related with the jumping process $y(t)$. Such research, however, requires a more sophisticated apparatus of the martingale theory and its applications (Neveu 1975, Shirjaev 1980) and deserves separate consideration.

## 7. EXAMPLES

1) Assume that entries into the transition intensity matrix do not depend on time, i.e., $q_{ij}(t)=q_{ij}$. The expression for $\bar{N}_{ij}(t)$ will be

$$\bar{N}_{ij}(t) = q_{ij}\int_0^t P_i(s)ds = q_{ij}\bar{T}_i(t)$$

where $\bar{T}_i$ is the expected time an individual should spend in group i during time interval [0,t]. If N=2 and j=2 represent a terminal state, then $P_1(s)$ is the exponential probability of survival

$$P_1(s) = e^{-q_{12}s}$$

So when $t = \infty$, then $\bar{N}_{12}(\infty) = q_{12}\int_0^\infty P_1(s)ds = 1$

Note that $\int_0^t P_i(s)ds$ is the expected time which an individual spends in state i during the time interval [0,t]. In the case when N=2 and J=2 is a terminal state, this time coincides with the expected time of life $\bar{T}$, and if $q_{12}(t)$ is constant

$$\bar{T} = \frac{1}{q_{12}}$$

2) Consider now the population consisting of two groups of living individuals: the first group being "healthy" and the second, "ill". The third, auxiliary group consists of the population that has died -- an absorbing state. Assume that the elements of the transition intensity matrix are constants

$$Q = \left\| \begin{matrix} q_{11} & q_{12} & q13 \\ q_{21} & q_{22} & q_{23} \\ 0 & 0 & 0 \end{matrix} \right\|$$

It turns out that the Kolmogorov equations for the probabilities of states can be solved in the explicit form in this case. The expressions for these probabilities are as follows:

$$P_1(t) = \Big\{ e^{\lambda_2 t}\Big[(q_{21}+q_{23}+\lambda_2)P_1(o) + q_{21}[1-P_1(o)]\Big] - e^{\lambda_1 t}\Big[(q_{21}+q_{23}+\lambda_2)P_1(o) + q_{21}[1-P_1(o)]\Big]\Big\}/(\lambda_2-\lambda_1)$$

$$P_2(t) = \Big\{ e^{\lambda_2 t}\Big[(q_{12}+q_{13}+\lambda_1)[1-P_1(o)] + q_{12}P_1(o)\Big] - e^{\lambda_1 t}\Big[(q_{12}+q_{13}+\lambda_1)[1-P_1(o)] + q_{12}P_1(o)\Big]\Big\}/(\lambda_2-\lambda_1)$$

$$P_3(t) = 1 + \Big\{ e^{\lambda_2 t}\Big[\lambda_1+q_{13}P_1(o)+q_{23}[1-P_1(o)]\Big] - e^{\lambda_1 t}\Big[\lambda_2+q_{13}P_1(o)+q_{23}[1-P_1(o)]\Big]\Big\}/(\lambda_2-\lambda_1)$$

where $\lambda_2$ and $\lambda_1$ are given by the expressions

$$\lambda_1 = \left(q_{11}+q_{22} - \sqrt{(q_{11}-q_{22})^2 + 4q_{12}q_{21}}\right)/2$$

$$\lambda_2 = \left(q_{11}+q_{22} + \sqrt{(q_{11}-q_{22})^2 + 4q_{12}q_{21}}\right)/2$$

The expected number of transitions from state 1 to state 2 is given in the following expressions

$$N_{12}(t) = \frac{q_{12}}{(\lambda_2-\lambda_1)}\Big\{\frac{1}{\lambda_2}\Big[(-q_{22}+\lambda_2)P_1(o)+q_{21}[1-P_1(o)]\Big](e^{\lambda_2 t}-1) - \frac{1}{\lambda_1}\Big[(q_{22}+\lambda_1)P_1(o)+q_{21}[1-P_1(o)]\Big](e^{\lambda_1 t}-1)\Big\}$$

See the similar calculations in Chiang (1968), Tuma et al. (1979). In the cases of four and more number of states or if the elements of the transition matrix depend on time, the formulas obtained from theorems 1, 2, 3, and 4 give convenient computational expressions for statistical characteristics in the random number of events.

3) Consider a population consisting of the same groups of people as above.

In the tables below, $q_{ij}$, where i,j=1,2,3, denotes the transition coefficient for the discrete time model; p(i), where i=1,2,3, represents the probability of being in state i; $N_{ij}$, where i,j=1,2,3, is the expected number of transitions from i to j; T(i), where i=1,2,3, denotes the time spent by individuals in groups (i), and t is the current time, which changes from 1 to 11. The three groups of individuals may be interpreted as healthy (i or j=1), ill (i or j=2), or dead (j=3).

The first three tables show the results of calculations based on constant transition probabilities ($q_{ij}$, where i,j=1,2,3). In these cases, $N_{ij} = q_{ij} \cdot T(j)$, for any time moment t. (The dependence of the variables on t is omitted in this formula.)

Table 1 shows a high probability of recovery ($q_{21}$=0.8), which generates a relatively high probability of individuals being in the "healthy" group ($P_1$=0.441) over 11 units of time. The expected transitions from "ill" to "healthy" ($N_{21}$) over 11 time units is 2.629. The expected time that individuals spend in the healthy state ($T_1$) is 6.009 time units and in the ill state ($T_2$) is 3.287.

Table 2 differs from Table 1 in that there is a lower probability of recovery ($q_{21}$=0.1). As a result, the probability of being healthy at the end of the time interval is also lower ($P_1$= 0.092) and the expected number of recoveries is 0.559. The expected time that individuals spend in the healthy state is 2.549, as against 5.592 in the ill state.

Table 3 is characterized by the high probability of transition from "ill" to "dead" ($q_{23}$=0.8). As a result the probability of being healthy is 0.004. The expected number of transitions from "ill" to "healthy" is 0.124 and the expected time that individuals spend in the healthy state is short: 1.844.

The last three tables show the results of calculations based on changing some of the transition probabilities $q_{ij}$.

Table 4 shows the transition probability from "healthy" to "ill" changing the variable from 0.5 to 0.9, over time, which results in a high level of transition probability from "ill" to "dead". As a result the probability of a person dying is 0.999. Table 5 represents the case where the probability of remaining ill is high ($q_{22}$=0.8) and morbidity ($q_{12}$) changes as in Table 4. Table 6 shows an increasing morbidity ($q_{12}$) and an increasing probability of dying ($q_{23}$).

## 8. CONCLUSION

The expected number of events which are related to the Markov transition model may be calculated successfully if the corresponding transition probabilities (in discrete time) or transition intensities (in continuous time) are known. The initial probability distribution functions over the states are supposed to be known too. In reality the transition coefficients are the functions of time and the individual's age. For instance, some of these coefficients in medico-demographic models demonstrate age specific morbidity, recovery, and mortality patterns. In the case of multiregional migration they are the age specific migration patterns and so on.

The estimation of the transition coefficient is a very important problem which depends on the available description of the individual's behavior, statistical data, and some additional hypotheses, which explain the motivation or necessity of the transition. The review of these methods deserve special consideration. The expected number of events is not the only important output characteristic of medico-demographic models. The expected time spent in selected states is another characteristic of the population that is essential to health care managers. Combining the expected number of transitions with the expected time span in a selected state provides useful information for decision makers who are concerned with the health of a population.

Table 1. Constant transition probabilities: high recovery rates.

| Variable | Time unit 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Transition probabilities from state i to state j* | | | | | | | | | | | |
| $q_{11}$ | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 |
| $q_{12}$ | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 |
| $q_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{21}$ | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 |
| $q_{22}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{23}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{31}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{32}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{33}$ | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| *Probabilities of being in state 1, 2, or 3* | | | | | | | | | | | |
| p(1) | 0.800 | 0.560 | 0.616 | 0.566 | 0.555 | 0.531 | 0.513 | 0.494 | 0.476 | 0.458 | 0.441 |
| p(2) | 0.200 | 0.420 | 0.322 | 0.340 | 0.317 | 0.309 | 0.296 | 0.286 | 0.275 | 0.265 | 0.256 |
| p(3) | 0. | 0.020 | 0.062 | 0.094 | 0.128 | 0.160 | 0.191 | 0.220 | 0.249 | 0.277 | 0.303 |
| *Expected number of transitions from state i to state j* | | | | | | | | | | | |
| $N_{11}$ | 0.400 | 0.680 | 0.988 | 1.271 | 1.543 | 1.814 | 2.070 | 2.317 | 2.555 | 2.784 | 3.004 |
| $N_{12}$ | 0.400 | 0.680 | 0.988 | 1.271 | 1.548 | 1.814 | 2.070 | 2.317 | 2.555 | 2.784 | 3.004 |
| $N_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $N_{21}$ | 0.160 | 0.496 | 0.754 | 1.026 | 1.279 | 1.527 | 1.764 | 1.992 | 2.213 | 2.425 | 2.629 |
| $N_{22}$ | 0.020 | 0.062 | 0.094 | 0.128 | 0.160 | 0.191 | 0.220 | 0.249 | 0.277 | 0.303 | 0.329 |
| $N_{23}$ | 0.020 | 0.062 | 0.094 | 0.128 | 0.160 | 0.191 | 0.220 | 0.249 | 0.277 | 0.303 | 0.329 |
| *Expected times in state 1, 2, or 3* | | | | | | | | | | | |
| T(1) | 0.800 | 1.360 | 1.976 | 2.542 | 3.097 | 3.627 | 4.140 | 4.634 | 5.109 | 5.567 | 6.009 |
| T(2) | 0.200 | 0.620 | 0.942 | 1.282 | 1.599 | 1.908 | 2.205 | 2.491 | 2.766 | 3.031 | 3.287 |
| T(3) | 0. | 0.020 | 0.082 | 0.176 | 0.304 | 0.464 | 0.655 | 0.876 | 1.125 | 1.401 | 1.704 |

Table 2. Constant transition probabilities: low recovery and mortality rates.

| Variable | Time unit 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Transition probabilities from state i to state j* | | | | | | | | | | | |
| $q_{11}$ | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 |
| $q_{12}$ | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 |
| $q_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{21}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{22}$ | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 |
| $q_{23}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{31}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{32}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{33}$ | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| *Probabilities of being in state 1, 2, or 3* | | | | | | | | | | | |
| p(1) | 0.800 | 0.420 | 0.266 | 0.199 | 0.165 | 0.145 | 0.131 | 0.120 | 0.110 | 0.101 | 0.092 |
| p(2) | 0.200 | 0.560 | 0.658 | 0.659 | 0.627 | 0.584 | 0.540 | 0.498 | 0.458 | 0.421 | 0.387 |
| p(3) | 0. | 0.020 | 0.076 | 0.142 | 0.208 | 0.270 | 0.329 | 0.383 | 0.433 | 0.478 | 0.521 |
| *Expected number of transitions from state i to state j* | | | | | | | | | | | |
| $N_{11}$ | 0.400 | 0.610 | 0.743 | 0.842 | 0.925 | 0.998 | 1.063 | 1.123 | 1.178 | 1.228 | 1.274 |
| $N_{12}$ | 0.400 | 0.610 | 0.743 | 0.842 | 0.925 | 0.998 | 1.063 | 1.123 | 1.178 | 1.228 | 1.274 |
| $N_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $N_{21}$ | 0.020 | 0.076 | 0.142 | 0.208 | 0.270 | 0.329 | 0.383 | 0.433 | 0.478 | 0.521 | 0.559 |
| $N_{22}$ | 0.160 | 0.608 | 1.134 | 1.662 | 2.163 | 2.631 | 3.063 | 3.461 | 3.827 | 4.164 | 4.474 |
| $N_{23}$ | 0.020 | 0.076 | 0.142 | 0.208 | 0.270 | 0.329 | 0.383 | 0.433 | 0.478 | 0.521 | 0.559 |
| *Expected times in state 1, 2, or 3* | | | | | | | | | | | |
| T(1) | 0.800 | 1.220 | 1.486 | 1.685 | 1.850 | 1.996 | 2.127 | 2.246 | 2.356 | 2.456 | 2.549 |
| T(2) | 0.200 | 0.760 | 1.418 | 2.077 | 2.704 | 3.289 | 3.829 | 4.326 | 4.784 | 5.205 | 5.592 |
| T(3) | 0. | 0.020 | 0.096 | 0.238 | 0.446 | 0.716 | 1.045 | 1.428 | 1.860 | 2.339 | 2.859 |

Table 3. Constant transition probabilities: high mortality rates.

| | Time unit | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
| *Transition probabilities from state i to stage j* | | | | | | | | | | | |
| $q_{11}$ | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 |
| $q_{12}$ | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 | 0.500 |
| $q_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{21}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{22}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{23}$ | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 |
| $q_{31}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{32}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{33}$ | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| *Probabilities of being in state 1, 2, or 3* | | | | | | | | | | | |
| p(1) | 0.800 | 0.420 | 0.252 | 0.151 | 0.091 | 0.054 | 0.033 | 0.020 | 0.012 | 0.007 | 0.004 |
| p(2) | 0.200 | 0.420 | 0.252 | 0.151 | 0.091 | 0.054 | 0.033 | 0.020 | 0.012 | 0.007 | 0.004 |
| p(3) | 0. | 0.160 | 0.496 | 0.698 | 0.819 | 0.891 | 0.935 | 0.961 | 0.976 | 0.986 | 0.992 |
| *Expected number of transitions from state i to state j* | | | | | | | | | | | |
| $N_{11}$ | 0.400 | 0.610 | 0.736 | 0.812 | 0.857 | 0.884 | 0.901 | 0.910 | 0.916 | 0.920 | 0.922 |
| $N_{12}$ | 0.400 | 0.610 | 0.736 | 0.812 | 0.857 | 0.884 | 0.901 | 0.910 | 0.916 | 0.920 | 0.922 |
| $N_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $N_{21}$ | 0.020 | 0.062 | 0.087 | 0.102 | 0.111 | 0.117 | 0.120 | 0.122 | 0.123 | 0.124 | 0.124 |
| $N_{22}$ | 0.020 | 0.062 | 0.087 | 0.102 | 0.111 | 0.117 | 0.120 | 0.122 | 0.123 | 0.124 | 0.124 |
| $N_{23}$ | 0.160 | 0.496 | 0.698 | 0.819 | 0.891 | 0.935 | 0.961 | 0.976 | 0.986 | 0.992 | 0.995 |
| *Expected times in state 1, 2, or 3* | | | | | | | | | | | |
| T(1) | 0.800 | 1.220 | 1.472 | 1.623 | 1.714 | 1.768 | 1.801 | 1.821 | 1.832 | 1.839 | 1.844 |
| T(2) | 0.200 | 0.620 | 0.872 | 1.023 | 1.114 | 1.168 | 1.201 | 1.221 | 1.232 | 1.239 | 1.244 |
| T(3) | 0. | 0.160 | 0.656 | 1.354 | 2.172 | 3.063 | 3.998 | 4.959 | 5.935 | 6.921 | 7.913 |

Table 4. Changing transition probabilities: increasing morbidity rates and high mortality rates.

| | Time unit | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
| *Transition probabilities from state i to stage j* | | | | | | | | | | | |
| $q_{11}$ | 0.500 | 0.500 | 0.400 | 0.400 | 0.300 | 0.300 | 0.200 | 0.200 | 0.100 | 0.100 | 0.100 |
| $q_{12}$ | 0.500 | 0.500 | 0.600 | 0.600 | 0.700 | 0.700 | 0.800 | 0.800 | 0.900 | 0.900 | 0.900 |
| $q_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{21}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{22}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{23}$ | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 |
| $q_{31}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{32}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{33}$ | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| *Probabilities of being in state 1, 2, or 3* | | | | | | | | | | | |
| p(1) | 0.800 | 0.420 | 0.210 | 0.113 | 0.050 | 0.024 | 0.009 | 0.004 | 0.001 | 0.001 | 0.000 |
| p(2) | 0.200 | 0.420 | 0.294 | 0.155 | 0.095 | 0.044 | 0.024 | 0.010 | 0.005 | 0.002 | 0.001 |
| p(3) | 0. | 0.160 | 0.496 | 0.731 | 0.856 | 0.931 | 0.967 | 0.986 | 0.994 | 0.998 | 0.999 |
| *Expected number of transitions from state i to state j* | | | | | | | | | | | |
| $N_{11}$ | 0.400 | 0.610 | 0.694 | 0.739 | 0.754 | 0.762 | 0.763 | 0.764 | 0.764 | 0.764 | 0.764 |
| $N_{12}$ | 0.400 | 0.610 | 0.736 | 0.804 | 0.839 | 0.856 | 0.863 | 0.867 | 0.868 | 0.868 | 0.869 |
| $N_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $N_{21}$ | 0.020 | 0.062 | 0.091 | 0.107 | 0.116 | 0.121 | 0.123 | 0.124 | 0.125 | 0.125 | 0.125 |
| $N_{22}$ | 0.020 | 0.062 | 0.091 | 0.107 | 0.116 | 0.121 | 0.123 | 0.124 | 0.125 | 0.125 | 0.125 |
| $N_{23}$ | 0.160 | 0.496 | 0.731 | 0.856 | 0.931 | 0.967 | 0.986 | 0.994 | 0.998 | 0.999 | 1.000 |
| *Expected times in state 1, 2, or 3* | | | | | | | | | | | |
| T(1) | 0.800 | 1.220 | 1.430 | 1.543 | 1.593 | 1.617 | 1.627 | 1.631 | 1.632 | 1.633 | 1.633 |
| T(2) | 0.200 | 0.620 | 0.914 | 1.069 | 1.164 | 1.209 | 1.232 | 1.242 | 1.247 | 1.249 | 1.250 |
| T(3) | 0. | 0.160 | 0.656 | 1.387 | 2.243 | 3.174 | 4.141 | 5.127 | 6.121 | 7.118 | 8.117 |

Table 5. Changing transition probabilities: increasing morbidity rates and low recovery and mortality rates.

| Variable | Time unit 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Transition probabilities from state i to state j* | | | | | | | | | | | |
| $q_{11}$ | 0.500 | 0.500 | 0.400 | 0.400 | 0.300 | 0.300 | 0.200 | 0.200 | 0.100 | 0.100 | 0.100 |
| $q_{12}$ | 0.500 | 0.500 | 0.600 | 0.600 | 0.700 | 0.700 | 0.800 | 0.800 | 0.900 | 0.900 | 0.900 |
| $q_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{21}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{22}$ | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 | 0.800 |
| $q_{23}$ | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 | 0.100 |
| $q_{31}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{32}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{33}$ | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| *Probabilities of being in state 1, 2, or 3* | | | | | | | | | | | |
| p(1) | 0.800 | 0.420 | 0.224 | 0.160 | 0.117 | 0.102 | 0.082 | 0.074 | 0.060 | 0.055 | 0.050 |
| p(2) | 0.200 | 0.560 | 0.700 | 0.694 | 0.667 | 0.616 | 0.574 | 0.525 | 0.486 | 0.443 | 0.404 |
| p(3) | 0. | 0.020 | 0.076 | 0.146 | 0.215 | 0.282 | 0.344 | 0.401 | 0.454 | 0.502 | 0.547 |
| *Expected number of transitions from state i to state j* | | | | | | | | | | | |
| $N_{11}$ | 0.400 | 0.610 | 0.700 | 0.763 | 0.799 | 0.829 | 0.846 | 0.860 | 0.866 | 0.872 | 0.877 |
| $N_{12}$ | 0.400 | 0.610 | 0.744 | 0.840 | 0.922 | 0.994 | 1.059 | 1.118 | 1.172 | 1.221 | 1.266 |
| $N_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $N_{21}$ | 0.020 | 0.076 | 0.146 | 0.215 | 0.282 | 0.344 | 0.401 | 0.454 | 0.502 | 0.547 | 0.587 |
| $N_{22}$ | 0.160 | 0.608 | 1.168 | 1.724 | 2.257 | 2.750 | 3.209 | 3.629 | 4.019 | 4.373 | 4.696 |
| $N_{23}$ | 0.020 | 0.076 | 0.146 | 0.215 | 0.282 | 0.344 | 0.401 | 0.454 | 0.502 | 0.547 | 0.587 |
| *Expected times in state 1, 2, or 3* | | | | | | | | | | | |
| T(1) | 0.800 | 1.220 | 1.444 | 1.604 | 1.721 | 1.823 | 1.905 | 1.979 | 2.039 | 2.093 | 2.143 |
| T(2) | 0.200 | 0.760 | 1.460 | 2.154 | 2.822 | 3.438 | 4.012 | 4.537 | 5.023 | 5.466 | 5.870 |
| T(3) | 0. | 0.020 | 0.096 | 0.242 | 0.457 | 0.740 | 1.083 | 1.485 | 1.938 | 2.441 | 2.987 |

Table 6. Changing transition probabilities: increasing morbidity and mortality rates.

| Variable | Time unit 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Transition probabilities from state i to state j* | | | | | | | | | | | |
| $q_{11}$ | 0.500 | 0.500 | 0.400 | 0.400 | 0.300 | 0.300 | 0.200 | 0.200 | 0.100 | 0.100 | 0.100 |
| $q_{12}$ | 0.500 | 0.500 | 0.600 | 0.600 | 0.700 | 0.700 | 0.800 | 0.800 | 0.900 | 0.900 | 0.900 |
| $q_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{21}$ | 0.600 | 0.600 | 0.500 | 0.500 | 0.400 | 0.400 | 0.300 | 0.300 | 0.200 | 0.200 | 0.100 |
| $q_{22}$ | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 | 0.200 |
| $q_{23}$ | 0.200 | 0.200 | 0.300 | 0.300 | 0.400 | 0.400 | 0.500 | 0.500 | 0.600 | 0.600 | 0.700 |
| $q_{31}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{32}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $q_{33}$ | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| *Probabilities of being in state 1, 2, or 3* | | | | | | | | | | | |
| p(1) | 0.800 | 0.520 | 0.428 | 0.371 | 0.246 | 0.205 | 0.112 | 0.086 | 0.035 | 0.024 | 0.008 |
| p(2) | 0.200 | 0.440 | 0.400 | 0.337 | 0.327 | 0.238 | 0.211 | 0.132 | 0.104 | 0.052 | 0.032 |
| p(3) | 0. | 0.040 | 0.172 | 0.292 | 0.427 | 0.558 | 0.676 | 0.782 | 0.861 | 0.924 | 0.960 |
| *Expected number of transitions from state i to state j* | | | | | | | | | | | |
| $N_{11}$ | 0.400 | 0.660 | 0.831 | 0.980 | 1.054 | 1.115 | 1.137 | 1.155 | 1.158 | 1.160 | 1.161 |
| $N_{12}$ | 0.400 | 0.660 | 0.917 | 1.140 | 1.312 | 1.455 | 1.545 | 1.614 | 1.645 | 1.667 | 1.674 |
| $N_{13}$ | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. | 0. |
| $N_{21}$ | 0.120 | 0.384 | 0.584 | 0.752 | 0.883 | 0.978 | 1.042 | 1.081 | 1.102 | 1.113 | 1.116 |
| $N_{22}$ | 0.040 | 0.128 | 0.208 | 0.275 | 0.341 | 0.388 | 0.431 | 0.457 | 0.478 | 0.488 | 0.495 |
| $N_{23}$ | 0.040 | 0.128 | 0.248 | 0.349 | 0.480 | 0.575 | 0.681 | 0.747 | 0.809 | 0.840 | 0.863 |
| *Expected times in state 1, 2, or 3* | | | | | | | | | | | |
| T(1) | 0.800 | 1.320 | 1.748 | 2.119 | 2.365 | 2.570 | 2.682 | 2.768 | 2.803 | 2.827 | 2.835 |
| T(2) | 0.200 | 0.640 | 1.040 | 1.377 | 1.704 | 1.942 | 2.153 | 2.285 | 2.389 | 2.441 | 2.473 |
| T(3) | 0. | 0.040 | 0.212 | 0.504 | 0.931 | 1.488 | 2.165 | 2.947 | 3.808 | 4.732 | 5.692 |

## APPENDIX A: The Proof of Theorem 1

In order to calculate the value of $\overline{N}_{ij}(t)$, consider the increment of the $N_{ij}(t)$ at an arbitrary moment in time t:

$$\Delta N_{ij}(t) = N_{ij}(t) - N_{ij}(t-1), \quad t=1,2,\ldots,.$$

It is not difficult to see that for $\Delta N_{ij}(t)$ the following equality is true

$$\Delta N_{ij}(t) = I[y(t-1)=i]\ I[y(t)=j]$$

where by $I(\cdot)$ we denote the indicator of random event $(\cdot)$.

Let $F_t$ be the history of the process $y(t)$ up to time t. The conditional mathematical expectation of $\Delta N_{ij}(t)$ given $F_{t-1}$ may be written as follows

$$E[\Delta N_{ij}(t)/F_{t-1}] = I[y(t-1)=i]P_{ij}(t) \tag{A.1}$$

The fact that the indicator $I[y(t-1)=i]$ is measurable with respect to $F_{t-1}$ was used here. Using the definition of $\Delta N_{ij}(t)$ we can represent the expected number of transitions $\overline{N}_{ij}(t)$ with the help of the following expression

$$\overline{N}_{ij}(t) = E \sum_{k=1}^{t} \Delta N_{ij}(k) = \sum_{k=1}^{t} E\,\Delta N_{ij}(k) \qquad (A.2)$$

Taking the mathematical expectation from both parts of equation (A.1) we get

$$E\,\Delta N_{ij}(t) = P_i(t-1)\; P_{ij}(t) \qquad (A.3)$$

and consequently from (A.2)

$$\overline{N}_{ij}(t) = E\, N_{ij}(t) = \sum_{k=1}^{t} P_i(k-1)\; P_{ij}(k) \qquad (A.4)$$

where probabilities $P_i(k)$, $k=0,1,2,\ldots$, may be received from the discrete time Kolmogorov equation

$$P_i(k) = \sum_{m=1}^{N} P_m(k-1)\; P_{mi}(k), \quad P_i(0), \quad i=1,\ldots N$$

A1. The Expected Number Entering State j

Let $N_j(t)$ be the number of process $y(t)$ transitions from arbitrary states to state j. The expected number of these transitions $\overline{N}_j(t) = EN_j(t)$ may be found from the evident relations

$$\overline{N}_j(t) = \sum_{i \neq j} \overline{N}_{ij}(t), \quad j=\overline{1,N}, \; t=0,1,2,\ldots$$

and consequently

$$\overline{N}_j(t) = \sum_{i \neq j} \sum_{k=1} P_i(k-1)\; P_{ij}(k), \quad j=\overline{1,N}, \; t=0,1,2,\ldots \qquad (A.5)$$

A2. The Expected Number Departing from State i

Denote by $N^i(t)$ the number of transitions from state i to an arbitrary state. The expected number of these transitions $\overline{N}^i(t)$ is given by the formula

$$\overline{N}^i(t) = \sum_{j \neq i} \sum_{k=1} P_i(k-1)P_{ij}(k) \qquad (A.6)$$

which can be obtained easily by summing both parts of the equation (1.4) over j.

A3. Some Generalizations

Some generalizations of these formulas for the expected number of transitions are related to the transitions from some set of states to another set of states. Assume that we are interested in the expected number of transitions from the set of states A to the set of states B, $A \cap B \neq \phi$, during the time interval [0,t]. Denote this variable by $\overline{N}_{A,B}(t)$. Using the equation (A.4) one can easily get

$$\overline{N}_{A,B}(t) = \sum_{i \in A} \sum_{j \in B} \sum_{k=1} P_i(k-1)P_{ij}(k)$$

Denote by $\overline{N}_B(t)$ the expected number of the transitions of the process y(t) from any arbitrary state to the set of states B during the time interval [0,t]. It is not difficult to get from (A.5) the following expression:

$$\overline{N}_B(t) = \sum_{j \in B} \sum_{i \notin B} \sum_{k=1} P_i(k-1)P_{ij}(k)$$

In the same way, if $\overline{N}^A(t)$ denotes the number of transitions from the set of the states A to any arbitrary state, from (A.6) one can easily get

$$\overline{N}^A(t) = \sum_{i \in A} \sum_{j \notin A} \sum_{k=1} P_i(k-1)P_{ij}(k)$$

## APPENDIX B: The Proof of Theorem 2

Consider the sequence of the divisions of the time interval $[0,t]$.

$$0=t_0^h,\ t_1^h,\ t_2^h,\ldots t_h^h = t\ ,\ \Delta t^h = t_k^h - t_{k-1}^h = \frac{1}{2^h}\ ,\ h=1,2\ldots$$

According to the definition of the transition intensities let $g_{ij}(t)$ be the probability of being in state j at time moment $t_k^h$ given that y(t) was in the state i at time moment $t_{k-1}^h$. Then

$$P_{ij}(t_{k-q}^h,\ t_k^h) = q_{ij}(t_{k-1}^h)\,\Delta t^h + o(\Delta t^h),\quad i\neq j$$

$$P_{ij}(t_{k-1}^h,\ t_k^h) = 1+q_{jj}(t_{k-1}^h)\Delta t^h + o(\Delta t^h) \qquad (B.1)$$

if the time interval $\Delta t_k^h$ is small enough.

Denote by $y^h(k)$ the discrete time Markov chain which is generated by the continuous time process y(t) at time $t_k^h$, $k=0,1\ldots h$. The transition probabilities for the discrete time process $y^h(k)$ are given by the expressions (B.1). We will denote with index h the variables which are concerned with the discrete time Markov chain $y^h(t)$. Thus, for the expected number of events $\bar{N}^h_{ij}(t)$, we have according to the formula (1)

$$\bar{N}^h_{ij}(t) = \sum_{k=1}^{h} P_i(t^h_{k-1})P_{ij}(t^h_{k-1}, t^h_k)$$

Tending $\Delta t^h$ to zero and using the equalities (B.1) we get

$$\lim_{h\to\infty} \bar{N}^h_{ij}(t) = \int_0^t P_i(s)q_{ij}(s)ds \qquad (B.2)$$

Denote as before by $N_{ij}(t)$, $\bar{N}_{ij}(t)$, $\bar{N}_j(t)$, $\bar{N}^i(t)$, $\bar{N}_{AB}(t)$, $\bar{N}_B(t)$, $\bar{N}^A(t)$, the variables having the same sense as in discrete time and referring to the continuous time processes $y(t)$.

It is clear from the definition of the Markov chain $y^h(k)$ that the following inequality is true for any $t \geq 0$:

$$N^h_{ij}(t) \leq N_{ij}(t), \quad i,j=\overline{1,N}$$

Moreover, when h tends to infinity, $N^j_{ij}(t)$ steadily tends to $N_{ij}(t)$. Changing the orders of the limits and the mathematical expectation on the left-hand side of the formula (B.2) we get

$$\bar{N}_{ij}(t) = \int_0^t P_i(s)q_{ij}(s)ds, \quad i,j=\overline{1,N} \qquad (B.3)$$

## APPENDIX C: The Proof of Theorem 3

Consider the expression for the product $\mu_{ij}(t)\cdot\mu_{km}(t)$ in discrete time. According to the definition of these processes $\mu_{ij}(t)$, $i,j=\overline{1,N}$, given by the expression (15), we have that

$$\mu_{ij}(t)\mu_{km}(t) = N_{ij}(t)N_{km}(t)$$

$$+ N_{ij}(t)\sum_{s=1}^{t} I_k(s-1)P_{km}(s)$$

$$+ N_{km}(t)\sum_{s=1}^{t} I_i(s-1)P_{ij}(s)$$

$$+ \sum_{s=1}^{t} I_i(s-1)P_{ij}(s)\sum_{s=1}^{t} I_k(s-1)P_{km}(s)$$

Taking the mathematical expectation from both parts of this equality, we receive the sum of the four addendums on the right-hand side. The values of each of these are then calculated separately.

Note that the product $N_{ij}(t)\ N_{km}(t)$ may be rewritten in another way

$$N_{ij}(t)N_{km}(t) = \sum_{l=1}^{t} N_{ij}(t-1)\Delta N_{km}(t)$$

$$+ \sum_{l=1}^{t} N_{km}(l-1)\Delta N_{ij}(l) + \sum_{l=1}^{t} \Delta N_{ij}(l)\Delta N_{km}(l)$$

First, consider the mathematical expectation from the first item of the right-hand side of the equation for $N_{ij}(t)N_{km}(t)$

$$E\left[\sum_{s=1} N_{ij}(s-1)\Delta N_{km}(s)\right] = E\left[\sum_{s=1}^{t} N_{ij}(s-1)I_k(s-1)P_{km}(s)\right]$$

where $P_{km}(s)$ denotes the transition probability for one step from the state k at time s-1 to the state m at time s (another notation may be $P_{km}(s-1,s)$. Now let us find the expression for

$$E\left[N_{ij}(s-1)I_k(s-1)\right]$$

We have

$$E\left[N_{ij}(s-1)I_k(s-1)\right] = E\left[I_k(s-1)\sum_{l=1}^{s-1} I_i(l-1)I_j(l)\right] \tag{C. 1}$$

$$= E\left[\sum_{l-1}^{s-1} I_i(l-1)I_j(l)I_k(s-1)\right]$$

Using the Markovian property of the process y(t) we get from (C. 1)

$$E\left[N_{ij}(s-1)I_k(s-1)\right] = E\left[\sum_{l=1}^{s-1} I_i(l-1)I_j(l)P_{jk}(l,s-1)\right] \tag{C.2}$$

$$= \left[\sum_{l=1}^{s-1} P_i(l-1)\ P_{ij}(l)\ P_{jk}(l,s-1)\right]$$

Thus

$$E\left[\sum_{l=1}^{t} N_{ij}(l-1)\Delta N_{km}(l)\right] = \sum_{s=1}^{t}\sum_{l=1}^{s-1} P_i(l-1)P_{ij}(l)P_{jk}(l,s-1)P_{km}(s) \tag{C.3}$$

Making similar calculations, we derive the mathematical expectation of the second component

$$E\left[\sum_{l=1}^{t} N_{km}(l-1)\Delta N_{ij}(l)\right]$$

$$= \sum_{s=1}^{t}\sum_{l=1}^{s-1} P_k(l-1)\ P_{km}(l)P_{mi}(l,s-1)P_{ij}(s)$$

taking into account that $E\left[\Delta N_{ij}(t)\Delta N_{km}(t)\right]$

$$= \delta_{ij,km}\sum_{s=1}^{t} P_i(s-1)\ P_{ij}(s)$$

where $\delta_{ij,km}$ is the Kronecker's symbol

$$\delta_{ijmkm} = \begin{cases} 1 \text{ if } i=k,\ j=m \\ 0 \text{ in other cases} \end{cases}$$

the expression for the expected value of the product $N_{ij}(t)N_{km}(t)$ becomes

$$E\left[N_{ij}(t)N_{km}(t)\right] = \sum_{s=1}^{t}\sum_{l=1}^{s-1} P_i(l-1)P_{ij}(l)P_{jk}(l,s-1)P_{km}(s)$$

$$+ \sum_{s=1}^{t}\sum_{l=1}^{s-1} P_k(l-1)P_{km}(l)P_{mi}(l,s-1)P_{ij}(s) \qquad (C.4)$$

$$+ \delta_{ij,km}\sum_{s=1}^{t} P_i(s-1)\; P_{ij}(s)$$

The product $N_{ij}(t)\sum_{s=1}^{t} I_k(s-1)\; P_{km}(s)$ may be rewritten as follows

$$N_{ij}(t)\sum_{s=1}^{t} I_k(s-1)P_{km}(s) = \sum_{l=1}^{t} N_{ij}(l-1)I_k(l-1)P_{km}(l) \qquad (C.5)$$

$$+ \sum_{l=1}^{t}\sum_{s=1}^{l} I_k(s-1)\; P_{km}(s)\Delta N_{ij}(l)$$

Taking the mathematical expectation from both parts of equality (C.5) and using the expression (C.2) for $E[N_{ij}(l-1)I_k(l-1)]$, we get

$$E\left[N_{ij}(t)\sum_{s=1}^{t} I_k(s-1)P_{km}(s)\right] = \sum_{l=1}^{t}\sum_{s=1}^{l-1} P_i(s-1)P_{ij}(s)P_{jk}(s,l-1)P_{km}(l) \qquad (C.6)$$

$$+ \sum_{l=1}^{t}\sum_{s=1}^{l} P_k(s-1)P_{km}(s)P_{ki}(s-1,l-1)P_{ij}(l)$$

Making the similar calculations we can get for

$$E\left[N_{km}(t)\sum_{s=1}^{t} I_i(s-1)\; P_{ij}(s)\right]$$

the following expression:

$$E\left[N_{km}(t)\sum_{s=1}^{t} I_i(s-1)P_{ij}(s)\right] = \sum_{l=1}^{t}\sum_{s=1}^{l-1} P_k(s-1)P_{km}(s)P_{mi}(s,l-1)P_{ij}(l-1) \qquad (C.7)$$

$$+ \sum_{l=1}^{t}\sum_{s=1}^{l} P_i(s-1)P_{ij}(s)P_{ik}(s-1,l-1)P_{km}(l)$$

The product $\sum_{s=1}^{t} I_i(s-1)P_{ij}(s)\sum_{s=1}^{t} I_k(s-1)P_{km}(s)$ may be rewritten as follows:

$$\sum_{s=1}^{t} I_i(s-1)P_{ij}(s)\sum_{s=1}^{t} I_k(s-1)P_{km}(s) = \sum_{s=1}^{t}\sum_{l=1}^{s} I_i(l-1)P_{ij}(l)I_k(s-1)P_{km}(s)$$

$$+\sum_{s=1}^{t}\sum_{l=1}^{s} I_k(l-1)P_{km}(l)I_i(s-1)P_{ij}(s)$$

$$-\sum_{s=1}^{t} I_k(s-1)I_i(s-1)P_{km}(s)P_{ij}(s) \qquad (C.8)$$

Taking the mathematical expectation from both parts of this equality and taking into account the Markovian property of the process y(t), we get from (C.8)

$$E\left[\sum_{s=1}^{t} I_i(s-1)P_{ij}(s)\sum_{s=1}^{t} I_k(s-1)P_{km}(s)\right] = \sum_{s=1}^{t}\sum_{l=1}^{s} P_i(l-1)P_{ij}(l)P_{ik}(l-1,s-1)P_{km}(s)$$

$$+\sum_{s=1}^{t}\sum_{l=1}^{s} P_k(l-1)P_{km}(l)P_{ki}(l-1,s-1)P_{ij}(s)$$

$$-\ {}_{ik}\sum_{s=1}^{t} P_k(s-1)P_{km}(s)P_{ij}(s) \qquad (C.9)$$

Summarizing the expressions (C.4), (C.6), (C.7), and (C.9), it is not difficult to get the assertion of theorem 3.

## APPENDIX D: The Proof of Theorem 4

Let $y(t)$ be the continuous time Markov process with the transition intensity matrix $[q_{ij}(t)]$, $i,j=\overline{1,N}$. As in Appendix B we will use the auxiliary Markov chain $y^h(k)$ which is generated by the process $y(t)$ at time $t_0^h$, $t_1^h, \ldots t_h^h = t$, with the one step transition probabilities $P_{ij}(t_{n-1}^h, t_n^h)$, $i,j=\overline{1,N}$. Let $\mu_{ij}^h(t)$, $i,j=\overline{1,N}$ be the processes which correspond to the Markov chain $y^h(k)$ in accordance with Appendix B.
The analogue of the expression (C.1) is the formula

$$\begin{aligned}\mu_{ij}^h(t)\mu_{km}^h(t) &= N_{ij}^h(t)N_{km}^h(t)\\ &+ N_{ij}^h(t)\cdot\sum_{s=1}^{h} I_k^h(t_{s-1}^h)P_{km}(t_{s-1}^h,t_s^h) \qquad (D.1)\\ &+ N_{km}^h(t)\cdot\sum_{s=1}^{h} I_i(t_{s-1}^h)P_{ij}(t_{s-1}^h,t_s^h)\\ &+ \sum_{s=1}^{h} I_i(t_{s-1}^h)P_{ij}(t_{s-1}^h,t_s^h)\sum_{s=1}^{h} I_k(t_{s-1},t_s)P_{km}(t_{s-1}^h,t_s^h)\end{aligned}$$

where $I_k^h(t_{s-1}^h)$ is the indicator of the event $\{y^h(s-1) = k\}$

It is not difficult to prove that the product $\mu_i^h(t)\mu_{km}^h(t)$ tends to the product $\mu_{ij}(t)\mu_{km}(t)$ when h tends to infinity where the processes $\mu_{ij}(t)$ are defined by the formula (18). The mathematical expectation $E[\mu_{ij}^h(t)\mu_{km}^h(t)]$ tends also to the $E[\mu_{ij}(t)\mu_{km}(t)]$ Therefore it is necessary to find the corresponding expressions for the right-hand side in (D.1) and pass to the limit when h tends to infinity. Consider at the beginning the first addendum of the right-hand side of (D.1). Remembering the formula (C.4) for the discrete-time case we can easily write

$$E\left[N_{ij}^h(t)N_{km}^h(t)\right] = \sum_{s=1}^{t}\sum_{n=1}^{s-1} P_i(t_{n-1}^h)P_{ij}(t_n^h)P_{jk}(t_n^h,t_{s-1}^h)P_{km}(t_s^h)$$

$$+ \sum_{s=1}^{t}\sum_{n=1}^{s-1} P_k(t_{n-1}^h)P_{km}(t_n^h)P_{mi}(t_n^h,t_{s-1}^h)P_{ij}(t_s^h) \qquad (D.2)$$

$$+ \delta_{ij,km}\sum_{s=1}^{t} P_i(t_{s-1}^h)P_{ij}(t_s^h) + 0(\Delta t^h)$$

Tending the value of $\Delta t^h$ to zero or the same h to infinity and noting that the change of the operations leads to the limit with respect to h and taking the mathematical expectation on the left-hand side of the formula (D.2), as in Appendix B, one gets

$$E\left[N_{ij}(t)N_{km}(t)\right] = \int_0^t\int_0^s P_i(u)P_{jk}(u,s)q_{ij}(u)q_{km}(s)\,du\,ds$$

$$+ \int_0^t\int_0^s P_k(u)P_{mi}(u,s)q_{km}(u)q_{ij}(s)\,du\,ds$$

$$+ \delta_{ij,km}\int_0^t P_i(s)q_{ij}(s)\,ds \qquad (D.3)$$

In a similar way, we can get the following continuous time analogs of expressions for the discrete time processes:

$$E\left[N_{ij}(t)\int_0^t I_k(s)q_{km}(s)ds\right] = \int_0^t\int_0^s P_i(u)q_{ij}(u)P_{jk}(u,s)q_{km}(s)duds$$

$$= \int_0^t\int_0^s P_k(u)q_{km}(u)P_{ki}(u,s)q_{ij}(s)duds \qquad (D.4)$$

$$E\left[N_{km}(t)\int_0^t I_i(s)q_{ij}(s)ds\right] = \int_0^t\int_0^s P_k(u)q_{km}(u)P_{mi}(u,s)q_{ij}(s)duds$$

$$+ \int_0^t\int_0^s P_i(u)q_{ij}(u)P_{ik}(u,s)q_{km}(s)duds \qquad (D.5)$$

$$E\left[\int_0^t I_i(s)q_{ij}(s)ds\cdot\int_0^t I_k(s)q_{km}(s)ds\right] = \int_0^t\int_0^s P_i(u)q_{ij}(u)P_{ik}(u,s)q_{km}(s)duds \qquad (D.6)$$

$$+ \int_0^t\int_0^s P_k(u)q_{km}(u)P_{ki}(u,s)q_{ij}(s)duds$$

The probabilities $P_{ki}(u,s)$ in these formulas satisfy the following Kolmogorov equations

$$P_{ki}(u,s) = \int_0^t \sum_{l=1}^{N} P_{kl}(u,s)q_{li}(s)ds + \delta_{ki}$$

Collecting these expressions we get theorem 4.

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