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*Dedicated to Professor Ioan A. RUS on the occasion of his $70^{th}$ anniversary*

# A Markov model in cervical cancer screening strategy

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ABSTRACT. Cancer is an important public health problem. The cost of cancer therapy is very high. Meanwhile, the prevention of some types of cancer is effective. Generally, Markov models are used to modelling chronic disease for health care (see [1], [2], [5]). This paper introduces a Markov model for cervical cancer screening programme.

## 1. INTRODUCTION

Cervical cancer is the second most common cancer among women worldwide and is an important public health issue. Cervical cancer is one of the most preventable and treatable cancers, since it takes many years to develop from detectable precursor lesions. There are evidence-based interventions for effective early detection and treatment. Interest in health promotion and disease prevention strategies has grown in the last years. The cervical screening program consists in testing of asymptomatic women. We need to solve the following problem: how to design and implement a cervical cancer screening keeping into account the limited resources and the medical effect.

## 2. THE MARKOV MODEL

More precisely, in this paper we analyze no screening and 3 different screening strategies: testing every year, testing every 3 years and testing every 5 years. For this, we construct a Markov model with 15-states: Well (W), Low-grade SIL (L), High-grade SIL (H), unknown stage I cervical cancer (UC1), unknown stage II cervical cancer (UC2), unknown stage III cervical cancer (UC3), unknown stage IV cervical cancer (UC4), detected stage I cervical cancer (C1), detected stage II cervical cancer (C2), detected stage III cervical cancer (C3), detected stage IV (C4), cancer survivor (S) (in this state are included all patients who have got cervical cancer and who alive and remained in the same state during 5 years), dead from cervical cancer (DC), dead from other cause (D), loss of follow-up (A). The set of these states is denoted by $\chi$.

In a Markov model, the conditional distribution of the outcomes given an exposure status depends on prior outcomes observations only. Our model follows a simulated cohort of women from ages $\underline{t}$ through $\bar{t}$, dividing in $n$ group-age:

$$[t_1,\ t_2[, [t_2, t_3[, ..., [t_{n-1},\ t_n[,\ [t_n,\ t_{n+1}],$$

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| State | Possible transitions |
|---|---|
| W | W, L, H, D, A |
| L | W, L, H, D, A |
| H | W, L, H, UC1, D, A |
| UC1 | UC1, C1, UC2, D, A |
| UC2 | UC2, C2, UC3, D, A |
| UC3 | UC3, C3, UC4, D, A |
| UC4 | UC4, C4, UC2, D, A |
| D1 | D1, D2, S, DC, D, A |
| D2 | D2, D3, S, DC, D, A |
| D3 | D3, D4, S, DC, D, A |
| D4 | D4, S, DC, D, A |
| S | S, D, A |
| DC | Absorbing state |
| D | Absorbing state |
| A | Absorbing state |

TABLE 1. States and possible transitions between states: Markov model for cervical carcinogenesis

where

$$t_1 = \underline{t} \ and \ t_{n+1} = \overline{t}.$$

The probability of moving from one state to another during a given Markov cycle is considered. These probabilities depend on the group-age and the states. States and allowed transitions are shown in table 1.

The cohort can be any size because the model uses and generates probabilities. For a person, the model generates lifetime probabilities of being in a given health state.

**Assumptions of the model**

The following list outlines the main underling assumptions of the model and our reason for making them.

- The probability of the transition from state X to state Y is denoted by $p_{X,Y}$. Generally it is not a constant. It depends of the age of patient, but it is the same for the patients in a group-age. Therefore, we consider that $p_{X,Y}$ depends of a parameter $g \in \{1, ..., n\}$, and we use for this the notation $p_{X,Y}(g)$.
- The probability of the pass of a patient from group-age $g$ in the group-age $g+1$ is denoted by $p_{g,g+1}$ and the probability that a patient from group-age $n$ to surpass the age $\overline{t}$ is denoted by $p_{n,n+1}$

- We suppose that the probability that a patient dead from other cause than the cancer is the same for all states but it depend of the ages of the patients, i.e. for every $g \in \{1, ..., n\}$ there is a number $k(g) \in [0,\ 1]$, such that

$$p_{X,D}(g) = k(g), \text{ for all } X \in \chi.$$

- We suppose that the probability that a patient lost from screening is the same for each state and each group-age, i.e. there is a natural number $p_A \in [0,\ 1]$ such that

$$p_{X,A}(g) = p_A, \text{ for all } X \in \chi \text{ and all } g \in \{1, ..., n\}.$$

We want to see what is the number of women from the cohort in each state and each group-age at each Markov cycle. We know that

- the number of Markov cycles is equal to $n$.
- At moment $t_1$ the percent of women of cohort who are in state $X \in \chi \setminus \{A, D, DC\}$, and in group-age $g \in \{1, ..., n\}$, is given and it is equal to $p_{X,g}(1)$. Obviously

$$p_{A,g}(1) = p_{D,g}(1) = p_{DC,g}(1) = 0.$$

- By $p_{X,g}(t)$ we denote the percent of women of cohort who are in state $X$, in group-age $g$ at $t$ cycle and by $p_X(t)$ the percent of women of cohort who are in state $X$ at $t$ cycle.

If we denote by $n_{X,g}(t)$ the number of women of cohort who are in state X at $t$ cycle, then

$$\begin{aligned} n_{X,g}(t) &= \sum_{Y \in \chi} p_{Y,X}(g) \cdot (1 - k(g)) \\ &\cdot \quad (1 - p_A) \cdot (1 - p_{g-1,g}) \cdot n_{Y,g}(t-1) \\ &+ \sum_{Y \in \chi} p_{Y,X}(g-1) \cdot (1 - k(g)) \cdot (1 - p_A) \cdot p_{g-1,g} \cdot n_{Y,g-1}(t-1), \end{aligned}$$

for all $g \in \{1, ..., n\}$, where $p_{0,1} = 0$.

Obviously

$$n_X(t) = \sum_{g=1}^{n} n_{X,g}(t), \text{ for all } X \in \chi.$$

## 3. APPLICATION

We consider a very easy application. For our interest are only the states W, L, H, and C, where by C we denote the cancer state. Also we consider that we have not group-age sets. Then we have a homogeneous Markov tree. Its associated matrices in the natural case (no screening) and after the 3 screening strategies are applied are:

**Natural case**

| | W | L | H | C |
|---|---|---|---|---|
| W | 0.9 | 0.9 | 0.3 | 0 |
| L | 0.06 | 0 | 0.1 | 0 |
| H | 0.04 | 0.1 | 0.3 | 0 |
| C | 0 | 0 | 0.3 | 1 |

**Screening case**

| | W | L | H | C |
|---|---|---|---|---|
| W | 0.9 | 0.02 | 0.01 | 0 |
| L | 0.06 | 0.88 | 0.01 | 0 |
| H | 0.04 | 0.1 | 0.62 | 0 |
| C | 0 | 0 | 0.3 | 1 |

If we have a cohort with 100 women: 90 in state L and 10 in state H, then after 5 years the situation is the following

- card W = 77, card L =5, card H=5 and card C = 13, if the screening is applied each year;
- card W = 76, card L =5, card H=5 and card C = 14, if the screening is applied each 3 year.
- card W = 64, card L =13, card H=9 and card C = 14, if the screening is applied each 5 year.
- card W = 5, card L =50, card H=19 and card C = 26, if the screening is not applied.

It is easy to see that the screening testing every year and testing every 3 years are the better and the results are, roughly speaking, the same. Keeping into account the cost of the test, we deduce that the screening testing every 3 years is the best.

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