

СПОСОБ ПРОГНОЗИРОВАНИЯ ЗЛОКАЧЕСТВЕННЫХ НОВООБРАЗОВАНИЙ ЖЕНСКОЙ ПОЛОВОЙ СФЕРЫ

© В.Н. Малащенко, Ю.В. Ершова, А.М. Ершов

ФГБОУ ВО Ярославский государственный медицинский университет
Минздрава России, Ярославль, Россия

Цель. Упрощение и увеличение точности анкетного метода прогнозирования злокачественных новообразований (ЗН) женской половой сферы для последующей компьютерной обработки данных и автоматизированного формирования диспансерных групп риска без участия врача. **Материалы и методы.** Работа выполнена на основе статистической обработки данных, полученных методом анкетирования 226 женщин. Первая группа: больные, имеющие ЗН женской половой сферы (n=125); вторая группа: условно здоровые женщины (n=101). Анкета включала 82 пункта: 19 открытых вопросов и 63 – с выбором ответа. Далее была создана многофакторная модель, при разработке которой, кроме данных анкетирования, использовались материалы историй болезней анкетированных пациентов и данные гистологических исследований. Анализ данных выполнен с помощью программ Statistica 10.0 и MedCalc 12.7.0. **Результаты.** По результатам ROC-анализа анкетных данных выявлено 18 значимых предикторов ЗН женской половой сферы. На их основе выведена формула для подсчета прогностического коэффициента (ПК) риска развития ЗН женской половой сферы с чувствительностью 72,8% и специфичностью 95,0%, с помощью которого можно создать компьютерную программу для автоматизированной обработки анкет по формированию групп риска и диспансерного наблюдения через интернет сайты больниц, без участия врачей. **Выводы.** 1) Выявлено 18 статистически значимых предикторов ЗН женской половой сферы, с помощью которых можно обоснованно формировать группы риска для проведения регулярных профилактических мероприятий. 2) Выполненные разработки позволят создать компьютерную программу автоматизированной обработки анкет по формированию групп риска ЗН женской половой сферы и диспансерного наблюдения. Внедрение анкетного скрининга через интернет с последующей компьютерной обработкой результатов без непосредственного участия врачей позволит увеличить охват женского населения РФ профилактическими мероприятиями ЗН женской половой сферы. Данная программа может освободить время врачам на прием первичных больных, облегчить их работу по созданию базы данных большого контингента женщин, а также повысить онкологическую настороженность.

Ключевые слова: злокачественные новообразования; женская половая сфера; анкетный скрининг; группы риска.

COMPUTER MODEL FOR IDENTIFICATION OF GROUPS OF RISK FOR MALIGNANT NEOPLASMS OF FEMALE SEX SPHERE USING QUESTIONNAIRE

V.N. Malashenko, Yu.V. Ershova, A.M. Ershov

Yaroslavl State Medical University, Yaroslavl, Russia

Aim. To identify predictors of malignant neoplasms (MN) of female sex sphere, to evaluate their sensitivity and specificity, to calculate prognostic coefficient (PC) and to create a computer



program on its basis for automated processing of questionnaire data for arrangement of groups of risk for regular medical check-ups through the Internet (without participation of a physician) or on computers of women's health clinics. **Materials and Methods.** The work was performed in two steps. The 1st step was an open questioning survey of 226 women, divided into 2 groups: the 1st group included women with MN of the sex sphere (n=125); the 2nd group included conventionally healthy women. The questionnaire included 82 positions: 19 open questions and 63 questions with a choice of an answer. The second stage consisted in a «blind» questioning of 120 women who visited a women's health clinic. The questionnaire included 18 earlier identified predictors. A multifactor model was developed on the basis of questionnaire data and also using the material of medical histories and of histological examinations. **Results.** Using ROC-analysis of the questionnaire data, 18 significant predictors of MN of female sex sphere were identified. On their basis a formula was derived for calculation of PC for the risk of development of MN of female sex sphere with 72.8% sensitivity and 95% specificity, which was used for creation of a computer model for automated processing of questionnaire data with the aim of identification of groups of risks and for medical check-ups without participation of physicians through Internet sites of hospitals. Then, in result of closed questioning of women (n=120) by 18 predictors, 70 women got into a group of risk, in 47 of them (67%) MN of sex sphere were identified, 50 fell into a group of conventionally healthy women, of them 45 (90%) were healthy, and 5 (10%) had MN. **Conclusions.** 1) Multifactor statistical ROC-analysis of 82 questions and answers permitted to identify 18 predictors of MN of female sex sphere which can be used to scientifically substantiate identification of groups of risk for organization of regular prophylactic measures. 2) The conducted work permitted to create a computer program for automated processing of questionnaires for formation of groups of risk and for regular medical check-ups. We believe that introduction of questionnaire screening through the Internet with subsequent computer processing of the results without participation of physicians with permit to increase the coverage of women's population of the Russian Federation with prophylactic measures against MN of the female sex sphere and to provide more time for receipt of primary patients, to simplify the work for creation of data base, and to increase the oncological alertness of women's population.

Keywords: malignant neoplasms; female ex sphere; questionnaire screening; groups of risk.

Malignant neoplasms (MN) of the female sex sphere (FSS) are the second most common neoplastic disease (19.1%) after the breast cancer (20.9%). Mortality rate from cervical cancer in the Yaroslavl region (YR) in 2018 made 4%, from endometrium cancer – 5.3%, from ovarian cancer – 7.5% (per 100 000 of population) [1]. The causes of high mortality rate are late identification of the diseases because of long-term asymptomatic course and difficulties of identification of MN in the preclinical period, late seeking for medical care, absence of mass screening for endometrial and ovarian cancer, low oncological alertness of primary care physicians and of patients [2-4].

The golden standard of early diagnosis of MN is identification of tumors in the

preclinical stage through formation of dispensary groups and their annual examination in the preclinical period [4-6]. However, most primary care physicians do not create dispensary groups of risk, one of reasons for which being the absence of automation of questionnaire-laboratory screening [7,8].

At present there is no system of questionnaire screening in the practical health-care system for formation of dispensary groups of risk for endometrial, cervical and ovarian cancer [9,10]. Questionnaire screening of Russian women does not provide evaluation of statistically significant risk factors for MN of FSS with modern mathematical methods.

Aim – to identify statistically significant predictors of MN on the basis of multifactorial analysis of the results of questionnaire screening of conventionally healthy women and women with MN of female sex sphere that could help develop a computer program for formation of groups of risk for regular medical observation without participation of a physician.

Materials and Methods

The work was conducted on the basis of statistical processing of the data of questioning of 226 women divided to two groups: with MN of FSS (n=125) and conventionally healthy women (n=101), by a method of creation of a multifactorial model. Besides the questionnaire data, in the work materials of medical histories of patients and the data of histological research were used.

The data were analyzed using Statistica 10.0 (Stat Soft Inc., USA) and MedCalc 12.7.0 (MedCalc Software, Belgium) programs. Multifactorial statistical analysis was applied. The quality of prediction of the studied phenomenon by predictors of MN of FSS was determined using ROC-analysis. The probability for development of MN of FSS on the basis of the most significant predictors was verified using statistical modeling. The method was described earlier in more detail [2,11].

Results and Discussion

In result of the conducted analysis it was found that a statistically significant risk factor in the block of individual characteristics of patients was age ($p<0.0001$). The most important risk factors in the block of questions concerning sex function and ways of contraception were: late age for starting sex life – after 22 years ($p=0.0002$), installation of intrauterine spiral (IUS) in life ($p=0.0164$), and also a history of abortions ($p<0.0001$).

Among clinical manifestations of the disease, the most significant predictors of MN were bleeding from the genital tract (BGT) ($p<0.0001$) and a sharp loss of weight (LW)

before the diagnosis. Analysis of questions concerning the way of life and the type of occupation showed that patients with MN more commonly had occupations associated with hard physical labor ($p=0.0023$), and more of them were living for a long time in military garrisons of air defense forces (ADF) ($p=0.0086$). Active way of life (AWL) was more common among conventionally healthy women ($p=0.0576$), while stresses, mental overloads (PS) were prevailing in the group of women with MN of FSS ($p=0.0001$).

Analysis of the block of questions about the existence of genital and extragenital diseases in women revealed the most common predomination of menstrual cycle disorders (MCD) ($p=0.0011$), of uterine myoma (UM) ($p=0.0231$), diabetes mellitus (DM) ($p=0.0003$), and also of cardiovascular diseases (CVD) ($p<0.0001$) in the group of women with MN of FSS. Besides, women with MN of FSS had problems with conception ($p=0.0057$), and in deliveries they had a higher incidence of cervical traumas in the form of ruptures ($p=0.0006$).

A block of questions concerning heredity revealed a higher incidence of breast cancer ($p=0.0007$) and cancer of other localization ($p=0.0135$) in relatives of patients with MN of FSS.

It should be noted that questions concerning diagnostics and awareness of women of prevention and diagnosis of MN of FSS, and their oncological alertness, demonstrated tactical mistakes of doctors: 85% of women with MN were not aware of methods of their prevention and of early diagnostics, while 65% women of the healthy group possessed this information ($p<0.0001$). The question 'Do you have the Internet at home so that could you enter the site of our clinic to answer the questionnaire?' was answered negatively by 67% of women. We think that this result shows the necessity for organization of computer places in women's health clinics for questioning of women in the electronic network of medico-prophylactic institutions.

Finally, on the basis of application of multifactorial statistical ROC-analysis of 82 questions and answers of women, 18 statistically significant predictors of MN of FSS were identified that can be used to form groups of risk:

1. Age (A) ($p<0.0001$);
2. Menstrual cycle disorders (MCD) ($p=0.0011$);
3. Late start of sexual life (LSSL) ($p=0.0002$);
4. Existence of intrauterine spiral in life (IUS) ($p=0.0164$);
5. Active way of life with a negative coefficient (AWL) ($p=0.0576$);
6. Abortions in history (Ab) ($p<0.0001$);
7. Rupture of uterine cervix in deliveries (RUC) ($p=0.0006$);
8. Existence of uterine myoma (UM) ($p=0.0231$);
9. Occupation associated with a hard physical labor (HPL) ($p=0.0023$);
10. Loss of weight before diagnosis (LW) ($p<0.0001$);
11. Long-term living in garrisons of air

defense forces (ADF) ($p=0.0086$);

12. Problems with conception (PC) ($p=0.0057$);

13. Psychological stresses, rueful feelings (PS) ($p=0.0001$);

14. Bleeding from genital tracts before diagnosis (BGT) ($p<0.0001$);

15. Existence of diabetes mellitus (DM) ($p=0.0003$);

16. Existence of cardiovascular diseases (CVD) ($p<0.0001$);

17. Breast cancer in relatives (BC in R) ($p=0.0007$);

18. Cancer of other localization in relatives (OC in R) ($p=0.0135$).

Results of ROC-analysis are given in Figure 1. The statistically significant level was $p\leq 0.0001$. The surface area below ROC-curve was 0.902; standard error – 0.0199; percentage of correctly classified cases – 72.8% (indicated confirmation of MN of FSS in 73 cases).

Measure of value and coordinate of ROC-curve were all meanings > 0.3267 with sensitivity 72.8% and specificity 95.0% (Figure 2).

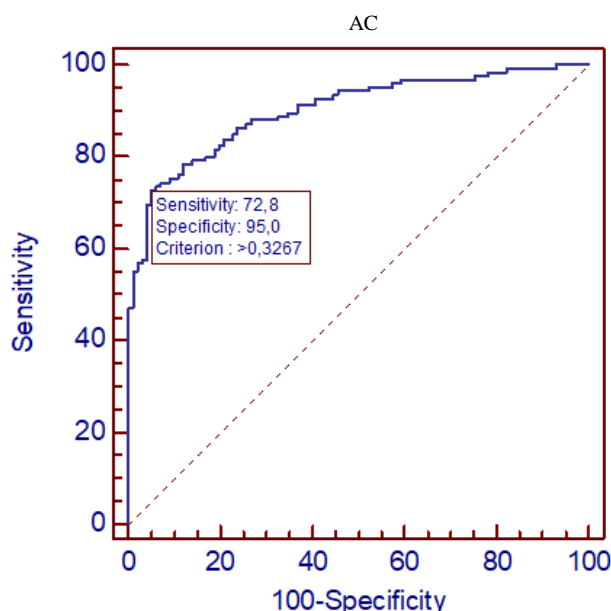


Fig. 1. Forecasting of malignant neoplasms of female sex sphere using questioning

Note: surface area under ROC-curve was 0.902; AC – associated, or prognostic coefficient

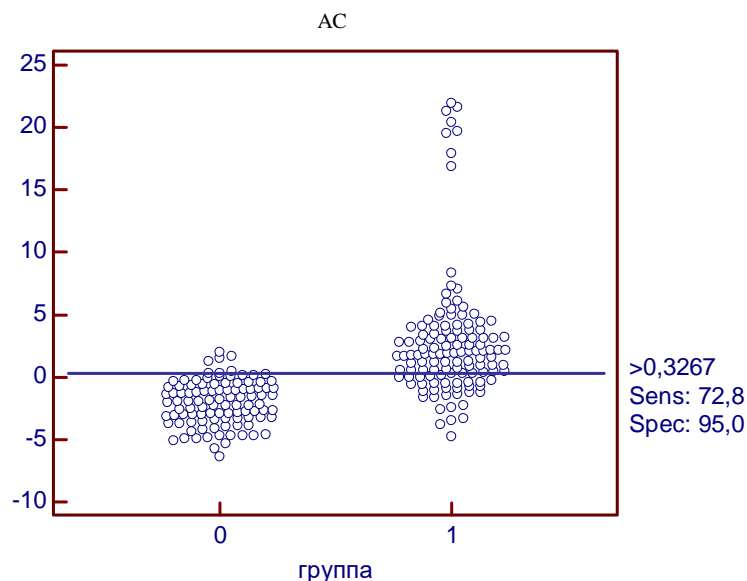


Fig. 2. Associated coefficient (AC)

Note: measure of value and coordinate of ROC-curve were all meanings > 0.3267 with sensitivity 72.8% and specificity 95.0%

These parameters reflect the chances to make a correct diagnosis in ill and healthy individuals. Sensitivity was determined as a share of patients having a real disease among those with a positive test. Specificity was de-

termined as a share of individuals having no disease among those with a negative test. Correlations of development of MN of FSS with the identified statistically significant risk factors are given in Table 1.

Table 1

***Correlation of Development of MN of FSS
with Identified Statistically Significant Risk Factors***

Related Signs	Correlation Coefficient (R)	p
MN of FSS – abortions in history	0.2772	$p < 0.0001$
MN of FSS – active way of life	-0.1274	$p = 0.0576$
MN of FSS – IUS installed in life	0.1605	$p = 0.0164$
MN of FSS – living in garrisons of air defense troops	0.1755	$p = 0.0086$
MN of FSS – age	0.6009	$p < 0.0001$
MN of FSS – other cancers in relatives	0.1651	$p = 0.0135$
MN of FSS – bleeding from genital tract before diagnosis	0.3478	$p < 0.0001$
MN of FSS – uterine myoma	0.1521	$p = 0.0231$
MN of FSS – late start of sexual life	0.2438	$p = 0.0002$
MN of FSS – disorders in menstrual cycle	-0.2164	$p = 0.0011$
MN of FSS – problems with conception	-0.1876	$p = 0.0057$
MN of FSS – occupation associated with hard physical labor	0.2030	$p = 0.0023$
MN of FSS – ruptures of uterine cervix in deliveries	0.2482	$p = 0.0006$
MN of FSS – reduction of body mass before diagnosis	0.3805	$p < 0.0001$
MN of FSS – breast cancer in relatives	0.2246	$p = 0.0007$
MN of FSS – diabetes mellitus	0.2376	$p = 0.0003$
MN of FSS – cardiovascular diseases	0.4514	$p < 0.0001$
MN of FSS – stresses, rueful feelings, overloads	0.2677	$p = 0.0001$

Logit regression of development of MN of FSS with the identified statistically significant

risk factors is given in Table 2.

Table 2

Logit Regression of Development of Malignant Tumors of Female Sex Sphere with Identified Statistically Significant Risk Factors

Risk Factors	Coefficient	Standard Error	p
MN of FSS – abortions in history	0,04823	0,5660	0,9321
MN of FSS – active way of life	-1,0828	0,6831	0,1129
MN of FSS – IUS installed in life	-0,1923	0,5906	0,7447
MN of FSS – living in garrisons of air defense troops	18,8194	2331,9512	0,9936
MN of FSS – age	0,05850	0,02747	0,0332
MN of FSS – other cancers in relatives	0,2615	0,8336	0,7538
MN of FSS – bleeding from genital tract before diagnosis	1,2056	0,5774	0,0368
MN of FSS – uterine myoma	-0,3486	0,5670	0,5387
MN of FSS – late start of sexual life	0,1386	0,1532	0,3654
MN of FSS – disorders in menstrual cycle	-0,1036	0,6001	0,8629
MN of FSS – problems with conception	-2,0947	1,0903	0,0547
MN of FSS – occupation associated with hard physical labor	0,7483	0,6909	0,2788
MN of FSS – ruptures of uterine cervix in deliveries	1,7209	0,6463	0,0077
MN of FSS – reduction of body mass before diagnosis	1,6171	0,8248	0,0499
MN of FSS – breast cancer in relatives	1,2262	0,8590	0,1534
MN of FSS – diabetes mellitus	0,8841	1,2704	0,4865
MN of FSS – cardiovascular diseases	0,5632	0,6828	0,4095
MN of FSS – stresses, rueful feelings, overloads	0,7538	0,6463	0,2435
Constant	-6,6071		

On the basis of mathematical processing of the results according to R. Fischer method, normative signs were obtained, and a method was formed for prognosis of MN of female sex sphere based on determination of prognostic coefficient (PC or AC) according to the formula developed by us:

$$PC = -6.6071 + (0.04823 \cdot Ab) + (-1.0828 \cdot AWL) + (-0.1923 \cdot IUS) + (18.8194 \cdot ADF) + (0.0585 \cdot A) + (0.2615 \cdot OC \text{ in } R) + (1.2056 \cdot BGT) + (-0.3486 \cdot UM) + (0.1386 \cdot LSSL) + (-0.1036 \cdot MCD) + (-2.0947 \cdot PC) + (0.7483 \cdot HPL) + (1.7209 \cdot RUC) + (1.6171 \cdot LW) + (1.2262 \cdot BC \text{ in } R) + (0.8841 \cdot DM) + (0.5632 \cdot CVD) + (0.7538 \cdot PS).$$

PC values below 0.3267 forecasts a low risk; PC values 0.3267 and above forecast a higher risk for development of MN of FSS [11].

Conclusion

Thus, multifactorial statistical ROC-analysis of 82 questions and answers of surveyed women (n=226) permitted to identify 18 statistically significant predictors of malignant neoplasms of female sex sphere which may substantiate formation of groups of risk to be covered by regular prophylactic examinations.

A formula was derived for calculation of prognostic (associated) coefficient with sensitivity 72.8% and specificity 95.0%

Besides, the obtained results were used for creation of a computer program and development of an automated system for testing on the Internet sites of hospitals and polyclinics. Introduction of questionnaire screening through the Internet with subsequent computer processing without direct participation of physicians will permit them to give more time for reception of primary patients, and also to raise oncological alertness of female population of the RF.

Литература

1. Сборник медицинской статистики. Ярославль; 2018.
2. Ершов А.М., Малашенко В.Н., Ершова Ю.В. Способ прогнозирования злокачественных новообразований женской половой сферы с помощью анкетирования // Исследования и практика в медицине. 2018. Т. 5, №S1. С. 32-33. doi: 10.17709/2409-2231-2018-5-S1
3. Организация проведения диспансеризации и профилактических медицинских осмотров взрослого населения. М.; 2013.
4. Никогосян С.О., Кузнецов В.В. Современная диагностика рака яичников // Российский онкологический журнал. 2013. №5. С. 52-56.
5. Каприн А.Д., Старинский В.В., Петрова Г.В. Состояние онкологической помощи населению России в 2014 году. М.; 2015.
6. Горяева А.Э., Петров Ю.А. Скрининг рака шейки матки // Международный журнал прикладных и фундаментальных исследований. 2018. №4. С. 171-175.
7. Мешков А.В., Вазиев И.К., Герасимова Л.И., и др. Анкетный скрининг – метод первичной профилактики рака (на примере канцерогеноопасных производств) // Современные проблемы науки и образования. 2015. №2-1. Доступно по: <https://science-education.ru/ru/article/view?id=18771>. Ссылка активна на 15 февраля 2019.
8. Вилянский М.П., Углев Н.Н. Скрининг в массовых профилактических осмотрах: автоматизированная система. М.; 1987.
9. Vesco K.K., Whitlock E.P., Eder M., et al. Screening for cervical cancer: a systematic evidence review for the U.S. Preventive Services Task Force. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
10. Frederiksen M.E., Lynge E., Rebolj M. What women want. Women's preferences for the management of low-grade abnormal cervical screening tests: a systematic review // An International Journal of Obstetrics and Gynaecology. 2012. Vol. 119, №1. С. 7-19.
11. Малашенко В.Н., Ершов А.М., Ершова Ю.В. Способ прогнозирования риска развития злока-

чественных новообразований женской половой сферы. Патент РФ на изобретение №2687780.

References

1. *Collection of Medical Statistics*. Yaroslavl; 2018. (In Russ).
2. Ershov AM, Malashenko VN, Ershova YuV. A method for predicting malignant tumors of the female genital through questionnaires. *Research and Practice in Medicine*. 2018;5(S1):32-3. (In Russ). doi:10.17709/2409-2231-2018-5-S1
3. *Organization of the clinical examination and preventive medical examinations of the adult population. Guidelines*. Moscow; 2013. (In Russ).
4. Nikoghosyan SO, Kuznetsov VV. Modern Diagnosis of Ovarian Cancer. *Russian Journal of Oncology*. 2013;(5):52-6. (In Russ).
5. Kaprin AD, Starinsky VV, Petrova GV. *The state of oncological assistance to the population of Russia in 2014*. Moscow; 2015. (In Russ).
6. Goryaeva AE, Petrov YuA. Cervical cancer screening. *International Journal of Applied and Fundamental Research*. 2018;(4):171-5. (In Russ).
7. Meshkov AV, Vaziev IK, Gerasimov LI, et al. Questionnaire screening is a method of primary cancer prevention (for example, carcinogenic production). *Modern Problems of Science and Education*. 2015;(2-1). Available at: <https://science-education.ru/ru/article/view?id=18771>. Accessed: 2019 February 15. (In Russ).
8. Vilansky MP, Uglev NN. *Screening in mass preventive examinations: automated system*. Moscow; 1987. (In Russ).
9. Vesco KK, Whitlock EP, Eder M, et al. *Screening for cervical cancer: a systematic evidence review for the U.S. Preventive Services Task Force*. Rockville, MD; 2011.
10. Frederiksen ME, Lynge E, Rebolj M. What women want. Women's preferences for the management of low-grade abnormal cervical screening tests: a systematic review. *An International Journal of Obstetrics and Gynaecology*. 2012;119(1):7-19.
11. Malashenko VN, Ershov AM, Ershova YuV. *A method for predicting the risk of developing malignant tumors of the female genital sphere*. Patent RUS for invention №2687780. (In Russ).

Дополнительная информация [Additional Info]

Источник финансирования. Бюджет ФГБОУ ВО Ярославский государственный медицинский университет Минздрава России. [Financial of study. Budget Yaroslavl State Medical University.]

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, о которых необходимо сообщить в связи с публикацией данной статьи. [Conflict of interests. The authors declare no actual and potential conflict of interests which should be stated in connection with publication of the article.]

Участие авторов. Ершов А.М. – сбор и обработка материала, статистическая обработка, написание текста. Ершова Ю.В. – сбор и обработка материала, статистическая обработка, написание текста, редактирование. Малашенко В.Н. – концепция и дизайн исследования, написание текста, редактирование. [Participation of authors. A.M. Ershov – acquisition and processing of the material, statistical processing, writing the text. Yu.V. Ershova – acquisition and processing of the material, statistical processing, writing the text, editing. V.N. Malashenko – concept and design of the study, writing the text, editing.]

Информация об авторах [Authors Info]

Малашенко Виктор Николаевич – д.м.н., профессор, заведующий кафедрой онкологии с гематологией, ФГБОУ ВО Ярославский государственный медицинский университет Минздрава России, Ярославль, Россия. [Victor N. Malashenko – MD, PhD, Professor, Head of the Department of Oncology with Hematology, Yaroslavl State Medical University, Yaroslavl, Russia.]
SPIN: 4229-9481.

***Ершов Алексей Михайлович** – врач-ординатор, ФГБОУ ВО Ярославский государственный медицинский университет Минздрава России, Ярославль, Россия. [Alexey M. Ershov – Resident, Yaroslavl State Medical University, Yaroslavl, Russia.]
SPIN: 1988-0031, ORCID ID: 0000-0002-4166-479X. E-mail: alesha95951@mail.ru

Ершова Юлия Владимировна – к.м.н., доцент кафедры акушерства и гинекологии, ФГБОУ ВО Ярославский государственный медицинский университет Минздрава России, Ярославль, Россия. [Yulia V. Ershova – MD, PhD, Associate Professor of the Department of Obstetrics and Gynecology, Yaroslavl State Medical University, Yaroslavl, Russia.]
SPIN: 9484-9860, ORCID ID: 0000-0003-4328-9150.

Цитировать: Малашенко В.Н., Ершова Ю.В., Ершов А.М. Способ прогнозирования злокачественных новообразований женской половой сферы // Российский медико-биологический вестник имени академика И.П. Павлова. 2019. Т. 27, №2. С. 219-226. doi:10.23888/PAVLOVJ2019272219-226

To cite this article: Malashenko VN, Ershova YuV, Ershov AM. Computer model for identification of groups of risk for malignant neoplasms of female sex sphere using questionnaire. *I.P. Pavlov Russian Medical Biological Herald.* 2019;27(2):219-26. doi:10.23888/PAVLOVJ2019272219-226

Поступила/Received: 22.02.2019
Принята в печать/Accepted: 17.06.2019