

ANNOTATION

dissertation by Alfiya Gumarovna Shamsutdinova, titled "Scientific Approaches to Enhancing the Implementation of Bioethical Principles in Screening Programs for Detecting Oncopathology of the Reproductive System," is submitted in the requirements for the degree of Doctor of Philosophy (PhD) in the specialty 6D110200 - "Public Health"

Relevance of the research topic

Cancer remains one of the most serious and prevalent health issues globally, contributing to high mortality rates and profoundly affecting the quality of life for patients and their families [1]. According to GLOBOCAN data from the International Agency for Research on Cancer (IARC), cancer ranks as the second leading cause of death worldwide, following cardiovascular diseases. In 2020, there were approximately 19.3 million new cancer cases, with fatalities exceeding 9.9 million [2].

The Global Burden of Disease (GBD) 2019 study identifies the most prevalent cancers globally as prostate, lung, and colorectal cancer (CRC) in men, and breast, CRC, and lung cancer in women. The primary causes of cancer-related deaths are lung, liver, and stomach cancer in men, and breast, lung, and CRC in women [3]. For adolescents and young adults (aged 15–39 years), where prevention and early detection are crucial, the most common cancers are breast and cervical cancer [4]. In Kazakhstan, cancer incidence and mortality rates align closely with global trends [5].

Cancer poses a significant global health threat, necessitating a comprehensive approach to its prevention, diagnosis, and treatment [6, 7]. A critical component of cancer prevention (primary prevention) is its early detection through screening (secondary prevention) [8]. Screening is recognized as one of the essential methods for identifying cancer at early stages, when treatment outcomes are most favorable [9]. Population-based or organized screening is defined by its focus on specific population groups, centralized organization and planning, systematic monitoring of participation across social groups, scientifically determined screening intervals, and the presence of a quality assurance system. In contrast, opportunistic screening occurs spontaneously when a patient seeks medical care, leading to higher healthcare costs and limited impact on overall cancer incidence and mortality rates [10]. Organized screening is typically more effective, optimizes resource use, and minimizes potential adverse effects [11].

In Kazakhstan, population screening for breast and cervical cancers was launched in 2008 as part of the state healthcare reform and development program for 2005-2010, which provided a guaranteed package of free medical services [12]. Between 2012 and 2016, the country implemented the "Oncology Care Development Program," allowing for a gradual expansion of the national screening program: breast, cervical, and colorectal cancer screenings were conducted nationwide, while screenings for prostate, esophageal, stomach, and liver cancers

were introduced in 11 out of 16 regions [13]. Following an evaluation of these screening programs by international experts from WHO, IARC, and IAEA, and under the direction of Kazakhstan's Ministry of Health, since 2019, organized national screening has focused solely on three cancers: breast, cervical, and colorectal [14]. Annually, approximately 3 million men and women in target age groups (30 to 70 years) participate in screening for early cancer detection [15].

Currently, breast cancer screening is conducted biennially for women aged 50-70, with mammography recognized as the most effective method for early disease detection [16]. Cervical cancer screening is performed every five years for women aged 30-70, using the Papanicolaou test (Pap test) as the primary screening tool for detecting precancerous and cancerous cervical conditions [17]. Prostate cancer screening involves an immunochemiluminescent blood test to measure prostate-specific antigen (PSA) levels in the blood serum of men aged 50-66, conducted every four years [18].

Screening programs are considered effective if they reach 70% or more of the eligible population within the specified age ranges [19]. In Kazakhstan, during the initial years of preventive examination programs, coverage for cervical cancer screening reached 40.4%, while breast cancer screening reached 45.1% among eligible women [13, p. 11]. By 2019, coverage had increased to 89% for cervical cancer screening and 60% for breast cancer screening according to the Register of Attached Population [15, p. 5]. Prostate cancer screening was conducted in a pilot phase, covering 428,483 men from 2013 to 2016 [20].

Women's participation in breast and cervical cancer screening programs has been widely studied across various countries and from multiple viewpoints. One of the primary obstacles to participation is the high cost of medical services, including screening, as well as the lack of health insurance in countries where these services are not covered by public programs [21–23]. In countries with lower economic development, the primary barriers include limited infrastructure and a shortage of qualified healthcare personnel [24]. Sociocultural factors that discourage participation include low awareness of available services, fear of the procedure and potential positive results, social stigma, embarrassment, and concerns about confidentiality [25, 26]. In Kazakhstan, as in other CIS countries, additional barriers for women include concerns about discovering a malignant tumor, doubts regarding the necessity of screening, and a general indifference toward personal health [27, 28].

Male participation in prostate cancer (PCa) screening has been less extensively studied, but most research indicates that a major barrier is men's limited knowledge about prostate cancer and low motivation or intention to undergo screening [29]. Among those aware of screening, barriers included mixed feelings about PCa screening due to the trade-off between its benefits and drawbacks, primarily the risk of overdiagnosis. Additional concerns included fear of a loss of "masculinity" and the potential need for further testing in the case of a positive result [30].

Public participation in screening programs also relies on trust in the program's implementation, service accessibility, and adherence to ethical principles at both the individual and population levels, ensuring a "fair" allocation of limited healthcare resources [31, 32, 33].

Ethical adherence in screening programs involves providing participants with thorough information on the benefits, risks, and limitations of screening; ensuring equitable access; and safeguarding privacy and confidentiality [34, 35]. Upholding bioethical principles at the individual level fosters adherence to ethical standards at the population level, enhancing the effectiveness of screening programs [36].

In Kazakhstan, conditions such as government support, funding, and staffing are in place to support screening programs. However, the level of public participation in these programs has not been extensively studied, nor is there information on the follow-up of participants. Given that screening programs for reproductive system cancers are particularly sensitive to ethical considerations [37], it is plausible that compliance with bioethical standards could significantly influence male and female participation in these programs. Research into bioethical compliance within breast, cervical, and prostate cancer screening programs could reveal the impact of these standards on the participation and adherence of target population groups. In this regard, the study aims to identify possible reasons for the insufficient coverage of the population by screening programs for oncological diseases of the reproductive system with an emphasis on the ethical issues that arise during their implementation. We believe that to answer this question, it is necessary to consider the following aspects: reliability and ethical validity of the screening tools used; behavioral factors and the level of public awareness of screening programs; organizational and practical difficulties, as well as compliance with bioethical principles by health workers when organizing and conducting screening.

The aim of this dissertation research is to enhance bioethical principles within screening programs for reproductive system cancers by developing a comprehensive algorithm for ethical review. This algorithm will be based on assessing participant commitment and analyzing ethical dilemmas encountered in screening organization, with the goal of safeguarding participants' rights and safety and improving the quality and effectiveness of screening practices.

Research objectives

1. To analyze the trends in incidence, prevalence, and coverage among target population groups participating in screening programs for detecting reproductive system cancers, considering regional variations across Kazakhstan for the period 2021-2023.
2. To determine the primary reasons for low adherence to screening programs through an analysis of behavioral characteristics and public awareness levels regarding screening for reproductive system cancers.
3. To examine the organizational and practical challenges faced by healthcare workers in screening for reproductive system cancers through in-depth interviews and to develop an educational program aimed at enhancing the competencies of

medical staff in screening organization, improving patient communication, and raising public awareness of the importance of preventive exams.

4. To develop a comprehensive algorithm for the ethical review of screening for reproductive system cancers, including breast, cervical, and prostate cancers, to ensure the protection of participants' rights and safety, thereby increasing adherence and expanding population coverage in screening programs.

Object and Subject of Research:

Data for this retrospective study were drawn from the Health Statistics database of the S. Kairbekova National Scientific Center for Health Development, covering the years 2021-2023. Surveys of participants were conducted from 2019 to 2023. The study took place at six city polyclinics in Almaty (No. 1, 9, 11, 13, 18, and 25), selected from both central and peripheral areas of the city. These polyclinics were included based on management consent to participate in the study.

The study was conducted in the following stages:

1. Evaluation of epidemiological data on breast and cervical cancer screening in Kazakhstan for the period 2021-2023.
2. Survey of patients in Almaty clinics, including women who underwent mammography and/or a cervical cytology (Pap test) and men who had a PSA blood test, in accordance with Kazakhstan's screening guidelines, to identify reasons for low adherence and barriers to screening for reproductive system cancers.
3. In-depth interviews with healthcare personnel to uncover obstacles in screening for reproductive system cancers.
4. Development of a training program for healthcare personnel aimed at improving public commitment to screening for reproductive system cancers.
5. Creation of an algorithm for the ethical review of screening for reproductive system cancers.

Research Methods:

1. Retrospective analysis of epidemiological data on breast, cervical, and prostate cancer screening, sourced from the Health Statistics database of the S. Kairbekova National Scientific Center for Health Development for the years 2021-2023.
2. Development of questionnaires assessing general knowledge about screening, as well as specific knowledge related to breast, cervical, and prostate cancers.
3. Evaluation of the reliability and internal consistency of the questionnaires using Cronbach's alpha coefficient.
4. Survey of screening participants on general and specific knowledge about breast, cervical, and prostate cancer screenings. The study was conducted in six city polyclinics in Almaty (No. 1, 9, 11, 13, 18, and 25) with sample sizes of 674 women for breast cancer screening, 565 women for cervical cancer screening, and 386 men for prostate cancer screening.
5. In-depth interviews with healthcare personnel to identify barriers to screening for reproductive system cancers, using a semi-structured questionnaire (sample size: 22 healthcare employees).

6. Development of the educational program “Adherence to Bioethical Principles in Screening for Reproductive System Cancers” for doctors and mid-level medical staff involved in the organization and implementation of screenings.

Provisions Presented for Defense:

1. Despite high coverage levels of screening for breast and cervical cancers among target groups of women, the cancer detection rate remains consistently low across Kazakhstan. Additionally, significant regional variations in these indicators highlight the need for region-specific adaptations and strengthened screening standards.
2. Low adherence to screening programs for reproductive system cancers is linked to insufficient public awareness about screening processes before and after testing, limited understanding of diagnostic procedures, lack of clear information on screening outcomes, and psychological discomfort and anxiety during testing and while awaiting results
3. The educational program developed for healthcare providers, which focuses on optimizing screening processes, improving communication skills, and raising public awareness of preventive examinations, helps reduce staff turnover by enhancing professional competencies. This program boosts patient adherence to screening, leading to earlier detection of cancers and overall improvement in the quality of healthcare services.
4. The comprehensive algorithm developed for ethical review in screening programs for reproductive system cancers, including breast, cervical, and prostate cancers, fosters an ethically sound system that safeguards participants' rights and safety, enhances the quality of screening programs, and addresses essential ethical concerns such as informed consent, data confidentiality, and equitable access to healthcare services.

Scientific Novelty

1. Developed and validated questionnaires to assess adherence to breast and cervical cancer screening in women and prostate cancer screening in men, from the perspective of ethical principles compliance (Registered in the state register of copyright-protected objects, Certificate No. 2434, dated March 26, 2019. “Questionnaire to Assess Adherence to Breast and Cervical Cancer Screening in Women and Prostate Cancer Screening in Men from an Ethical Compliance Perspective” // Shamsutdinova A.G.).
2. Created a training program for healthcare professionals focused on adherence to bioethical principles in screening for reproductive system cancers (Registered in the state register of copyright-protected objects, Certificate No. 49050, dated August 15, 2024. “Training Program on Compliance with Bioethical Principles in Screening for Reproductive System Cancers” // Shamsutdinova A.G.).
3. Developed a checklist for conducting ethical reviews of screening programs, based on established criteria and indicators (Registered in the state register of copyright-protected objects, Certificate No. 50447, dated October 15, 2024. “Checklist for Ethical Review of Screening Programs, Illustrated with Breast, Cervical, and Prostate Cancer Screening” // Shamsutdinova A.G.).

4. Designed a comprehensive algorithm for the ethical assessment of screening programs for reproductive system cancers, including breast, cervical, and prostate cancers (Registered in the state register of copyright-protected objects, Certificate No. 50451, dated August 15, 2024. “Algorithm for Ethical Assessment of Cancer Screening Programs” // Shamsutdinova A.G.).

Practical Significance of the Results

1. The developed questionnaires, which assess respondents' general knowledge and subjective perceptions regarding breast, cervical, and prostate cancer screenings, can be utilized to objectively evaluate knowledge levels and attitudes, aiding in the identification of low adherence to screening programs.
2. The educational program created for healthcare professionals can be applied to optimize screening processes, enhance communication skills, and increase public awareness about the importance of preventive exams. This program also supports reducing staff turnover through improved professional competencies, thereby fostering greater patient compliance with screening.
3. The comprehensive algorithm developed for the ethical assessment of screening programs for reproductive system cancers helps to enhance the quality and ethical integrity of these programs by safeguarding participants' rights, ensuring data confidentiality, and promoting equitable access to healthcare.

Personal contribution of a doctoral student

The doctoral candidate, with guidance from scientific consultants, independently conducted all stages of the research, including comprehensive data analysis, statistical processing, interpretation of the findings, and formulation of well-founded conclusions.

Conclusions

1. In 2023, breast cancer screening coverage declined to 61.9%, compared to 85.2% in 2021 and 91.8% in 2022. The proportion of benign breast neoplasms detected dropped from 23.4% in 2021 to 4.9% in 2023, while the rate of breast cancer detection remained steady at 0.25%. For cervical cancer, screening coverage fell to 54.9% from 92.9% in 2021 and 92.0% in 2022, with the detection rate of benign conditions decreasing from 5.8% in 2021 to 1.9% in 2023, and the cancer detection rate remaining at 0.04%. In the Karaganda region, disease detection reached 57.9% with 86.2% coverage; in the Akmola region, breast cancer detection was 3.2% with 78.9% coverage; and in the Kostanay region, breast cancer detection was 5.3% with 57.1% coverage.
2. Low adherence to screening programs for reproductive system cancers is attributed to limited public awareness of screening procedures post-testing (up to 56% were unaware of the process, $p = 0.001$), insufficient knowledge about diagnostic tests (78.8% of prostate cancer screening participants had minimal knowledge, $p = 0.001$), lack of clear information on screening results (over half of the participants were not informed about the timing and methods for receiving results, $p = 0.001$), and psychological discomfort and anxiety during and while awaiting tests (up to 46.7% reported anxiety, $p = 0.001$), along with restricted access to diverse information sources ($p = 0.001$).

3. The educational program developed for healthcare professionals, focused on optimizing screening processes, enhancing communication skills, and increasing public awareness about the importance of preventive exams, helps reduce staff turnover by improving professional competencies. This, in turn, boosts patient commitment to screening, facilitating early detection of cancers and improving the overall quality of healthcare services.
4. The comprehensive algorithm developed for the ethical review of screening for reproductive system cancers, including breast, cervical, and prostate cancers, establishes an ethically sustainable system that upholds participants' rights and safety. It enhances the quality of screening programs and addresses critical ethical concerns such as informed consent, data confidentiality, and equitable access to healthcare services.

Results Approbation of the dissertation

The main provisions of the dissertation were presented and discussed at the following events:

- International Scientific and Practical Conference “Priorities of Public Health and Preventive Medicine in the 21st Century” (December 4, 2015, Almaty, Kazakhstan). Report title: “Screening Programs as an Indicator of the Readiness of the Kazakh Population for Shared Responsibility in Health.”
- III International Scientific and Practical Conference of Students and Young Scientists “Science and Medicine: Modern View of the Youth,” dedicated to the 25th anniversary of Kazakhstan’s independence (April 24, 2016, Almaty, Kazakhstan). Report title: “Modern Perspectives on Screening Programs: A Literature Review.”
- XV Conference of Young Medical Scientists of CIS Countries “Modern Problems of Theoretical and Clinical Medicine,” in memory of Professor B. U. Dzharbusynov (May 19, 2017, Almaty, Kazakhstan). Report title: “Prostate Cancer Screening: Specialists’ Expectations and Public Attitudes.”
- 23rd Annual World Congress on Medical Law, 50th Golden Anniversary Meeting, Theme: Medical Law, Bioethics, and Multiculturalism (July 10-13, 2017, Baku, Azerbaijan). Report titles: “Ethical Issues in Cancer Screening” and “The Ethics of Cancer Screening at the Primary Healthcare Level.”
- Scientific and Practical Conference of Young Scientists “Akanovsky Readings: Current Issues in Medicine and Health Care” (April 19-20, 2018, Almaty, Kazakhstan). Report title: “Ethical Considerations in Reproductive Cancer Screening.”
- International Scientific and Practical Conference of the 12th General Assembly of the Asia-Pacific Organization for Cancer Prevention (September 19-21, 2024, Bishkek, Kyrgyzstan). Report title: “Analysis of the Effectiveness and Coverage of Breast, Cervical, and Colorectal Cancer Screening Programs in Kazakhstan for the Period 2021-2023: Regional Disparities and Coverage Dynamics.”

Implementation of research results into practice

Four author's certificate have been issued, including:

- Certificate of inclusion in the state register of rights to copyright-protected objects, No. 2434, dated March 26, 2019: “Questionnaire for Assessing Adherence to Breast and Cervical Cancer Screening in Women and Prostate Cancer Screening in Men from an Ethical Compliance Perspective.”
- Certificate of entry in the state register of rights to copyright-protected objects, No. 49050, dated August 15, 2024: “Training Program on Compliance with Bioethical Principles in Screening for Reproductive System Cancers.”
- Certificate of entry in the state register of rights to copyright-protected objects, No. 50451, dated October 15, 2024: “Algorithm for Conducting an Ethical Review of Cancer Screening Programs.”
- Certificate of inclusion in the state register of rights to copyright-protected objects, No. 50447, dated October 15, 2024: “Checklist for Conducting an Ethical Review of Screening Programs, with Examples of Breast, Cervical, and Prostate Cancer Screening.”

Four implementation acts have been approved:

- Act on the implementation of a training program for doctors and mid-level medical personnel involved in organizing and conducting screening for reproductive system cancers at the Central Clinical Hospital, JSC.
- Act on the implementation of a training program for doctors and mid-level medical personnel engaged in organizing and conducting cancer screening at the State Enterprise with Economic Management Rights "Rural Hospital of Panfilov Village" in Almaty Region.
- Act on the implementation of a training program for doctors and mid-level medical personnel involved in organizing and conducting reproductive system cancer screening at the TAN Clinic Medical Center in Almaty.
- Act on the implementation of the ethical review algorithm for reproductive system cancer screening programs at the TAN Clinic Medical Center in Almaty.

Publications:

Based on the dissertation research, 25 scientific papers have been published, including 6 abstracts in international conference proceedings, 8 articles in various journals, and 8 articles in scientific and practical journals recommended by the Committee for Quality Assurance in Education and Science of the Ministry of Science and Higher Education. These include Bulletin of AGIUM (4 articles), Bulletin of KazNMU (2 articles), Medicine (1 article), and Higher School of Kazakhstan (1 article). Additionally, 3 articles were published in journals indexed by Scopus: 2 articles in the Asian Pacific Journal of Cancer Prevention (ISSN: 1513-7368, CiteScore - 3.0, percentile - 46), and 1 article in the Siberian Oncology Journal (ISSN: 1814-4861, CiteScore - 0.3, percentile - 12). Four certificates of inclusion in the state copyright registry have also been received: No. 2434 dated March 26, 2019, for the “Questionnaire for Assessing Adherence to Breast and Cervical Cancer Screening in Women and Prostate Cancer Screening in Men from an Ethical Compliance Perspective,” and No. 49050 dated August 15, 2024, for the training program “Compliance with Bioethical Principles in Screening for Reproductive System Cancers.”

Volume and structure of the dissertation:

The dissertation spans 144 pages of typed text and includes a list of abbreviations and symbols, an introduction, a literature review, a description of materials and methods, results of the author's research, a discussion, a conclusion with key findings, practical recommendations, and a bibliography comprising 210 references. It also contains 34 tables, 26 figures, and 10 appendices.