COMPlex Quantitative estimation of medical, social and economic effect of cancer prophylactic programs

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The increase of cancer incidence and mortality rates makes the problem of cancer care system financing one of the sufficient social and economical problems of modern society. The treatment of cancer patients is extremely expensive, that is why the cost-benefit analysis of medical technologies applied in cancer care system is of great importance for rational use of resources.

Lots of research, conducted mostly by medical practitioners using factor analysis, show the great influence of the stage of disease (at the moment when cancer is firstly diagnosed) on medical results and cost of treatment of patient. But quite a few research deal with quantitative estimation of medical and economical effect of cancer prophylactic measures on the level of population. Our purpose is to answer, what changes we should expect in terms of average life duration and average cost of treatment of cancer patient in cancer care system because of introducing concrete prophylactic program in the region. Such cost-benefit analysis is necessary for making rational management decisions in cancer care system.

For achieving the purpose mentioned above, mathematical model of cancer patient states and transitions was developed based on international classification of
cancer patients taking into account latent period of disease. From mathematical
point of view, the model is a system of differential equations and could be classified as
Markov chains model.

Parameters of the model were estimated using breast cancer patients database of
Oncology Center of Republic of Bashkortostan. Numerical simulation let us predict
breast cancer situation on the territory of the Republic and evaluate the efficiency of
prophylactic program, proposed by medical specialists of the Center.

1. THE MODEL OF CANCER PATIENTS STATES AND TRANSITIONS
The model is developed on the basis of classification of cancer patients used in
oncology care system which takes into account the features of the disease.[1]

According the classification, there are four stages of cancer. If the disease is
diagnosed in the IV stage, radical treatment aimed at patient’s full recovery is
impossible and patient is directly classified as a patient of IV clinical group. Patients
of IV clinical group receive palliative care aimed at reducing suffering and supporting
patients life quality.

If the disease is diagnosed in I, II, III stages, the patient is classified as patient of II
clinical group. She/he receives radical treatment if it is possible, and after treatment
she/he moves to III clinical group. In the case of cancer progressing such patient
moves back to II clinical group if it is possible to do radical treatment again or she/he
moves to IV clinical group if radical treatment is impossible. Patients can move to IV
clinical group from II and III clinical groups in the case of cancer progressing.

The graph of patients states and transitions according to the classification
described above is shown on figure 1.

The classification does not take into consideration latent period of cancer.
According to cancer research, the duration of latent period can be 75% of the whole
disease duration (in the case of no treatment)[2]. That’s why we added additional
states of latent period of the disease. The graph of patients states and transitions used
for development of mathematical model is shown on figure 2.

The following states are shown on the figure 2.

\(S_0\) – people without cancer; \(S_1, S_2, S_3, S_4\) – patients with latent cancer, which will
be diagnosed relatively in I, II, III, IV stages; \(S_1^r, S_2^r, S_3^r, S_4^r\) – patients with cancer, having
been diagnosed relatively in B I, II, III stages and receiving radical treatment; \(S_1^r, S_2^r,
S_3^r\) – patients with cancer, having been diagnosed relatively in B I, II, III stages and not
receiving radical treatment; \(S_1^r, S_2^r, S_3^r, S_4^r\) are the states of II clinical group;
\(S_1^r, S_2^r, S_3^r, S_4^r\) – cancer patients of I, II, III stage relatively, having been treated radically.
\(S_1^r, S_2^r, S_3^r, S_4^r\) are the states of III clinical group; \(S_5\) – are the patients of IV clinical group
receiving palliative care; \(S_6\) – dead. The area bounded by dashed line includes states of
patients within oncology care system.
On the basis of the graph Markov model was developed. The following signs are used in formulas.

- $L_a(t)$ – the number of patients in the state $S_a$ at the moment of time $t$.
- $b(t)$ – birth rate at the moment of time $t$.
- $m(t)$ – death rate from different causes excluding cancer at the moment of time $t$.
- $g(t)$ – true cancer incidence rate at the moment of time $t$.
- $p_i(t)$ – the probability cancer is diagnosed in the $i$ stage $i \in [1..4]$.
- $\tau_{1,i}, \tau_{2,i}, \tau_{3,i}, \tau_{4,i}$ – average duration of latent period if cancer is diagnosed relatively in I, II, III, IV stage;
\[ \tau_{2}^{1}, \tau_{2}^{2}, \tau_{2}^{3} \] – average duration of radical treatment if cancer has been diagnosed relatively in I, II, III stage;

\[ \tau_{3}^{1}, \tau_{3}^{2}, \tau_{3}^{3} \] – average duration of patient’s staying in II clinical group if cancer has been diagnosed relatively in I, II, III stage and patient is not treated radically.

\[ \tau_{4}^{1}, \tau_{4}^{2}, \tau_{4}^{3} \] – average duration of patient’s staying in III clinical group if cancer has been diagnosed relatively in I, II, III stage.

\[ \tau_{5} \] – average duration of patient’s staying in IV clinical group.

\[ h_{1}^{1}, h_{2}^{1}, h_{3}^{1} \] – is a part of patients with cancer having been diagnosed relatively in I, II, III stages, which receive radical treatment.

\[ h_{1}^{2}, h_{2}^{2}, h_{3}^{2} \] – is a part of patients with cancer having been diagnosed relatively in I, II, III stages, which can be treated radically again in the case of cancer progression.

The dynamics of patients numbers in different states can be described by the system of differential equations below (1) – (6).

\[
\frac{dL_0}{dt} = b(t) \left( L_0 + \sum_{i=1}^{4} L_1^i + \sum_{i=1}^{3} L_2^i + \sum_{i=1}^{3} L_3^i + \sum_{i=1}^{3} L_4^i + L_5 \right) - (m(t) + g(t)) \cdot L_0(t) 
\] (1)

\[
\frac{dL_1^i}{dt} = g(t) \cdot p_i(t) \cdot L_0(t) - (m(t) \cdot L_1^i(t) - \frac{L_1^i(t)}{\tau_1^i})\cdot L_1^i(t), i = 1.4
\] (2)

\[
\frac{dL_2^i}{dt} = h_1^1 \cdot \frac{L_1^i(t)}{\tau_1^i} - \left( m(t) + \frac{1}{\tau_2^i} \right) \cdot L_2^i(t) + \frac{h_4^i}{\tau_4^i} \cdot L_4^i(t), i = 1..3
\] (3)

\[
\frac{dL_3^i}{dt} = (1 - h_1^1) \cdot \frac{L_1^i(t)}{\tau_1^i} - \left( m(t) + \frac{1}{\tau_3^i} \right) \cdot L_3^i(t), i = 1..3
\] (4)

\[
\frac{dL_4^i}{dt} = \frac{L_3^i(t)}{\tau_2^i} - \left( m(t) + \frac{1}{\tau_4^i} \right) \cdot L_4^i(t), i = 1..3
\] (5)

\[
\frac{dL_5}{dt} = \frac{L_1^i(t)}{\tau_1^i} + \frac{L_1^3(t)}{\tau_3^i} + \frac{L_2^3(t)}{\tau_3^i} + \frac{L_3^3(t)}{\tau_3^i} + \frac{(1 - h_1^4) \cdot L_4^i(t)}{\tau_4^i} + \\
\left( \frac{1 - h_4^2}{\tau_4^2} \right) \frac{L_4^3(t)}{\tau_4^3} + \left( \frac{1 - h_4^3}{\tau_4^3} \right) \frac{L_4^3(t)}{\tau_4^3} - \left( m(t) + \frac{1}{\tau_5^i} \right) \cdot L_5(t)
\] (6)

The important advantage of the model is its ability of predicting dynamics of patients numbers applying different variants of demographic and epidemiological situation dynamics (functions \( b(t), m(t), g(t) \)).
2. **THE ESTIMATION OF CANCER CARE SYSTEM EFFICIENCY ON THE BASIS OF THE MODEL OF PATIENTS STATES AND TRANSITIONS**

There are two main criteria of efficiency of cancer care system: average duration of patient’s life from the moment cancer diagnosis has been established till the moment of patient’s death from cancer (medical efficiency) and total cost of patients treatment in oncology care system (economic efficiency).

For evaluating average duration of patient’s life is necessary to trace paths from the moment cancer diagnosis has been established to the death from cancer. Formulas for estimating duration and probability of every path are shown at Table 1.

**Table 1: Paths from the moment cancer diagnosis has been established to the death from cancer**

<table>
<thead>
<tr>
<th>Path</th>
<th>The average duration of patient’s life for the path</th>
<th>The probability of the path</th>
</tr>
</thead>
<tbody>
<tr>
<td>$W_1$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_1 = \frac{\tau_1^1 + \tau_2^1 + \tau_3^1 + \tau_4^1}{1 - h_6^1}$</td>
<td>$v_1 = p_1 \cdot h_1^1$</td>
</tr>
<tr>
<td>$W_2$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_2 = \tau_1^1 + \tau_3^1$</td>
<td>$v_2 = p_2 \cdot (1 - h_1^1)$</td>
</tr>
<tr>
<td>$W_3$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_3 = \tau_1^1 + \tau_3^1 + \tau_4^1 + \tau_5$</td>
<td>$v_3 = p_3 \cdot h_1^1$</td>
</tr>
<tr>
<td>$W_4$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_4 = \tau_1^1 + \tau_3^1$</td>
<td>$v_4 = p_4 \cdot (1 - h_1^1)$</td>
</tr>
<tr>
<td>$W_5$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_5 = \tau_1^1 + \tau_3^1 + \tau_4^1 + \tau_5$</td>
<td>$v_5 = p_5 \cdot h_1^1$</td>
</tr>
<tr>
<td>$W_6$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_6 = \tau_1^1 + \tau_3^1$</td>
<td>$v_6 = p_6 \cdot (1 - h_1^1)$</td>
</tr>
<tr>
<td>$W_7$: $S_1 \rightarrow S_2 \rightarrow S_3 \rightarrow S_4 \rightarrow S_5 \rightarrow S_6$</td>
<td>$W_7 = \tau_1^1 + \tau_3^1 + \tau_4^1 + \tau_5$</td>
<td>$v_7 = p_7 \cdot h_1^1$</td>
</tr>
</tbody>
</table>

The average duration of patient’s life from the moment cancer diagnosis has been established till the moment of patient’s death from cancer is determined by formula (7):

$$W = \sum_{i=1}^{7} W_i \cdot v_i \quad (7)$$

The more $W$, the higher medical efficiency of cancer care system.

Total cost of all patients treatment in oncology care system can be evaluated by summing the cost of patients treatment in different states.

Let $c_i$ be average cost of patient’s treatment in state $S_i$ per year.

Total cost of patients treatment in the state $S_i$ during $[t_1, t_2]$ can be estimated using formula (8):
Total cost of all patients treatment in oncology care system during \([t_1, t_2]\) can be estimated using formula (9):

\[
Z = \sum_{i=1}^{3} Z_i(t_1, t_2) + \sum_{i=1}^{3} Z_i(t_1, t_2) + \sum_{i=1}^{3} Z_i(t_1, t_2) + Z_i(t_1, t_2)
\]

(9)

The less \(Z\), the higher economical efficiency of oncology care system.

3. THE APPLICATION OF THE MODEL FOR EVALUATING THE EFFICIENCY OF BREAST CANCER PROPHYLACTICS ON THE TERRITORY OF THE REPUBLIC OF BASHKORTOSTAN

The model described above was used for evaluating medical and economical efficiency of breast cancer prophylactic program developed by medical specialists of Republic Oncology Center.

Breast cancer prophylactic program is aimed at early diagnostics of breast cancer. In terms of our model it means increasing such model parameters as \(p_1\) and \(p_2\) and decreasing such model parameters as \(p_3\) and \(p_4\).

For evaluating the efficiency of breast cancer prophylactics two numerical experiments were realized. In the first one parameters \(p_1, p_2, p_3, p_4\) were constant describing the situation when prophylactic program is not applied. In the second experiment the parameters \(p_1, p_2\) increased gradually, the parameters \(p_3, p_4\) decreased gradually, describing the situation when prophylactic program is launched on the territory of Republic.

For measuring model parameters the data of 839 breast cancer patients of Oncology Center were used:

\[
p_1=0.1048; \quad p_2=0.4243; \quad p_3=0.3659; \quad p_4=0.1048; \quad h_1=0.8977; \quad h_2=0.8511; \quad h_3=0.8371; \quad h_{31}=0; \quad h_{32}=0; \quad h_{33}=0; \quad \tau_5=0.55 \text{ years}; \quad \tau_6=0.57 \text{ years}; \quad \tau_7=1.35 \text{ years}; \quad \tau_8=6.845 \text{ years}; \quad \tau_9=5.445 \text{ years}; \quad \tau_{10}=1.126 \text{ years}; \quad \tau_{11}=27.025 \text{ years}; \quad \tau_{12}=15.505 \text{ years}; \quad \tau_{13}=3.137 \text{ years}; \quad \tau_{14}=1.755 \text{ years}; \quad \tau_{1}=8.94 \text{ years}; \quad \tau_{2}=9.96 \text{ years}; \quad \tau_{3}=10.58 \text{ years}; \quad \tau_{4}=10.58 \text{ years}.
\]

Initial numbers of patients in different stages were determined using Oncology Center database.

The dynamics of average life duration is shown on figure 3.
As follows from Figure 3, applying prophylactic program leads to gradual increasing average life duration of breast cancer patient.

The dynamics of total cost of breast cancer patients treatment per year is shown on figure 4.

As follows from Figure 4, the application of prophylactic program leads to decreasing total cost of treatment (mostly because the cost of treatment of patients with I and II stages is sufficiently lower comparing with the cost of treatment of patients with III and IV stages.)
4. CONCLUSION
The model let us quantitatively estimate both medical and economical efficiency of breast cancer prophylactic program and therefore prove the rationality of its application on the territory of Republic. We suppose the model to be quite useful for predicting cancer situation and evaluating different types of measures directed on managing oncology situation.

5. REFERENCES