

USING A STOCHASTIC MODEL TO INVESTIGATE
TIME TO ABSORPTION DISTRIBUTIONS

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ABSTRACT

After testing a Markov chain model for goodness of fit, a researcher may use it to compare distinct cohorts with respect to stochastic movement among the states composing the chain. One may also use the model to compute time to absorption distributions which are useful in planning follow up studies. We demonstrate such inferential use of a Markov chain using data from a historical prospective study conducted in Skopje, Yugoslavia. We do this by testing a model of women's reproductive paths and using it to compare first pregnancy aborters to first pregnancy deliverers. Finally, within each of the above cohorts, we estimate time to delivery distributions, which may be useful in determining sample size for future studies of the effects of induced abortion.

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Researchers conducting follow-up studies must ensure that a sufficient number of individuals in the original cohort (homogeneous segment of study population) will "survive" to the end of the study period; for example, epidemiologists studying a group of smokers to detect the incidence of lung cancer must take into consideration the fact that some subjects will quit smoking or withdraw from the study. Consequently, cohort studies must use a large enough sample and follow sampled individuals over a sufficiently long period of time in order to obtain adequate estimates for the variables under study. Many conditions, such as lung cancer, are rare, thus data requirements for follow-up studies, which may involve complex variable interrelationships and confounding factors, are very expensive. Hence an analytic model that can provide estimates of required sample size, as well as insight into some of the key research questions, becomes a cost effective part of such studies.

In order to estimate sample size, researchers must consider the probability distribution of the length of time between initiating observation for the study and the appearance of the particular condition under investigation. In addition they will often be interested in the effect of various events on this time as well as in the comparison of such time intervals for different groups. To aid researchers this paper considers:

1. How a stochastic model may be used to investigate such epidemiologic or demographic questions.

2. Assuming that such a model is available,
 - (a) how its analytic assumptions may be validated, and
 - (b) how it may be used to compare the behavior of distinct cohorts.

In particular, this paper utilizes data from a historical prospective study (which creates chronological records by locating past records and "following" them to the present) of potential long term effects of induced abortion, Hogue (3), to compare two cohorts of fertile women, one consisting of first pregnancy aborters and the other of first pregnancy deliverers. Members of both cohorts were recruited at the termination of their initial pregnancy. After providing an abbreviated review of a Markov model designed to depict women's reproductive paths, Shachtman and Hogue (6), we present methodology for testing various hypotheses which is useful for formulating and solving the aforementioned research concerns. We then use the model to compare the cohorts and to estimate their respective time to delivery distributions.

There is apparently little existing information on the use of stochastic models in follow-up studies, but several references exist concerning the utilization of Markov chains in developing reproductive models similar to the one we employ in the example. These include models of human fertility, Chiang (2), pregnancy and post-partum periods in a fertility model, Perrin and Sheps (5), and birthrates as a function of fecundity, contraceptive effectiveness, and other parameters, Sheps and Menken (8), Sheps and Perrin (9).

1. TIME TO ABSORPTION DISTRIBUTIONS

To determine appropriate sample size and length of observation for an epidemiologic study, consider the following question: What is the relationship between length of observation and proportion of a designated sample expected to develop a prespecified condition (e.g., cancer)? Moreover, what is the difference in the time to appearance of this condition between two samples, one composed of subjects exhibiting a certain characteristic (e.g., smoking) and the other comprising subjects who do not exhibit the characteristic? When appropriate attributes make classification viable, we may define a set of states and observe movement among them. The basic goal is then to characterize a random variable to represent time to absorption in the end state (representing the appearance of the condition).

To characterize such a random variable we first define a function $t(\cdot)$ which, under the assumption that all subjects will be observed for the duration of the study, gives the proportion $t(n)$ of a specified cohort expected to develop the condition by time n . The function $t(\cdot)$ is the distribution function of the random variable representing the theoretical time to absorption (development of the condition). This assumption, however, may be impractical as some subjects will withdraw from most studies before the period of observation is terminated. A modification of the $t(\cdot)$ function will allow us to estimate, for various withdrawal patterns, the proportion of the cohort which we observe to develop the condition by time n . This modified function $c(\cdot)$ may then be used to calculate the number of subjects necessary in each cohort for a given period of follow-up. The function $c(\cdot)$ is the distribution function of the random variable representing the observed time to absorption.

2. PARAMETERIZATION

Proportions such as $t(n)$ are estimable directly from incidence (new case) rates; such estimates, however, are limited since the data must be time-censored (i. e., the period of observation will terminate at some distinct point in time). When the underlying process governing the cohorts is a stationary (time-homogeneous) Markov chain (MC) the effect of time-censoring on the data may be reduced by determining $t(n)$ from the MC. Assume that this indeed is the case and that available data make appropriate state definitions feasible. Then, consider one of the cohorts under study and let $p_{jk} = P(X_n = k \mid X_{n-1} = j)$ be the probability that a member of that cohort is in state k at time n given that it was in state j at time $n-1$; note that because of stationarity these probabilities do not depend on n . The chain's transition matrix is then $P = ((p_{jk}))$. We may obtain the n -step transition probabilities, $p_{jk}^{(n)} = P(X_n = k \mid X_0 = j)$, from this transition matrix by the well-known relationship $P^n = ((p_{jk}^{(n)}))$; i. e., $p_{jk}^{(n)}$ is the (j, k) -th element of P^n . Finally, we express the first-passage time probabilities, $f_{jk}^{(n)} = P(X_n = k; X_v \neq k, 1 \leq v \leq n-1 \mid X_0 = j)$, by

$$p_{jk}^{(n)} = \sum_{m=1}^n f_{jk}^{(m)} p_{kk}^{(n-m)} \quad n \geq 1 \quad (2.1)$$

and hence may obtain them iteratively by the formula

$$\begin{aligned} f_{jk}^{(n)} &= p_{jk}^{(n)} - \sum_{m=1}^{n-1} f_{jk}^{(m)} p_{kk}^{(n-m)} \quad n \geq 2 \\ f_{jk}^{(1)} &= p_{jk} \end{aligned}$$

These basic quantities may be used to obtain $t(n)$ from the chain. Let α and δ be states representing the initial state and the appearance of the condition, respectively, then consider

$$\begin{aligned}
 F_{\alpha\delta}(n) &= \sum_{m=1}^n f_{\alpha\delta}(m) \\
 &= \sum_{m=1}^n P(\text{state } \delta \text{ entered for first time at time } m \mid X_0 = \alpha) \\
 &= P(\text{state } \delta \text{ entered by time } n \mid X_0 = \alpha).
 \end{aligned}$$

Thus, $F_{\alpha\delta}(n)$ is the probability that a member of the cohort has reached state δ , i.e., exhibited the condition, by time n given that s/he was in state α at time 0; hence, assuming that all members are initially in state α , $t(n) = F_{\alpha\delta}(n)$. Note that equation (2.1) implies for absorbing, i.e., $p_{\delta\delta}(m) = 1$ for all m , that $t(n) = F_{\alpha\delta}(n) = p_{\alpha\delta}(n)$, which greatly simplifies computation. The assumption that δ be absorbing is common in many epidemiological settings, as it means that once the condition is contracted it remains.

To determine $c(n)$, the proportion of the cohort we observe to develop the condition by time n , we must modify $t(n)$. Letting $n_1 < n_2 < \dots < n_w$ represent the times at which a person may withdraw from the study, we depict the withdrawal distribution through the parameters r_i , $i = 1, 2, \dots, w$, where r_i is the probability that a randomly selected member of the cohort will withdraw at month n_i .

PROPOSITION 2.1:

$$c(n) = \sum_{k=1}^{u-1} r_k t(n_k) + r_u^* t(n)$$

where $u = [n] + 1$, $r_u^* = \sum_{k=u}^w r_k$, and $[a]$ represents the greatest integer in a .

PROOF: Let W_j represent the number of subjects withdrawing at time n_j and note that the set of random variables $\{W_j : j = 1, 2, \dots, w\}$ has a multinomial distribution with parameters $(N: r_1, r_2, \dots, r_w)$

where N is the size of the cohort. Now, of the W_j individuals observed until time n_j , some number, say D_j , will be observed to develop the condition. Conditioned on W_j and $t(n_j)$, D_j is a binomial random variable with parameters $(W_j, t(n_j))$. Thus,

$$E(D_j | W_j, t(n_j)) = W_j t(n_j)$$

and

$$\begin{aligned} E(D_j | t(n_j)) &= E_{W_j}(E(D_j | W_j, t(n_j))) \\ &= N r_j t(n_j) \end{aligned}$$

where we have assumed that $t(n_j)$ and W_j are independent. Now for $n_{j-1} < n < n_j$, the number of individuals we expect to observe develop the condition in $(0, n]$ is

$$E(D_1) + E(D_2) + \dots + E(D_{j-1}) + E(D^*)$$

where D^* is the number of the $\sum_{k=j}^w W_k$ individuals observed longer than time n_{j-1} who develop the condition by time n . By an argument similar to the one used to find $E(D_j)$ we obtain

$$E(D^*) = Nt(n) \sum_{k=j}^w r_k$$

Finally, the proportion of the original cohort we expect to observe develop the condition by time n is represented as

$$\begin{aligned} c(n) &= (1/N) (\text{expected number of individuals who we} \\ &\quad \text{will observe to develop the condition} \\ &\quad \text{by time } n) \\ &= \sum_{k=1}^{u-1} r_k t(n_k) + r_u^* t(n). \end{aligned}$$

□

By computing $t(.)$ and $c(.)$ for a given cohort, we obtain estimates of sample size requirements for future studies. For example, if we desire to observe m occurrences of the condition and must complete the study no later than time n , we must require that the initial sample contains at least N individuals, where $m = N c(n)$.

In addition to the sample size application, we may use the $t(.)$ function from MCs to compare cohorts with respect to their propensity to develop the condition. Such comparisons may also be carried out using incidence rates; however, those rates are usually affected by time-censoring the data. Thus a comparison of the model-based functions should be more meaningful. In addition, we may more fully contrast cohorts by a careful study of the transition matrices of their respective MCs. This latter comparison is a useful complementary analysis as it provides a more detailed look at the processes governing the cohorts. In particular, it is quite possible for cohorts to be different (i.e., described by MCs with statistically significant differences in their transition probability matrices) yet the individual probabilities interact in such a manner as to generate similar $t(.)$ functions. Likewise, similar transition matrices may result in significantly different $t(.)$ functions.

3. AN APPLICATION

We illustrate this methodology with an example using data from a historical prospective study of potential long term effects of induced abortion conducted by Hogue (3). These data were collected on Macedonian women residing in Skopje, Yugoslavia whose first pregnancies were terminated by induced abortion, a cohort of "aborters" (N=217), or delivery, a cohort of "deliverers" (N=711), during 1968-1969. Interviews with these women,

conducted in the fall and winter of 1972, produced full reproductive histories up to the time of the interview; data are therefore time-censored. Hogue (3) reported on the results of an intensive study of the quality and representativeness of these data to the population of Macedonian women.

The major purpose of Hogue's study was to investigate the relationship between induced abortion and risk of prematurity in subsequent pregnancies. Unfortunately, the attained samples were too small to provide time dependent conclusions. To obtain estimates for sample size and length of observation in future studies of consequences of induced abortion, we use these same Skopje data and a stochastic model to investigate the relationship between length of observation and proportion of a designated sample expected to deliver at least one child during the period of observation. Moreover, in this example we will also consider the difference in time to delivery between two samples, one composed of women who aborted their first pregnancy and the other composed of women who delivered their first pregnancy.

The function $t(\cdot)$, which is defined under the assumption that all women are observed until they deliver, gives the proportion of a specified cohort expected to deliver by time n . Since some women will withdraw from any study before they deliver and before the study is terminated, $t(\cdot)$ can not be used to compute sample size requirements. The modified function $c(\cdot)$, however, provides an estimate of the total number of women expected to have an observed delivery. Thus we may use it to calculate the number of women necessary in each cohort for a given period of follow-up.

The development of the stochastic model describing a woman's reproductive path between the onset of menstruation and menopause, which we use in this example, is detailed in Shachtman and Hogue (6).

This model is a 79-state discrete-time Markov chain with one month intervals and transition probabilities assumed to be stationary over a limited time period. The state space of this model is partitioned into three groups: I -- prior to the first pregnancy outcome (25 states); II--following a first pregnancy but prior to the first delivery (27 states); and III--following the first delivery (27 states). Each of these groups constitutes a Markov subchain and describes a portion of the reproductive period of a woman's life. All women are initially in group I; when they terminate their initial pregnancy, the women who deliver enter group III directly, while those who abort enter group II. The latter eventually enter group III if and when they deliver a subsequent pregnancy.

We need only consider the subchains corresponding to groups II and III for this example, which contrasts the post first pregnancy behavior of a cohort of first pregnancy aborters with that of a cohort of first pregnancy deliverers. In fact, we need the estimators of the transition probabilities in group III only for those women who deliver their first pregnancy, whom we will call group IIID; note that all transition probabilities employed are for group IIID, not group III. These subchains have a common state space, since the only difference in the cohorts they describe is initial pregnancy outcome. In Appendix I we list this state space, which includes 9 states of pregnancy, 4 states of pregnancy outcomes, 9 states of susceptibility to pregnancy, and 5 states of various levels of reduced susceptibility to pregnancy. The associated network flow diagram, Figure 1, serves to explain movement among these states.

Figure 1

A. STATISTICAL TESTS

1. Verifying Assumptions

We investigated the basic modeling assumptions before using the subchains of the model to study specific research questions. In particular, we considered the Markov property and stationarity.

HYPOTHESIS 1: First order Markov dependence is equivalent to second order Markov dependence; i. e., $p_{ijk} = p_{jk}$ for all states i, j, k of the chain, where

$$p_{jk} = P(X_n = k | X_{n-1} = j)$$

$$p_{ijk} = P(X_n = k | X_{n-1} = j, X_{n-2} = i).$$

Using a procedure proposed by Kullback, Kupperman, and Ku (4), we tested this hypothesis for both subchains. Letting f_{ijk} denote the observed frequency of transitions from state i to state j to state k , the test statistic is expressed as

$$\chi^2 = \sum_i \sum_j \sum_k f_{ijk} \ln(f_{ijk} / e_{ijk})$$

where $e_{ijk} = (f_{ij.})(f_{.jk}) / (f_{.j.})$ and

$$f_{ij.} = \sum_k f_{ijk}$$

$$f_{.jk} = \sum_i f_{ijk}$$

$$f_{.j.} = \sum_i \sum_k f_{ijk}$$

The above summations are over all states of the chain. Under the null hypothesis of equivalence this statistic has a central chi-square distribution with r degrees of freedom where r is the number of positive f_{ijk} 's.

Based on the Skopje data, the p-values for the tests of groups II and IIID were greater than 0.999 (based on 238 d.f.) and equal to 0.618 (based on 257 d.f.), respectively. We thus accept Hypothesis 1 and have confidence in using these chains for statistical inference since the state definitions themselves imply that higher order dependencies will be absent.

HYPOTHESIS 2: The first order Markov chain has stationary probabilities.

Unfortunately, data limitations prevented us from explicitly testing this hypothesis. Based on pre-data considerations, however, it appears quite reasonable to assume that stationarity holds over a short time period, say five to ten years. These considerations include such factors as the average (typical) age span of the women sampled, the formulation of the state definitions, and the choice of time interval. Furthermore, Hogue chose Yugoslavia for this study because of the non transiency of its population and the constancy of its societal attitudes towards abortion. In particular, since induced abortion had been legalized for many years previous to this study, there was no unfavorable social stigma associated with it, nor was there widespread religious opposition. Consequently, we do not believe that sociological issues would have introduced nonstationarity into the data; for further information see Shachtman and Hogue (6,7).

2. Comparing Cohorts

Having established that the chains corresponding to both groups II and IIID satisfy the Markov assumption, we may now use these chains to test whether the groups arise from (or can be described by) the same

underlying process. This comparison is possible since the basic state space is identical in both chains.

HYPOTHESIS 3: Based on the state space for the given Markov chain, movement in the aborter chain is the same as movement in the deliverer chain.

We investigated this hypothesis using a test proposed by Anderson and Goodman (1). Let m be the cardinality of the common state space associated with transition matrices P_1 (for group II) and P_2 (for group IIID); the test statistic, which under the null hypothesis of equivalence has a central chi-square distribution, is

$$\chi^2 = \sum_{i=1}^m \chi_i^2$$

where

$$\chi_i^2 = \frac{n_{i\cdot}^{(1)} n_{i\cdot}^{(2)}}{n_{i\cdot}^{(1)} + n_{i\cdot}^{(2)}} \sum_{j=1}^m \frac{[P_{ij}^{(1)} - P_{ij}^{(2)}]^2}{P_{ij}^{(\cdot)}}$$

$n_{ij}^{(1)}$ ($n_{ij}^{(2)}$) is the number of transitions from state i to state j among the paths used in estimating the first (second) transition matrix, and

$$\begin{aligned} n_{i\cdot}^{(1)} &= \sum_j n_{ij}^{(1)} & ; & & n_{i\cdot}^{(2)} &= \sum_j n_{ij}^{(2)} \\ P_{ij}^{(1)} &= n_{ij}^{(1)} / n_{i\cdot}^{(1)} & ; & & P_{ij}^{(2)} &= n_{ij}^{(2)} / n_{i\cdot}^{(2)} ; \\ P_{ij}^{(\cdot)} &= (n_{ij}^{(1)} + n_{ij}^{(2)}) / (n_{i\cdot}^{(1)} + n_{i\cdot}^{(2)}) . \end{aligned}$$

The degrees of freedom for this statistic is $t-m$ where $t = \sum_{i=1}^m t_i$ and, for each i , t_i is the number of n_{ij} 's which are positive

in one or both of the groups being tested. For our data the statistic was based on 92 degrees of freedom and obtained a value of 779.284, producing a corresponding p-value of less than 0.001. We thus reject Hypothesis 3 and conclude that the aborter and deliverer cohorts do not originate from the same process.

In addition to this comparison of the complete transition matrix, we may compare the individual states.

HYPOTHESIS: 4. i ($i = 1, \dots, 27$): Movement out of state i in the aborter chain is the same as movement out of state i in the deliverer chain.

We test Hypothesis 4. i using χ^2_i as defined above and noting that under the null hypothesis it has a central chi-square distribution with $t_i - 1$ degrees of freedom. From our data, we obtain significant differences ($p < .05$) for the following states: rsi, rsv4, s1, s4, s6, s7, ia, sa, m9, md. States ia ($\chi^2 = 353.02$ with 4 d. f.), rsv4 ($\chi^2 = 220.12$ with 5 d. f.), s1 ($\chi^2 = 42.48$ with 5 d. f.), sa ($\chi^2 = 32.80$ with 4 d. f.), and md ($\chi^2 = 21.97$ with 4 d. f.) are the states exhibiting the most highly significant differences ($p < .001$).

Note that three of the five states which reveal very significant differences (induced abortion, spontaneous abortion, and mature delivery) involve transitions from pregnancy terminations. The differences, with respect to transitions out of these states, indicate that a woman who delivers her first pregnancy is more likely to enter a contraceptive state immediately following a subsequent pregnancy than is a woman who aborts her initial pregnancy. On the other hand, first pregnancy aborters are more likely to enter either the state of assumed abstinence (following a subsequent abortion) or the state of susceptibility (following a

subsequent delivery). Note also that the other two of the five states which exhibit highly significant differences (assumed abstinence and first month susceptibility to pregnancy) indicate that first pregnancy deliverers are more likely to enter a contraceptive state than are first pregnancy aborters. These data also report that, given that she has already completed a pregnancy, a woman who is in a state of susceptibility to pregnancy will have a greater likelihood of becoming pregnant if she had aborted her first pregnancy.

Even though the stochastic processes governing these cohorts are significantly different, it is possible that the individual probabilities interact in such a way as to produce similar time to delivery distributions. We address this issue in the following section.

B. TIME TO DELIVERY

To investigate the time to delivery questions, we consider the following two chains which are (essentially) the two chains just tested.

$$C_A = \{ia_2, sa_2, sj_2 (j=1, \dots, 9), rsvj_2 (j=1, \dots, 4), rsi_2, \\ mjp_2 (j=1, \dots, 9), md_2, pd_2\}.$$

$$C_D = \{ia_3, sa_3, sj_3 (j=1, \dots, 9), rsvj_3 (j=1, \dots, 4), rsi_3, \\ mjp_3 (j=1, \dots, 9), md_3, pd_3\}.$$

Note that in order to avoid confusion we have added an additional subscript to the states defined in Appendix I. This subscript assumes the values 2, 3 to index groups II and IIID, respectively. Thus, C_A is the subchain representing the first-pregnancy aborters and C_D is the subchain representing first-pregnancy deliverers. The transition matrix P_A for C_A is the same as the corresponding submatrix for group II, except that, without loss of information, the states md_2 and pd_2 are made absorbing.

Since entrance into group IIID is through states md1 or pd1, we adjoin these states to group IIID when calculating time to next delivery. Hence the subchain used for group IIID is:

$$C_D = C_{D'} \cup \{md1, pd1\}$$

The transition matrix P_D for C_D is the same as the corresponding submatrix for group IIID with rows for states md1 and pd1 adjoined and states md3 and pd3 made absorbing. To simplify the notation let

$$\begin{aligned} \alpha &= \text{a group II induced abortion} && = ia2 \\ \beta &= \text{a group I mature delivery} && = md1 \\ \gamma &= \text{a group I premature delivery} && = pd1 \\ \mu_k &= \text{a group k mature delivery} && = mdk \\ \pi_k &= \text{a group k premature delivery} && = pdk. \end{aligned}$$

From the results presented above, we immediately obtain the time to delivery distribution for the aborters from C_A by $t_A(n) = \sum_{m=1}^n f_{\alpha\delta}(m)$ where $\delta = \{\mu_2\} \cup \{\pi_2\}$. Noting that the individual components defining δ are mutually exclusive, we may write $f_{\alpha\delta}(m) = f_{\alpha\mu_2}(m) + f_{\alpha\pi_2}(m)$ and hence

$$t_A(n) = \sum_{m=1}^n f_{\alpha\mu_2}(m) + \sum_{m=1}^n f_{\alpha\pi_2}(m).$$

Finally, since both μ_2 and π_2 are absorbing in C_A , it follows that $p_{\alpha\mu_2}(n) = \sum_{m=1}^n f_{\alpha\mu_2}(m)$ and $p_{\alpha\pi_2}(n) = \sum_{m=1}^n f_{\alpha\pi_2}(m)$; thus we obtain

$$t_A(n) = p_{\alpha\mu_2}(n) + p_{\alpha\pi_2}(n)$$

where the parameter n runs through the months of interest. Therefore, $t_A(n)$ is the distribution of the time to delivery random variable for the

cohort represented by C_A . Fractiles are obtained directly from a graph since $p_{\alpha\mu_2}(\cdot) + p_{\alpha\pi_2}(\cdot)$ is a cumulative distribution function.

To determine the expected time to delivery proportions for the cohort defined by C_D , the pertinent equation is

$$t_D(n) = P(\{X_n = \mu_3\} \cup \{X_n = \pi_3\} | \{X_0 = \beta\} \cup \{X_0 = \gamma\}) \\ = \Delta (p_{\beta\mu_3}(n) + p_{\beta\pi_3}(n)) + (1-\Delta)(p_{\gamma\mu_3}(n) + p_{\gamma\pi_3}(n))$$

where $\Delta = P(X_0 = \beta)$ and the initial distribution for group IIID is defined over the states $\beta = md1$ and $\gamma = pd1$.

To determine values for Δ , we can use the prematurity rate for group I. If we let Γ be the probability of a prematurity in group I and write $j = 7, 8, 9$ for $m_j p$ ($j=7, 8, 9$), it follows that $\Gamma = p_{78} + p_{78} p_{8\gamma} + p_{78} p_{89} p_{9\gamma}$ and $\Delta = 1 - \Gamma$. Using the Skopje data, $\Delta = 0.9494$.

To obtain the time to observable delivery distributions $c_j(n)$ within each cohort, $j=A, D$, we used the withdrawal probability distribution from the Skopje data; however, any other discrete distribution may be substituted in order to assess the effect of different withdrawal patterns. (Note in Proposition 2.1 the heavy dependence of $c(\cdot)$ on the withdrawal distribution.)

Table 1 contains a few cumulative model values, $t(n)$ and $c(n)$, for both the aborter and deliverer cohorts.

TABLE 1

This table indicates that even though the two cohorts are stochastically different (since in Section 3.A.2 we rejected the hypothesis that they have similar transition matrices), they appear to have very similar time to delivery distributions. Sensitivity analysis performed on $t_D(n)$ for Δ

varying in the interval $[0.92, 0.98]$ determined that in this range the value of Δ has little effect on $t_D(n)$. Furthermore, for the withdrawal patterns of the Skopje study, the cohorts also have similar time to observable delivery distributions.

The distribution function for the time to observable delivery random variable is always less than or equal to that of the time to delivery random variable, i. e., $c_j(n) \leq t_j(n)$ for all n and $j = A, D$. It is interesting to note from numerical results that even though $t_D(n)$ is slightly greater than $t_A(n)$ for all n , both functions have the same basic shape. On the other hand, $c_A(n) \leq c_D(n)$ holds only for $n \leq 50$; for larger n the particular withdrawal pattern of the Skopje data is such that $c_A(n) > c_D(n)$ even though $t_A(n) \leq t_D(n)$. This relationship between the time to observable delivery random variables in the two cohorts, however, is not generalizable to other samples or to other withdrawal distributions because of the strong dependence on the withdrawal patterns.

4. DISCUSSION

We have further explored a MC model originally developed to examine the epidemiologic relationship between induced abortion and subsequent reproductive performance in a Yugoslav population. After validating the modeling assumptions, we used the model to formally compare the reproductive behavior of a cohort of first pregnancy aborters to that of a cohort of first pregnancy deliverers. In addition, we have shown that (1) this model may be used to study additional fertility problems, e. g., comparison of time to delivery for aborters and deliverers, and (2) functions of the transition matrix may be used to compute sample sizes for denominators for rates or proportions of particular interest.

In the example presented here, the model predicts that one-fourth of a cohort will deliver within the next 30 months, regardless of whether the members had aborted or delivered their first pregnancy, while the second one-fourth will deliver within the subsequent 20 months. Since some women will have no future deliveries, the probability of a future delivery will never reach unity. Not all deliveries, however, will be observable. Using the withdrawal pattern associated with the Skopje study to adjust the model results, we expect that one-fourth of the respective cohorts will report an observable delivery within 30 months; all of the second one-fourth, however, still will not have reported an observable delivery some 30 months later. Furthermore, even though the aborter and deliverer cohorts are significantly different, the differences are not reflected in their respective time to delivery or time to observable delivery distributions.

These rates reflect biological and behavioral components such as minimal time required to deliver, utilization of abortion and contraception for child-spacing and desired family size. The MC model is not affected by the truncation of data which limits the range of direct incidence measures; hence we believe it gives improved estimates over the period in which we can justify the stationarity assumption. Thus, this model may be applied to other data bases and simulated samples to compare the robustness of estimates under varying behavioral settings.

Many demographers will find these time to delivery results counterintuitive; hence an important future investigation would be to perform sensitivity analysis on transition probabilities of the chains to reflect various reproductive behavioral changes. For example, we may investigate the effect of restricting intervening abortions by treating that state as a taboo state. That is, within each cohort we estimate the

taboo first passage time probabilities

$$h_{j k}^f(n) = P(X_n = k; X_m \notin \{h, k\}, 1 \leq m \leq n-1; X_0 = j)$$

where $h = ia2$, $j = ia2$, $k = md2$ or $pd2$ for the aborter chain and $h = ia3$, $j = md1$ or $pd1$, $k = md3$ or $pd3$ for the deliverer chain. The expression $h_{j k}^F(n) + h_{j r}^F(n)$ where $h_{j k}^F(n) = \sum_{m=1}^n h_{j k}^f(m)$ and $h_{j r}^F(n) = \sum_{m=1}^n h_{j r}^f(m)$, $k = md$ and $r = pd$ in either chain gives the corresponding taboo time to delivery distribution. A comparison of these taboo distributions with the non-taboo expressions will evaluate the effect of restricting induced abortion. We may, of course, treat other states as taboo; of particular interest would be the state $s1$, implying consideration of only those future pregnancies resulting from contraceptive failures.

We could also perform sensitivity analysis on contraceptive use patterns by postulating new (increased or decreased) values for the transition probabilities associated with transitions into, out of, and among contraceptive states. We may then compute time to delivery distributions for each hypothesized pattern and compare the resulting distributions. For example, consider the chain describing deliverers; let $j = md$ and $k = rsvk$ for $k = 1, 2, 3$. If $p_{j1} = 0.3$, $p_{j2} = 0.1$, and $p_{j3} = 0.4$, we could investigate the effect of increasing the propensity to utilize an effective means of contraception by postulating the values $p_{j1} = 0.1$, $p_{j2} = 0.2$, and $p_{j3} = 0.5$ and calculating $t(n)$ and $c(n)$. Note that since the cohorts studied here differed significantly with respect to contraceptive use and yet had similar time to delivery distributions we, a priori, might expect that this distribution is robust to moderate changes in these probabilities.

Another way of studying the sensitivity of time to delivery on behavioral characteristics is to change the state definitions and

estimate the transition matrix and resulting time to delivery distributions for the new chain. For example, the state rsi (reduced susceptibility, involuntary) is presently entered only after nine consecutive months of susceptibility. Data indicate that there may be little difference between this state and the last three months of susceptibility (s7, s8, s9); hence, we may investigate a different assumption by combining these four states into one state of involuntary reduced susceptibility and reanalyzing.

Investigations similar to those suggested for further evaluation of the time to delivery distributions may be performed using Markov chains designed for other epidemiologic studies. Such analyses serve not only to study the sensitivity of time to absorption distributions on various parameters, but also to lend insight into the probabilistic structure of the phenomena which are under investigation -- insight which does not appear to be available using incidence rates and the traditional chi-square analysis of cohorts.

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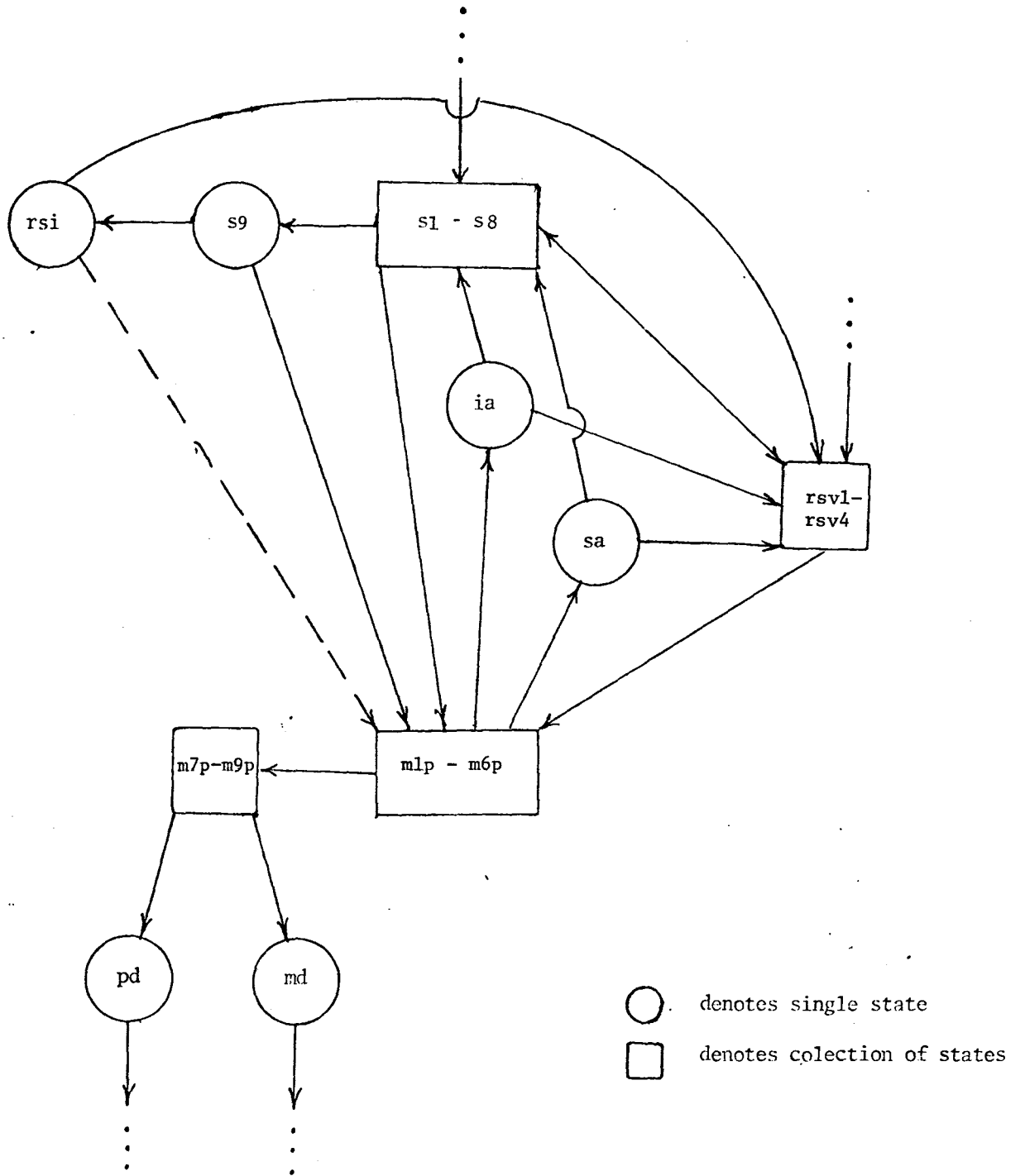


FIGURE 1: TYPICAL NETWORK FOR SUBCLASSES OF THE MARKOV CHAIN

TABLE 1

TIME TO DELIVERY DISTRIBUTIONS

Month	t(n)		c(n)	
	Aborters	Deliverers	Aborters	Deliverers
12	.0392	.0397	.0392	.0397
24	.2047	.2180	.2034	.2176
36	.3382	.3541	.3346	.3521
48	.4465	.4613	.4019	.4106
60	.5344	.5488	.4160	.4143

APPENDIX I: STATE DEFINITIONS *

State	Descriptive Definition
rsi	reduced susceptibility to pregnancy, involuntary
rsvj	reduced susceptibility to pregnancy, voluntary j, j = 1,2,3,4, for contraceptive methods which are ineffective, moderately effective, effective, and assumed abstinence, respectively.
s1 - s9	first (to ninth) month susceptibility to pregnancy
m1p - m9p	first (to ninth) month pregnancy
ia	induced abortion
sa	spontaneous abortion
md	mature delivery
pd	premature delivery

* These state definitions are common to both subchains analyzed. In order to prevent confusion in the text, we shall attach an additional subscript k which will take on the value 2,3 depending on whether we are discussing the aborters (Group II) or the deliverers (Group IIID), respectively. Thus m3p2 represents the third month of (a subsequent) pregnancy for a woman who delivered her first pregnancy.