

**Cancer screening in Ukraine: When a theory answers reality.  
Socioeconomic feasibility of population screening for cervical cancer  
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**Summary.** Cervical cancer is a leading cause of disease in the world. Cervical cancer is the second most common cancer and third on a death rate among women worldwide. The great majority of the disease burden occurs in developing countries. At present, cancer screening in oncology it is the basic method of prophylaxis that reduces the level of death rate from malignant tumors. For Ukraine, as the states with the limited financial resources is a necessity socioeconomic feasibility of population screening for cervical cancer with definition of quantitative estimation «cost-effectiveness analysis» and qualitative estimation «cost benefits-disbenefits analysis». In addition, organizational events must be definition for his introduction. In this study, we carried out assessed of an analysis the parameters to measure aggregate criteria and indicators that characterize the economic side conducting of population screening for cervical cancer.

**Key words:** screening, primary prophylaxis, early cancer detection, cervical cancer, algorithm of the screening program, socioeconomic feasibility of cancer screening.

Experience of the countries (USA, Central and Western) developed in a socio-economic relation shows that systematic work in the direction of primary prophylaxis, allows objectively to reduce the level of oncological incidence and mortality rate. A major role this process replace a purposeful and persistent cancer control. One way around this problem is a primary and secondary prophylaxis. In every country the choice of priorities of medical elective that most extensive, and usually the most effective efforts must involve features of socio-economic, political, ecological, oncoepidemiology and other situations.

At that, it is necessary to consider not only potential efficiency of prophylactic measures but also presence of terms that allow them to realize.

In WHO resolution, known as on cancer prevention and control (WHA58.22) adopted in May 2005 («WHO Global Action Plan Against Cancer», 2005), and in appendix this resolution the «The World Health Organization's Fight Against Cancer: Strategies That Prevent, Cure and Care» is described a complex strategy Cancer Control, that contains four basic components: prophylaxis and diagnostics, screening and treatment, palliative care and organizational events [1, 2].

In modern Ukraine, it is impossible correctly to choose priority directions of primary prophylaxis, without regard to three major oncologic risk factors that influence on oncological incidence of population in our country: poverty, strong chronic stress and low public awareness or absence about reasons, early signs of cancer and prophylaxis. Taking the above-mentioned into consideration and experience of Cancer Control in the World, we should also present modern priority directions of primary prophylaxis for our country. This is being done by implementing the four components of cancer control:

- creation delegated legislation and methodical base for cancer primary prophylaxis;
- cancer control and educational work among a population;
- prophylaxis in high-risk groups patients;
- prevention for cancer professionals and early detection;
- government and regional prevention cancer control programmes.

At first glance, they have a substantial difference of priority directions that is confessed in the world. However, we must apply such tactics that answers a present socio-economic situation and possibilities of our country. Strategic aim there must be a reduction of oncologic-attributable incidence and mortality among a population.

In Ukraine, basic indexes of cancer early diagnostics and quality of treatment are in 2–2.5 any number of times a good deal worse, than in the developed countries. In particular, during first-year

after cancer diagnostics oncological patients die in Ukraine twice as much, than in other countries of Europe [3].

A recent meta-analysis and an estimate of cancer treatment in Western Europe and North America concluded at the first to that, their systems of health care attain stabilizing of cancer mortality rate and then his decline. First of all, it was related to full-scale implementation of the national screening programs.

From the socio-economic point of view, was recommended WHO to organized cancer screening in Ukraine is subject to cancer of the uterine cervix that mainly causes negative influence on workforce potential and demographic potential of our state.

A problem of early Cervical Cancer detection and prevention is very important and actual for today. Because this oncological disease involve women of reproductive age and reduced the working performance capability.

In the world Cervical Cancer remains one of the most widespread cancer forms and takes a 2th place on frequency and 3th place on a death rate among all cancer in women.

On estimated of data for 184 countries of the world on the project of GLOBOCAN - 2008 (International Agency for Research on Cancer, department of WHO), the greatest level of Cervical Cancer incidences was recorded in Romania – 34,9 expressed per 100 000 of the population ( $^0/0000$ ), cancer mortality rate – 14,2  $^0/0000$ . Among the countries of Europe, Ukraine takes a 11 place with indexes incidence and mortality 19,2 and 7,8  $^0/0000$ , last Switzerland – 4,2 and 1,6  $^0/0000$  accordingly [4, 5, 6, 7].

From informative data of European Cancer Observatory on the program Eucan-2012 the relative frequency of 5 leading cancer sites by age group in population women's the Cervical Cancer ranked 5<sup>th</sup> position. The incidence and mortality rate was 13,4  $^0/0000$ , 4,9  $^0/0000$ . The specific weight Cervical Cancer among reproductive organs for women make up 3,6 % and this placed aside on 3th grade place [8, 9].

Due to wide implementations of population cervical cancer screening programs and his treatment, a death rate from Cervical Cancer revised down for past 30 years. For women 20-60 years to 31 %, 60-65 years to 48 %, and for women by age over 65 years in a less degree , to 23 %. In spite of these positive changes, today 1 women from 25 000 dies from Cervical Cancer in European Region from data of WHO [10, 11, 12].

A patient's prognosis for Cervical Cancer has a relatively favourable. A relative five-year survival on the early stages is about 90 %. A cumulative five-year survival in Europe is 67 % [13].

According to the data of National cancer registry of Ukraine was based on age-standardised indexes (world standard) the incidence rate of Cervical Cancer are increasing during 1998-2010 and reached a level 15  $^0/0000$  in 2010. The mortality rate of Cervical Cancer was 5.6 deaths per 100,000 women per year and had a tendency toward weakening.

The greatest relative frequency of leading cancer sites in 2011 had cervical cancer patients in reproductive age make up 47.0 % and the working performance capability – 60.8 %.

On estimated from stage distribution of new cases Cervical Cancer in Ukraine established that more than 70 % oncological patients had the early stages (stage I – 35,9 %, stage II – 40,3 %) was increasing on advanced stages (– 25 %), that have a relatively favourable prognosis.

The 2003–2005 database of the surveillance, epidemiology, and end results programme of the Ukrainians National Cancer Institute was analysed by period analysis. They included data and important rates calculated based on the on-line data of regional registries according to the age and stage of the cervical cancer. Estimates of 5-year relative survival rates for types of cervical cancer according to the stage were stage I – 86.1 %, stage II – 50.7 %, stage III – 29,8 %, stage IV – 7,8 %, respectively, by period analysis. A cumulative five-year index of survival was 56.9 %.

For patients with the different stages was established the variation in quantities of this index for stages. The survival of cervical cancer patients for stage II were half as much again the group of patients from stage I, for stage III were 1.7 times larger, more for patients from stage II [3, 14].

On based international data, exactly systematic screening allows to prevent **exceeded** 80% cases of invasion Cervical Cancer. Analysis the efficiency of Cervical Cancer Screening Programs was estimated for the countries of Europe and North America. It was achieved the high-level decrease high level of mortality rates due to these programs. By period analysis, 20–30-year mortality rates were

close to 80% for Iceland, exceeded 50 % for Finland, about 34 % for Sweden, exceeded 75 % for Canada (A province is Britannic Colombia for 30 years) [15].

The efficiency of these programs in Europe and North America also are characterizing the relative survival rates. These estimates were close to 100% for cervical dysplasia, and of about 99,3 % for carcinoma in situ, 96,8 % for cervical microinvasive carcinoma and for Cervical Cancer stages I, II, III, IV 78.1 %, 57 %, 31 %, 7.8 %, respectively.

At this time, these programs are conducted on five continents, in 11 countries in the world, in 38 institutes. In Europe the Population Cervical Cancer Screening put into practice in nine countries: Denmark, Iceland, Netherlands, Norway, Slovenia, United Kingdom Great Britain, Finland, Sweden and, partly, Italy [16].

In the world really exist two types of Cytological Cervical Cancer Screening: systematic, that is directed to all the population of women what is subject to screening, determined to periodicity of realization and unsystematic (sporadic) or conservative women that appealed to curative in hospital or seek medical advice from other occasion. Certainly, systematic screening is most effective, especially through a possibility to overcome by cytological research most of the population [17].

In our study, we based oneself upon on official data the biomedical implication of systematic screening, recommendations of WHO and UICC according to realities and possibilities in Ukraine the real to do the needful for the country carrying out of Population Cervical Cancer Screening, inasmuch as Cervical Cancer is frequent disease in Ukraine and the important problem of health care. In addition, there are prolonged period developments of the disease, possibility for the further improvement of verification and treatment methods, reliable screening test – colposcopy and colposcopic cytological examinations with loop biopsies [7, 18, 19].

On based identifying data of National cancer registry of Ukraine by the means of epidemiology, medical and mathematical statistics were established: age peak for carcinoma in situ was accounted for by women age of 30-34 – 9.3 ‰, while an age peak incidence for Cervical Cancer was in women age of 45-49 – 37.9 ‰ (Fig. 1.) [3].

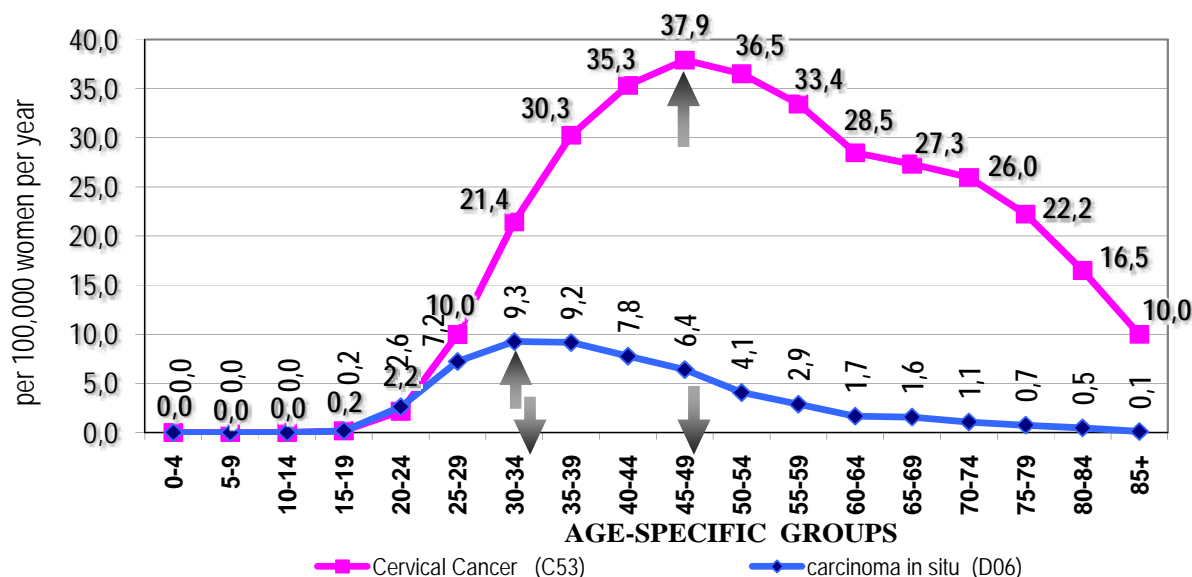


Fig. 1. Age-specific incidence rate for carcinoma *in situ* and Cervical Cancer in Ukraine (2002–2010)

At presents, the problem of Cervical Cancer has very important for Ukraine, because this oncological disease involve women of reproductive age and reduced the working performance capability. Therefore, implementation Cervical Cancer Screening is extremely a necessity for Ukraine. It must provide to decline of the mortality rate from Cervical Cancer and to reduce disabilities resulting from an illness improve survival and quality of life cervical cancer patients and in the future to reduce the incidence rate.

It is necessary to mark that an efficiency of Cervical Screening from positions of evidential medicine influences the next factors:

- coverage of the women by Cervical Cancer Screening;
- rate of the frequency;
- sensitivity of screening test;
- quality of biological material for research;
- adequate patients examination and appropriate treatments.

The intermediate signs of program efficiency usually are an increase of frequency and diagnosed precancer and cancer on the early stages. This allows providing the appropriate treatments for cervical cancer patients. The goal of Cervical Screening must be reduce the mortality rate in population.

The implementation of the screening program has the next steps:

- establish a database;
- invitation on examination;
- process of examination;
- treatment;
- patient monitoring;
- feedback with patients.

Methodology of Cervical Screening must be including the study of home population, age-specific characteristics and community disease awareness about precancer, cancer and risk factors, risk assessment is to be carried out. Without of such work it is impossible to attain necessary efficiency of screening. The condition of the screening proper organization is the simultaneous participating in medical care (primary, second and, tertiary), residency training for screening, intersectoral collaboration all health profession medical specialties supportive personnel.

The Cervical Screening Programs shall be for the next steps:

- computer step;
- clinical step;
- laboratory step;
- examination step, Sub-study and ancillary tests;
- treatment step;
- monitoring and clinical supervision;
- account and clinical supervision;
- palliative care.

The problem of Cervical Cancer Screening must decide with the help of creating government program, by the means of mass-media communications and lectures of medical experts.

The important aspect of the screening efficiency is not only the study of home population but also monitoring and clinical supervision patients with factors of risk and subsequent organizational work with them. Most patients do not see a requirement in a further supervision because does not know the symptoms of illness without asymptomatic disease course and feedback with them flicker out. Therefore they have need of this deserves further comment in relation to the necessity of clinical supervision with the purpose of state cost effectiveness and budget savings.

Determination accuracy of cervical cancer in the woman differs according to the two basic descriptions: sensitiveness and specificity [18].

Over 100 types of human papilloma virus (HPV) well-known for today, but in fact, only two types of oncogenic virus – HPV-16 and HPV-18 cause in 70 % cervical cancer. Pre-morbid status of cervical carcinogenesis lasts for years close to 12-16 years and all of period when development of invasion cervical cancer – more than 20 years. It means that exists enough time for realization of prophylactic and prevention measures [16].

The analysis of mathematical model has revealed the following, a decision factor that influences on benefit-disbenefit and cost effectiveness of screening is validity of the diagnostics test (sensitivity and diagnostic specificity). The Papanicolaou test (also called Pap smear, Pap test, cervical smear, or smear test) is a screening test used to detect potentially pre-cancerous (called cervical intraepithelial neoplasia (CIN)) and cancerous processes in the endocervical canal (transformation zone) of the female reproductive system. Unusual findings are often followed up by more sensitive diagnostic procedures, and, if warranted, interventions that aim to prevent progression to cervical cancer. Pap screening test is prevalent in various country of the world. So far as known, when sensitivity and specificity of Pap test below the limit of quantification 80 % and 86 % respectively, from a medical and economical standpoint, implementations the Cervical Screening does not make economic sense.

According to international criteria, from 84 schedules of screening for today the cost effectiveness are having got 12 schedules, with whom 7 allow to save the maximal number of Quality-Adjusted Life Year (2.45) in the absence of spending. Using the first method of «Pap test + colposcopy» and «Pap test + HPV» it is possible go for a win outcome for example, minimization expenses and maximization number of Quality-Adjusted Life Year under existing conditions such as coverage population by screening not less than 80 % and sensibility cytological of Pap test exceeded 86 % and over [20].

It is important to note that, at present times for diagnostics Cervical Cancer in healthcare system in Ukraine are using the conservative cytology (cervical smear). Deficiency this method is:

- Absence of the standardized biological sampling of Pap smear samples (in a conventional Pap smear, samples are smeared directly onto a microscope slide after collection.).

- The problem of false positive cytological conclusion (e.g., cervical intraepithelial neoplasia).

More cost effectiveness would be application of Pap test based on the innovation technology – Liquid thin-layer based cytology (the Pap smear sample is put in a bottle of preservative for transport to the laboratory, where it is then smeared on the slide. In addition, an HPV test may be performed either as indicated for abnormal Pap results, or in some cases dual testing is done, where both a Pap smear and HPV test are done.

Also she gives an opportunity to prepare additional preparations that can be used for realization of auxiliary screening researches such as virus HPV by the PCR-based diagnostics, immunohistological analysis of oncomarker P-16, P-18 [20, 21, 22, 23, 24].

Screening guidelines vary from country to country. In general, Screening is typically recommended every three to five years, as long as results are normal but this question is debatable. Different intervals are used in some countries in the world. For instance, the interval for Cervical Cancer Screening in Netherlands was 6-years, on Finland – 5-years, in Sweden – 4-years-old, in Denmark – 3-years, and in Iceland and China – each 2-3 years.

In general, screening starts about the age of 20 or 25 and continues until about the age of 50 or 65 and at the first 2 years in succession than every three to five years, as long as results are normal. The purpose cytological screening should be exception of false negative result and the sensibility must be makes up from 60 % to 83 % [25].

Due to the prolonged period developments of the Cervical Cancer an efficiency of screening differs according to the coverage of population by cytological research. From informative data of international researches, the screening efficiency is almost identical at intervals researches between 1 and 2 years. In the process of research which was conducted annually and 1 time per 3 years for same women population found out a difference only in 2 % nevertheless an economic expenses were three times greater [6, 11].

In consideration of the foregoing and age peak incidence for Cervical Cancer (Fig. 1), life expectancy in Ukraine – 73 years and others recommend based oneself on world evidential medicine experience it must be emphasized that starting Cervical Cancer Screening at age 20-59 years. The succession must be within the next 2 years and than 1 time per 3 years [3, 17, 18, 23, 26].

With a purpose a socio-economic effectiveness and makes economic sense for implementation of Cervical Screening Program in Ukraine, we carried-out of the cost effectiveness analysis. It is important to note that on a given time is impossible makes cost of Screening Program due to lack of authentic coefficient. Therefore, the authors of this project were calculated benefit and cost effectiveness for cytological screening without participation of economists, that is why an orientation was.

Taking the above mentioned into consideration in a cost one cytological research was included only spendings on:

- nominal basic wages of doctor (specialization: oncological gynecology) (unified wage rate scale);

- nominal basic wages of staff members the cytological laboratory (two-stage system of microscopic research);

- expendable material.

According to the unified wage rate scale for doctor, laboratory assistants of the centralized cytological laboratory on 50 000 cytological examinations it is need in a year: 1 doctor, 3 laboratory assistants and 1 hospital attendant. Amount of women population by age 20-59 years capitalized on State Statistics Service of Ukraine was 13 848 861 (as on January, 2012). For examinations of this

category of population needed 277 doctors-histologists, 831 laboratory assistant, 277 hospital attendants.

According to loading instructions of doctors for Consultation at Polyclinics for examination, one patient required 12 minutes. The oncogynecology that is receiving patients has 33 workings hours in a week over five-day working week. This is the way a one doctor may examined of 33 patients or 7 260 persons for a year (220 workings days without a weekend and vacations). For the inspection of population, taking in consideration the above for subject screening it is necessary 1 908 oncogynecology doctors (Table 1).

Table 1. Basic amount of doctors (gynecology), required for Cervical Cancer Screening

Admission of one patient, (min.)	12
Working a day in Polyclinics, (hours)	6,6
Amount of patients per one doctor in a day, (persons)	33
Amount of patients per one doctor in a year, (persons)	7 260
Amount of patients, required for screening, (persons)	13 848 861
Amount of doctors is needed for screening (persons)	1 908

The average wages of doctor in Ukraine presents a 1 600 UAH, laboratory assistant – 1 300 UAH, hospital attendant – 1 147 UAH. The annual wages of staff members are 4 894 019 UAH (Table. 2).

Table 2. Annual wages of staff members required for Cervical Cancer Screening

Staffing position	Number of staffing position	Average wages, (UAH) *	
		Position held (one person)	Total
doctors-gynecology	1 908	1 600	3 052 800
doctors-histologists	277	1 600	443 200
laboratory assistant	831	1 300	1 080 300
hospital attendants	277	1 147	317 719
Total (one examination)			0,35338 (≈ 0,35)
Total (in a year)		3 293	5 647
			4 894 019

\* Capitalized on State Statistics Service of Ukraine (as on January, 2012). (<http://www.ukrstat.gov.ua>).

During realization of Cervical Screening will be used next expendable materials (Table. 3).

Table 3. Amounts and cost of expendable materials for Cervical Cancer Screening

Expendable materials	Number		Cost, (UAH) **		
	package amount (total)	Examination (for one)	Number		
			package amount	unit	Examination (for one)
Slide 24x24, (un.)	1000	1	100	0,10	0,10
Slide 76x76, (un.)	72	1	13	0,18	0,18
Smear staining by Romonovckiy, (ml)	1000	2	60	0,06	0,12
Gloves, (un.)	100	1	60	0,60	0,60
Cervical brush, (un.)	100	1	64	0,64	0,64
Total (one examination)					1,64
Total (in a year)					22 712 132

\*\* Prise of company «ЕксімКаргоТрейд» (as on January, 2013). (<http://www.labprice.ua/company/eksimkargotrejd>).

Total spendings for Cervical Cancer Screening of women population equal 27 612 984 UAH (Table. 4).

Table 4. Total cost for Cervical Cancer Screening

Spendings	Cost, in a year (UAH)	Examination (for one), (UAH)
Average wages	4 894 019	0,35
Expendable materials	22 712 132	1,64
Total	27 606 151	1,99

For the economic efficiency calculation of Cervical Cancer Screening was applied the next formula 1:

$$EECS = SFS - (TUTD + PDPLP + LLP), \quad (1)$$

EECS – economic efficiency for carrying out of cervical screening;

SFS – spendings for screening;

TUTD – total unpaid taxes in result of death;

PDPLP – payment of disability pension in labor pool;

LLP – low-limit of pension.

On based identifying data of National cancer registry of Ukraine 2 170 women died of Cervical Cancer, that is to say from them 1 282 - by age 20-59, that is to say this persons was of working-age, which in the case implementation of the screening program would remain alive and, that is why working, should be paid taxes. Total unpaid taxes in result of death from Cervical Cancer were applied the next formula 2:

$$TUT = \frac{AW \times ABT}{100} \times TEPD \times 12, \quad (2)$$

TUT – total unpaid taxes;

AW – average wages;

ABT – accrual based taxation;

TEPD – total employable population died from an illness;

12 – amount of months

On based oneself on official data of State Statistics Service of Ukraine an average wages was 3 377 UAH in December, 2012. Sum of accrual based taxation were close to 21 %. Therefore, as a result of death cervical cancer patients the state did not get taxes to the amount of a 10 909 871 UAH (Table. 5).

Table 5. Total unpaid taxes

Number of cervical cancer patients that died, (persons)		Total unpaid taxes in result of death, (UAH)
Working performance capability (persons)	1282	10 909 871
Total	2170	

Common amount of labor pool women with Cervical Cancer and in a future potentially can become invalids and get a pension on disability were 3 720 persons in 2010. Low-limit of pension in Ukraine (January 2013) was 884 UAH. Consequently, the state will be spend 39 461 760 UAH in a year in payment of pensions on disability from Cervical Cancer. Total Spendings due to the fact of death and disability resulting will be 50 371 631 UAH in a year (Table. 6).

Table 6. Total Spendings due to the fact of death and disability resulting from an illness

Number of cervical cancer patients would get a pension on disability, (persons)	3 720
Low-limit of pension, (UAH)	884
Spendings on pension due to the fact of disability (in a year, UAH)	39 461 760
Total unpaid taxes in result of death, (UAH)	10 909 871
Total Spendings due to the fact of death and disability resulting, (UAH)	50 371 631

In the cost treatment of cervical cancer patients was included only chemotherapy as a most high-cost comparatively with surgical and radial. We analyzed standard schedule of chemotherapy for patients on stages III-IV including palliative care. Sum The amount of such women were 863 persons in 2011. They would get treatment on next schedules (Table. 7) [10].

Table 7. Total cost chemotherapy on conventional management for Cervical Cancer Patients

Treatment schedule	cost of treatment, (UAH)			
	one course		for 4 course	
	n=1	n=863	n=1	n=863
Monochemotherapy*** Bleomycin Sulfate 300 mg in sum			3 396,80	2 931 438,40
Cisplatin+Bleomycin+Etoposid	1 760,41	7 041,64	1 518 795,49	6 075 181,95
CAP	1 567,40	6 269,60	1 352 666,20	5 410 664,80
PC	1 162,02	4 648,08	1 002 823,26	4 011 293,04

\*\*\* The dose of chemotherapeutic medicine we was counted on persons weighing 70 kg and by a height a 170cm. The cost of medicines used for calculations we are taken from Register of wholesale-vacation prices on medicinal facilities Ukraine's Ministry (on February 20 in 2013).

Spendings for chemotherapeutic treatment of cervical cancer patients will have been from 2 931 438.40 UAH to 6 075 181.91 UAH depending on the schedule of treatment.

Comparing the charges of the for Cervical Cancer Screening and type of schedule chemotherapeutic and also spendings on pension due to the fact of disability, total unpaid taxes in result of death, state may have budget savings (Table. 8) .

Table 8. Total Spendings of budget funds for Cervical Cancer Screening

Type of spendings	validity period of screening	
	the first two year, (UAH)	It is starting with 3th year, (UAH)
Program of Screening	27 606 151,04	9 202 050,35
unpaid taxes		10 909 871,00
pension on disability		39 461 760,00
Chemotherapeutic treatment (schedules): conventional management		2 931 438,40
pricier conventional management		6 075 181,95
budget savings, include:		
conventional management	25 696 918,36	44 101 019,05
pricier conventional management	28 840 662,91	47 244 763,61

Therefore, during the first and second years from a moment implementation of Cervical Cancer Screening the state annually may have budget savings from 25 696 918 UAH to 28 840 662 UAH (formula 1). Beginning from 3th year of action this program the state annually may have budget savings from 44 101 019 UAH to 47 244 763 UAH. Conclusion, for today population cytological screening is the only method of Cervical Cancer prevention according to realities and economical possibilities in Ukraine for today.



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