



University of Georgia
School of Health Sciences
Doctoral Program: Public Health

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**Organizational Barriers of pain management
in the process of cancer treatment**

**Academic degree holder of Doctor
of Public Health**

Doctoral Dissertation Bulletin

(Specialty - 0904 - Public Health)

Tbilisi

2022

**The thesis was completed at the University of Georgia
in the School of Health Sciences.**

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The thesis defense will be held on January 31, 2023 at 03:00 (pm)

in hybrid mode with the Zoom platform, UG, 4th building, auditorium 519

The dissertation can be viewed in the library of the University of Georgia

Dissertation bulletin sent on December 31, 2022

Secretary of Dissertation Council:
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Relevance of the problem, research issues:

Recently, there has been a decrease in cancer mortality (WHO, 2018) and an increase in cancer survival (Siegel RL, et al. 2019); However, the frequency of pain, which is 55% of cases during treatment, does not decrease (Marieke H. J, 2018). According to the World Cancer 2020 report, in parallel to the increase of the survival rate of cancer patients, the incidence of pain is also increasing. This is as a result of the shortcomings of preventive strategies which are most common in developing countries (Li Z., 2018). Based on these aspects, in Georgia, which is a mixture of Soviet and Western medicine, a different environment has been created, where it is relevant to determine the pain frequency and management barriers during cancer treatment. For this, it is necessary to study the following issues:

- Determination of cancer incidence using the database of population that is registered with cancer;
- Studying the effectiveness of pain assessment and management during the treatment of cancer patients from medical cards, as well as clarifying the same issues by telephone survey of the same patients;
- Survey of patients undergoing cancer treatment to determine pain frequency, intensity, prescribed analgesics, outcomes, and some barriers to pain management;
- Research and analysis of the current regulatory documents of medical opioids in Georgia.

Concept hypothesis:

Research will make it possible to identify barriers to adequate pain assessment and management in cancer treatment, create educational programs, plan to eliminate barriers to opioid access - early detection, correct assessment and management of pain, which will alleviate the burden of pain - suffering - torture for thousands of patients;

Reason for Research:

Identifying barriers to pain management in the process of cancer treatment and developing their preventive measures.

1. Comparison and characterization of cancer incidence in Georgia from 2015-2019;
2. During the treatment of cancer patients, determining the frequency and intensity of pain in different groups (age, gender, location of cancer, types of treatment), evaluating the prescribed analgesics and the obtained results;
3. Identifying barriers to pain management associated with patients and physicians;
4. Identifying barriers associated with regulating medical opioid use.

Scientific novelty and practical value of research results:

In the field of public health protection, in the field of oncology, new and complete knowledge was obtained through scientific research, based on evidence as follows:

1. Using standardized indicators, the structure of cancer incidence and the ranking of 5 main locations from 2015-2019 in Georgia, in the regions and in Tbilisi among male and female populations were determined. Compared to the same data of 2008, it was established that despite the decrease in the number of population in the country, the morbidity rate for cancer in all locations is increasing;

2. It was established for the first time that in 2015-2019 in Georgia, cancer was diagnosed at zero stage in both sexes only 0.2%. More than 50% of cases were diagnosed in stage III-IV. Especially noteworthy is the highest frequency of cancer verification in stage IV.

3. From 2015-2019, a total of 52,179 cases of cancer in 35 locations, including 989 cases of unknown and unclearly defined locations, were registered with cancer in both sexes of the population of Georgia. 737 (74.5%) of them are in IV stage. For the first time, it was established that the highest frequencies of diagnosis in the IV stage from the cancer organ locations were liver (64.8%), pancreas (61.6%), lung (61.2%), gallbladder (51.2%), stomach (43.8%), bone and joint system (43.5%), small intestine (42.0%) and retroperitoneum (41.5%) cancer.

4. It was determined for the first time that from 2015-2019, cancer in both sexes of the Georgian population was diagnosed in stage I in 22.1% of cases, stage II in 18.5%, stage III in 19.7%, stage IV in 24.1%. Out of all the regions within Georgia, cancer in the IV stage was diagnosed with the highest frequency in Guria (ASR=56.2%000; AAR=85.7%000; CR64=3.6. CR74= 6.4), in Tbilisi (ASR=54.2%000; AAR=79.2%000; CR64=3.2; CR74= 6.5), in Adjara (ASR=54.2%000; AAR=79.2%000; CR64=3.4; CR74= 5.7), in Racha-Lechkhumi (ASR=46.2%000; AAR=75.5%000; CR64=2.9; CR74= 5.2) and in Samegrelo-Zemo Svaneti (ASR=43.0%000; AAR=62.9.5%000; CR64=2.9; CR74= 5.1).

5. It was revealed that the population that has been registered with cancer and are oncology patients, do not register the cases of pain syndrome, their quality, and do not provide follow-up for monitoring. Clinical groups, according to which treatment of oncological patients and management of pain syndrome are carried out in Georgia, are also not registered.

6. In 44,119 cases of oncology patients, with stage III and IV stages, by modeling the frequency of pain, the estimated minimum (19,000 cases, 43.1%) and maximum (29,000 cases, 65.7%) pain syndromes were determined for the first time.

7. It was established for the first time that in Georgia, cancer-related pain occurs in 62.7-66.4% of patients during the cancer treatment ($p < 0.001$);

8. It was revealed for the first time that during the treatment of cancer patients, 73.9%-75.3% of patients had moderate and severe pain, which, according to the WHO pain management recommendation, requires opioid management;

9. In Georgia, it was established for the first time that in the process of treatment of patients with cancer, there was pain both in the early/intermediate stages - 43.7%, and in the IV stage - 56.3%; In early/intermediate stages, pain was more frequent in women (50.5%) than in men (37.8%), and in IV stage - on the contrary, pain was more frequent in men (62.2%) than in women (49.5%);

10. During the treatment, pain is most common in lung (92.5%), gastrointestinal (78.5%) and urogenital tract ($p<0.001$);

11. It was established for the first time that the frequency of pain during palliative chemo-radiation therapy is 1.7 times higher than during radical therapy ($p<0.001$). During palliative treatment, 87.6% of patients had pain of medium and strong intensity ($p<0.001$);

12. It was found for the first time that opioids are prescribed only in 9.6% - 14.6% of patients with moderate/severe pain during cancer treatment ($p<0.001$). Because of this, patients experience suffering, a decrease in the quality of life and the effectiveness of treatment;

13. It was revealed for the first time that the pain was relieved by analgesia in 23%-46.8% of cases ($p<0.001$), the pain management index was 29.4%-36.9%, that is when the treatment had low effectiveness; In total, 13.7% of patients were prescribed an opioid for moderate/severe pain; All patients were considered incurable/terminal and transferred to IV clinical group;

14. It was established for the first time that pain syndrome was associated with chemotherapy in 43.7% of the cases ($p<0.001$). During chemotherapy, 75.3% had moderate and severe pain. During chemotherapy, pain lasts up to 1 week in 65.1% (OR=1.8, 95%CI – 1.12-2.8, $p<0.001$), which is why opioid premedication was indicated;

15. In 10-15 days after radiation therapy, pain of various intensity develops which includes severe pain. The issue needs further study;

16. The lethality of patients with pain in 1 month was 11.9%, and among those without pain - 2.5% ($p<0.001$); 90% of the 31 patients who died had Moderate to severe pain. Because of this, cancer pain syndrome can probably be considered as a predictor of the spread of the disease, although it requires further in-depth research;

17. Despite the effective management of cancer pain, its frequency in 1 month decreased by only 49.8% and amounted to 50.2% of the initial number;

18. Classification of patients according to clinical groups ($p<0.001$) was considered to be the main barrier to prescribing opioids for those with moderate/severe pain in 97.7% of cases, which is not used anywhere except for the post-Soviet country hospitals;

19. On the basis of new knowledge obtained based on reliable evidence, recommendations developed in the direction of public health policy in the field of oncology legally paves the way for cancer control advocacy, protection of patients' constitutional rights and freedoms, reduction of suffering caused by pain in the treatment process, increase of treatment efficiency, increasing the chances of survival and life expectancy of patients, improving the quality of life, new directions of research, and socio-economic progress.

The main provisions of the justification:

1. In order to advocate the health of oncology patients, division into clinical groups should be removed from cancer management practices, guidelines, pain syndrome management legislation and subordinate regulatory acts.

- ✓ Classification of oncological diagnoses worldwide is carried out by clinical stages and TNM system classifiers. Division of oncology patients into clinical groups was used only in the Soviet Union and, as a remnant, is still used today in less developed post-Soviet countries, including Georgia. Moderate to severe pain can be managed with opioids 97% of the time, as the bylaw prescribes opioids for medical purposes only to untreated patients in the terminal phase for 6 months.
- ✓ Division of oncology patients into clinical groups and management of pain syndrome according to it reduces the effectiveness of treatment, deprives patients of the chances of survival and life extension, sacrifices them for suffering and torture, is inhumane and violates the constitutional rights and freedoms of a person.

2. Pain syndrome is most likely a prognostic factor for cancer progression and needs further research.

- ✓ Cancer pain is often experienced by patients both during the incurable phase and during the treatment of the disease (62.7%). At this time, more than 2/3 of patients with cancer pain (75.3%) have pain of medium and severe intensity, which require opioid management in accordance with WHO pain management recommendations.
- ✓ Patients with moderate/severe cancerous pain are mostly (79%) treated with non-steroidal anti-inflammatory drugs; As a result, the pain management index is 36.9%, and patients do not receive proper help and suffer, thereby worsening their quality of life and the effectiveness of cancer treatment, losing their chances of survival and prolonging their lives;

3. Regulations for existing medical opioid use need to be harmonized with the recommendations of the 1961 Single Convention on Narcotic Drugs (PPSG 2013) and WHO pain management standards (Health Organization, 2011), with national laws based on medical indications for pain management.

Volume and structure of the work:

The dissertation consists of an introduction, and five chapters with literature review, research materials and methods, main research results (three chapters), research results and evidence-based conclusions, main conclusions and recommendations, bibliography and 17 appendices, as well as a list of scientific works published on the topic of the dissertation. The thesis is written on 230 pages, following APA requirements, and contains 113 tables and 68 diagrams. The list of references contains 136 sources. The attached CD contains the electronic versions of the doctoral dissertation and prospectus (in Georgian and English), used questionnaires, electronic database, published scientific works on the topic of the dissertation.

Approbation of the work:

Fragments of the dissertation were reported at the International Conference on Public Health and Welfare of the University of Georgia - Online (Tbilisi, Georgia, April 26-30, 2020), at the VI congresses of the World Institute of Pain (WIP) in February 2012 and at the XI congress of the same institute on August 25-27, 2022, at the session of the Scientific Advisory Dissertation Council of the School of Health Sciences of the University of Georgia (Tbilisi, December 23, 2022).

Target groups, research instruments and methods:

In order to study the incidence of cancer in Georgia, the population that registered with cancer from 2015-2019 was analyzed. Electronic database of 52,178 registered cancer cases. 5-year data on cancer incidence in male and female populations in Tbilisi and other regions of Georgia according to cancer organ locations and patients' place of residence were studied. Based on the absolute number of incidences, using the methods of descriptive epidemiological research, standardized indicators were calculated and the structure of 5 main cancers, by gender, in Georgia were determined. Databases were processed statistically using the software package of Microsoft Excel. A descriptive epidemiologic study was conducted using the methodology recommended by the International Agency for Research on Cancer (IARC, Lyon), the International Association of Cancer Registries (IACR, Lyon), the European Network of Cancer Registries (ENCR, Lyon) and the International Union Against Cancer (UICC, Geneva) (Ahlbom A., Norell S., 1984; Boyle P., Parkin D.M., 1988; Gardis L., 2004; Agostina R. et al., 2006; Bhopal R., 2008). Tables were made with the obtained statistical indicators, and graphs were made by means of the software package of PowerPoint. The following statistical indicators were calculated: crude rate of morbidity; Age-Specific Rate (Age-Specific Rate); Age-Standardized Rate (Age-Standardized Rate - ASR); 95% Confidence Interval (95% CI ASR) of the Age-Standardized Ratio; Age-Adjusted Rate (AAR); 95% Confidence Interval (95% CI AAR) of the Age-Adjusted Rate; Standardized Rate Ratio (SRR); 95% Confidence Interval of Standardized Rate Ratio (95% CI SRR); Cumulative Risk Indicator (Cumulative Risk-CR); 95% Confidence Interval (95% CI CR) of the Cumulative Risk Ratio (CR64, CR74).

Cancer Population Register from 2015-2019 the 5-year cancer survival rates (by direct calculation) and treatment methods of oncology patients for cancer of the main location were studied with the data.

To determine the status of cancer pain management, medical records of 354 patients treated for cancer, kept in archives, were retrospectively studied using a developed questionnaire; The questionnaire included diagnosis, stage, treatment methods, pain frequency, intensity, drugs prescribed for pain relief, results. Subsequently, the same oncology patients were interviewed 1 month after the end of treatment with a telephone questionnaire. In this process, the information obtained from the cards was checked with the patients, as well as the issues that could be associated with

the patients. With the data received, an electronic database dBase N1 was created, which was processed by the means of software package SPSS. In order to detect pain in real time during the treatment of oncological patients, to find out some issues related to pain with doctors and patients, 354 patients were prospectively studied in different clinics of Tbilisi and Batumi and were interviewed with Questionnaire 2. The results were verified with Questionnaire 4. With the data received, an electronic database dBase N2 was created, which was processed by means of the software package SPSS.

The main results of the research:

In order to study the incidence of malignant tumors in Georgia, the electronic database for the population that registered with cancer from 2015-2019 was used. 5-year data on cancer incidence within Georgia, in Tbilisi and other regions, among male and female populations for 5 cancer sites were analyzed.

From 2015-2019, 52,178 cancer cases were registered, 29,303 (56%) of them in women and 22,875 (44%) in men. It was established that women in Georgia get sick more often than men ($Z=17.8$; $P<0.001$).

From 2015-2019, according to crude rates, there were 258 cancer cases per 100,000 men annually in Georgia. According to age-standardized (ASR) rates, there were 183 cancer cases per 100,000 men in Georgia from 2015-2019.

Among cancer organ locations, the rank is as follows: I - lung (ASR=27.3), II - prostate (ASR=20.4), III - bladder (ASR=16.0), IV - colorectal (ASR=15.8), V - skin (ASR=14.8).

According to the age-adjusted (AAR) indicators, from 2015-2019, 258 cancer cases per 100,000 men were diagnosed annually in Georgia.

In terms of cancer organ locations, the rank is as follows: I - lung (AAR=38.8), II - prostate (AAR=30.9), III - bladder (ASR=23.3), IV - skin (AAR=23.2), V - colorectal cancer (AAR=23.1).

According to AAR indicators, there is very little difference between the prevalence rates of bladder, colorectal and skin cancer in the male population of Georgia. In comparison with ASR, AAR indicators IV and V are replaced by colorectal and skin cancer morbidities.

From 2015-2019, the cumulative risk of men with cancer in the age group under 65 years of age in Georgia was 10.5, the amount of which increases almost twice before the age of 75 and is 20.0

From 2015-2019, the highest cumulative risk of cancer in men with the age group under 65 years of age in Georgia according to location was lung cancer (CR64=1.8), the amount of which increases almost twice before the age of 75 (CR74=3.5).

From 2015-2019, 7,595 cases of males with cancer were registered in Tbilisi. In the analyzed 5-year period, according to rough indicators, 302 that were diagnosed with cancer felt unwell annually for every 100,000 men in Tbilisi.

According to the age-standardized (ASR) rates, from 2015-2019, 244 cancer cases occurred annually for every 100,000 men in Tbilisi. I - Lung cancer (ASR=34.1), II - prostate (ASR=32.5), III - colorectal (ASR=24.1), IV - urinary bladder (ASR=22.7), V - Skin cancer (ASR=17.3).

According to the age-adjusted (AAR) rates, from 2015-2019, for every 100,000 men in Tbilisi, 244 were diagnosed with cancer annually. The first cancer locations were lung cancer (AAR=34.1), II - prostate (AAR=32.5), III - colorectal (ASR=24.1), IV - bladder (AAR=22.7), V - skin cancer (AAR=17.3).

From 2015-2019, the cumulative risk of male cancer in Tbilisi in the age group under 65 was 13.0, the amount of which increased almost twice before the age of 75 to 25.8.

From 2015-2019, men in Tbilisi had a high cumulative risk of lung cancer in the age group under 65 according to locations (CR64=2.2), the amount which doubled in the age group under 75 (CR74=4.4).

According to the cumulative risk indicators, there is a small difference between the cumulative risk of bladder (CR64=1.3), colorectal (CR64=1.2) and prostate (CR64=1.1) cancer in men under 65 years of age in Tbilisi.

However, in the age group under 75, the cumulative risk of prostate cancer increases 4 times (CR74=4.6) and, in addition to cancer of the mentioned locations, it exceeds the risk of developing lung cancer (CR74=4.4).

From 2015-2019, 15,225 cases of male cancer were registered in the regions of Georgia. In the analyzed 5-year period, according to rough indicators, 240 cases of cancer occurred annually for every 100,000 men in the regions.

According to age-standardized (ASR) rates, from 2015-2019, 166 cases of cancer per 100,000 men were diagnosed annually in the regions.

The first cancer locations were lung cancer (ASR=25.6), II - prostate (ASR=16.8), III - skin (ASR=14.3), IV - bladder (ASR=14.1), V - Colon cancer (ASR=13.5).

According to the age-adjusted (AAR) rates, from 2015-2019, there were 240 cases of cancer per 100,000 men in the regions each year.

The first cancer locations were lung cancer (AAR=37.4), II - prostate (AAR=26.9), III - skin (ASR=23.4), IV - bladder (AAR=21.0), V - Colorectal cancer (AAR=20.2).

From 2015-2019, the cumulative risk of male cancer in the regions in the age group under 65 years was 9.7, which increased almost twice for the age of 75 years to 18.2.

From 2015-2019, the high cumulative risk of male cancer disease in the regions of Georgia for males under 65 years of age according to locations had lung cancer (CR64=1.7), the amount of which increased almost twice in the age group under 75 years (CR74=3.3).

According to the cumulative risk indicators, there is a small difference in the risk of bladder (CR64=0.8), colorectal (CR64=0.8), prostate (CR64=0.6) and skin (CR64=0.6) cancers among men under 65 years of age. In addition, in the age group under 75, the cumulative risk of prostate cancer increases 4 times (CR74=2.3) and is higher than the risk of developing cancer in these locations and is only lower than the risk of lung cancer (CR74=3.3).

Lung cancer is the first in the structure of male cancer morbidity in 5 main organ locations (ASR=27.3), in Tbilisi (ASR=34.1) and within regions of Georgia

(ASR=25.6). The standardized incidence rate ratio (SRR) shows that the incidence of lung cancer in Tbilisi is 1.3 times higher (SRR=1.3) than those in the regions. In the structure of men's cancer morbidity in Georgia, prostate cancer is second (ASR=20.4), in Tbilisi (ASR=32.5) and within regions of Georgia (ASR=16.8). In addition, according to SRR, the incidence of prostate cancer in Tbilisi is 1.9 times higher (SRR=1.9) than in the regions. In the structure of male cancer morbidity in Georgia, bladder cancer is third (ASR=16.0), which is fourth in Tbilisi (ASR=24.1) and regions (ASR=14.1). According to SRR, the incidence of bladder cancer in Tbilisi is 1.7 times higher (SRR=1.7) than those in the regions. In the structure of male cancer morbidity in Georgia, colon cancer is fourth (ASR=15.8), which in Tbilisi is third (ASR=24.1), and fifth in the regions (ASR=13.5). Colorectal cancer morbidity in Tbilisi with SRR is 1.8 times higher (SRR=1.8) than the level of cancer morbidity in this location in the regions. Skin cancer ranks fifth in the structure of men's cancer morbidity in Georgia (ASR=14.8), as well as in Tbilisi (ASR=17.3), and third in the regions (ASR=14.3). According to SRR, the incidence of bladder cancer in Tbilisi is 1.2 times higher (SRR=1.2) than the level of cancer incidence in regions of this location. From 2015-2019, the number of new cancer cases in Georgia ranged from 10,000 to 11,000. In 2008, when the population was larger, 7,000 cases were registered, or 1.5 times less. In 2008, the incidence of cancer in Georgia was 143.0 per 100,000 population, and by 2019, this rate increased almost doubled and amounted to 277.9 per 100,000 population. From 2015-2019, the diagnosis of cancer in the zero stage in both sexes of the population of Georgia is so meager (0.2%) that it is not even reflected graphically. More than half of the cases were diagnosed in the third and fourth clinical stages. The highest frequency of cancer verification in clinical stage IV is particularly noteworthy and worrisome. A total of 52,179 cases of cancer of 35 localizations, including 989 cases of unknown and poorly defined locations, were registered in both sexes of the population of Georgia from 2015-2019 by the Cancer Population Register, of which 737 (74.5%) were in the IV clinical stage. Among cancer locations, the highest frequencies of diagnosis in IV stage were observed in liver (64.8%), pancreas (61.6%), lung (61.2%), gallbladder (51.2%), stomach (43.8%), bone and joint system (43.5%), in small intestine (42.0%) and retroperitoneum (41.5%) cancers. Attention is drawn to the fact that in 14.5% of cases the clinical stage of cancer is unknown/not registered. In addition, 0.8% of cases registered no clinical stage, 0.2% indicated advanced stage. From 2015-2019, in both sexes of the population of Georgia, cancer was diagnosed in stage I in 22.1% of cases, II - in 18.5%, III - in 19.7%, IV - in 24.1% of cases. Among the regions, cancer in IV stage was diagnosed with high frequency in Guria (ASR=56.2%000; AAR=85.7%000; CR64=3.6. CR74= 6.4), Tbilisi (ASR=54.2%000; AAR=79.2%000; CR64=3.2; CR74= 6.5), in Adjara (ASR=54.2%000; AAR=79.2%000; CR64=3.4; CR74= 5.7), in Racha-Lechkhumi

(ASR=46.2%000; AAR=75.5% 000; CR64=2.9; CR74= 5.2) and Samegrelo-Zemo Svaneti (ASR=43.0%000; AAR=62.9.5%000; CR64=2.9; CR74= 5.1).

It is noteworthy that the population registry of cancer does not register the cases of pain syndrome, their intensity, and does not provide follow-up monitoring in oncology patients. Clinical groups, according to which treatment of oncological patients and management of pain syndrome are carried out in Georgia, are also not registered.

We modeled the frequency of pain in patients with oncological stages III and IV. In 44,119 patients with clinical staging, according to version 8, estimated pain syndrome rates were determined.

Estimated minimum (19,000 cases, 43.1%) and maximum (29,000 cases, 65.7%) pain frequency rates in patients with oncological stage III and IV stage in Georgia were determined.

The frequency and intensity of pain syndrome in oncology patients requires further study, mandatory registration and active follow-up monitoring.

Early/intermediate stage cancer detection correlates positively with five-year survival rates and vice versa. Five-year cancer survival rates in Georgia from 2015-2019 were high for thyroid gland (92.8%), Cancer In situ (89.1%), Hodgkin's Lymphoma (74.5%), kidney/pelvis (69.3%), uterine body (66.7%) and breast cancer (66.0%).

In Georgia, the five-year survival rate for all locations is 50.1%. According to the five-year cancer survival rates of 2015-2019, Georgia is among the countries with low survival compared to international data. This means that cancer treatment needs significant improvement. Low five-year cancer survival rates are observed in developing countries, where pain is common, affecting treatment outcomes. In 2019, 15,971 different types of treatment were performed on cancer patients in Georgia. Out of those, 7316 (40.8%) were surgical, 8655 (54.2%) were chemo-, hormone-, immuno-, radiation therapy. Thus, in 2019, medical and radiation treatments were performed on more patients than surgical ones.

According to international experts, in 2018-2030, the number of new cancer cases in Georgia will increase by 5% in women, and by 7% in men.

Research of medical cards of oncology patients revealed that 138 or 39% of 354 patients experienced pain during cancer treatment (Chi-Square 17.19; $p < 0.001$); In the telephone survey of the same patients, pain was diagnosed in 235 or 66.4% (Chi-Square 38; $p < 0.001$), which is similar to the results of the prospective study is similar. In particular, out of 354 patients, 222 or 62.7% had pain (Chi2=22.88, $p < 0.001$). As for pain fixation in the cards, it was not written in 97 patients or 41.3% (OR=13.0, 95%CI-6.5-26.2, $p < 0.001$). This means that doctors do not record pain symptoms for certain reasons. They named the stressful environment when receiving patients, relieving pain with treatment, concentrating attention on treatment, etc. as such reasons. That is, doctors do not adequately assess the negative impact of pain on treatment, physical health, psycho-emotional status, which indicates their lack of knowledge about pain and the need to increase knowledge in this regard.

With the cards, out of 138 patients with pain, the intensity of pain was recorded in 81 patients, i.e. 58.7%, and in relation to 235 patients with pain, 34.5%, the remaining 65.5% (OR=7.3, 95%CI – 3.4-15.7, $p<0.001$) yes - not determined (diagram 2). Out of 81 patients with pain, 21.7% had mild pain (OR=5.7, 95%CI – 1.7-19.0, $p=0.005$), moderate pain – 24.6% (OR=9.9, 95%CI – 2.3-41.9, $p<0.001$), strong - 12.3% (OR=3.0, 95%CI – 0.9-10.5, $p=0.086$), and the rest 41.4% were unknown; With a partial assessment of the strength of pain, it is naturally impossible to judge the real strength. Therefore, it was determined how doctors rate pain intensity and whether they use a numerical or visual analogy rating scale. A survey of pain intensity in the cards revealed that out of 354 cancer patients, 5 (1.4%) patients were asked about numerical pain assessment (Chi-Square 166.39; $p<0.001$). Of those, pain intensity was recorded in 2 (0.6%) patients (Chi-Square 346.05; $p<0.001$) were assigned to clinical group IV due to severe pain with terminal condition and were prescribed opioid management. Data on pain assessment were confirmed by the same patient survey.

159 oncology patients or 44.9% stated that the oncologist did not ask them a question about the numerical assessment of pain intensity and therefore they believe that doctors evaluate pain based on personal experience. 190 patients or 53.7% did not know what method doctors use to assess pain intensity. (Chi-Square 166.39; $p<0.001$). Thus, during the treatment of patients with cancer, doctors assess the intensity of pain based on their personal experience and almost do not (1.4%) use a numerical pain assessment scale (Chi-Square 346.05). Consequently, during pain management, doctors prescribe analgesics inadequately, which influences the effectiveness of pain management. In particular, 12.8% (OR=3.3, 95%CI – 1.3-8.8, $p=0.016$) of pain was "relieved" by prescribed analgesics and "partial" – 33.5% (OR=9.5, 95%CI – 4.0-22.6, $p<0.001$), and the rest is "unknown" 52.8% (OR=8.0, 95%CI – 4.2-15.3, $p<0.001$) (see diagram 3). The effectiveness of drugs prescribed to manage all types of pain was 24.7%.

Thus, in the medical cards, oncologists prescribe analgesics to patients with pain not according to the intensity of the pain, but according to personal opinion; As a result, pain management is less effective, indicating a lack of knowledge among physicians in this area.

A survey of patients with pain revealed that physicians focus predominantly on cancer treatment and less on pain assessment and management. Such an approach sometimes leads to an incorrect assessment of pain. A 64-year-old man said: "I often told my doctor that despite the chemotherapy, I still had pain, and the doctor stubbornly insisted that he was treating me and that time and patience were necessary..., and he didn't even talk about pain relief" (P105). During the telephone survey, all 235 patients were evaluated for their pain intensity using a numerical scale. Among them, 50 patients or 21.3% had mild pain (OR=15.8, 95%CI – 3.8-66.2, $p<0.001$), 136 or 57.9% had moderate pain (OR=39.5, 95%CI – 14.1- 110.6, $p<0.001$), strong - 41 or 17.4% (OR=24.9, 95%CI – 3.4-183.7, $p<0.001$). A total of 177 patients or 75.3% had moderate/severe pain (Chi-Square 290.14, $p<0.001$); All of them

required opioid management according to WHO pain management step 3. Unfortunately, weak/strong opioids were prescribed to only 21 patients out of 177 patients or 11.9%, and the remaining 156 patients or 88.12% were left without proper help; In addition, all patients were prescribed opioids after transfer to the IV clinical group.

All other patients were prescribed: Non-steroidal anti-inflammatory drug - 147 patients (62.6%), Analgin with Diphenhydramine - 20 (8.5%) (Chi-Square 186.9, $p < 0.001$). 54 or 23.0%, partially - 139 or 59.1%, and 42 (17.9%) patients - pain of the same intensity remained (Chi-Square 198.58, $p < 0.001$). (Table 4),

For 235 pain patients, the pain management index was positive in 29.4%, which is 4.7% more than in the medical records - 24.7%. Thus, analgesic drugs prescribed for pain relief were effective in 29.4%, inadequately prescribed in 70.6% of cases. During the current treatment or prospective study, 58 or 26.1% of 222 cancer patients had mild pain, 118 or 53.2% had moderate pain, 46 or 20.7% had severe pain (Chi-Square 62.14, $p < 0.001$). Thus, moderate pain was the most common, as among those interviewed by telephone. A total of 164 patients, or 73.9%, who required opioid therapy had moderate and severe pain.

During the current treatment, as well as among those interviewed over the phone, doctors use Non-steroidal anti-inflammatory drug most often to relieve cancer pain - in 197 cases or 55.6%, which is 88.7% of all patients with pain;

164 patients with moderate and severe pain, who require the prescription of opioids according to the pain management recommendations of the WHO, as well as the pain management guidelines of the Ministry of Health of Georgia. However, it was prescribed to only 24 patients (Table 4). That means, out of 164 patients with moderate/severe pain, 24 patients or 14.6% received adequate help, while 140 (85.4%) patients remained without help. Analgesics prescribed for pain relief were effective for 104 patients or 46.8% of 222 patients with pain, when the pain was completely relieved, 118 patients or 53.2% were partially relieved of pain, in the case of 4 patients there was no result (Chi²=59.42, $p < 0.001$).

The adequacy of the prescribed means for pain relief was determined by calculating the pain management index. It was found that the management index was positive in 6.8% (118 patients) of moderate pain, 34.8% (46 patients) of severe pain, and 36.9% of 222 cases of all types of pain, which is 7.6%- It is higher than in the patients interviewed by phone (29.3%), but it is much less than can be reached.

Thus, in retrospective and prospective studies, pain during cancer treatment is very common (66.4-62.7%), especially moderate/severe (75.3-73.9%), which requires opioid management, and existing pain management is less effective (29.3-36.9%). That is why it is necessary to develop new approaches. For this, it is necessary to reveal the characteristics of pain distribution and barriers to management.

Research results were inconclusive for cancer pain by age group. However, it was determined that 10.2% of 235 pain patients interviewed by phone had pain under the age of 50, 26.0% at the age of 51-60, 40.9% at the age of 61-70, and the

frequency of pain over the age of 70 decreased to 23.0%. Similar results were obtained in a study of 222 pain patients on current treatment. In particular, 14.4% of patients under the age of 50 had pain, 23% at the age of 51-60, 41.4% at the age of 61-70, and only 21.2% of those over 70. Thus, as the age of patients with pain increases, the frequency of pain also increases, which reaches its maximum at the age of 51-70 years (66.8-64.4%), and significantly decreases after the age of 70. A survey of pain frequency by gender showed that 114 (55.1%) of 207 women interviewed by telephone had pain, and 121 (82.3%) of 147 men had pain. During the current treatment, 103 of 193 women with cancer had pain, or 53.4%, and 119 of 161 men, or 73.9% (Chi-Square 15.84; $p < 0.001$). Accordingly, pain in men during treatment is at least 1.4 times (73.9%/53.4%) more than in women.

Pain intensity was also studied according to gender. It was determined that 103 women with pain most often had moderate pain - 47 or 45.6% (Table 5); Men had the highest pain in average intensity of 71 or 59.7%, which is 1.3 times more than in women. A total of 98 men or 82.4% had moderate/severe pain, 72 or 69.9% in women. Opioid therapy is needed to manage pain of such severity, based on the WHO pain management scheme and the pain management guidelines of the Ministry of Health and Social Protection of Georgia (F. Dzotsenidze, T. Rukhadze, I. Abesadze, 2012).

Table 5. Current treatment of cancer patients Frequency and intensity of pain according to gender

Gender	Quantity, %	NRS >4	NRS =4-6	NRS ≤7
Woman	103/100%	31/30.1%	47/45.6%	25/24.3
Male	119/100%	27/22.7%	71/59.7%	21/17.6
All	222/100%	58/26.1%	118/53.2%	46/20.7%

Source: Research results

Patients interviewed by telephone had increased pain frequency with increasing cancer stage. 2.6% had pain at stage I, 13.2% at stage II, 3 times more at stage III - 40.4%, more at stage IV - 43.8% Chi-Square 36.22; $p < 0.001$). 56.2% had pain in the early/intermediate stages of 235, and 43.8% in the IV stage.

Similar trends were found in the patients interviewed during the current treatment. In particular, 2.3% had pain at stage I, 10.8% at stage II, 3 times more at stage III - 30.6%, at stage IV - 56.3% Chi-Square 67.42; $p < 0.001$). Out of 222 patients with pain, 43.7% had pain in stages I-III, and 56.3% in stage IV.

A study of the frequency of pain by sex and stage of 235 patients interviewed by telephone during cancer treatment showed that in early/intermediate stages, as well as in stage IV, pain was common in both women (53.8% / 46.2%) and men - 60.0% / 40%. During cancer therapy, the frequency of pain in stages I-III may be related to frequent aggressive drug therapy or their long-term infusion, as well as radiation therapy or combination of all, because in stage IV, sparing palliative therapy is mainly carried out. This opinion was partially reflected by a study of

222 patients with pain during current treatment, in which stage I-III pain was more frequent in women (50.5%) than men (37.8%), and on the contrary, stage IV pain was more frequent in men (62.2%) than in women (49.5%). Thus, as the stage of cancer increases during treatment, the frequency of pain also increases, which in early/intermediate stages is more common in women (50.5%) than in men (37.8%), on the contrary, in stage IV, pain is more common in men (62.2%) than in women (49.5%).

Comparing those with and without pain during cancer of a separate organ, it was determined that pain is common in lung (93.5%), stomach (80%) and colorectal (50%) cancers, and relatively less in breast (48.1%), ovarian (45%) and in the case of uterine body cancer (40.5%) (Chi-Square 68.57; $p < 0.001$).

During the treatment of patients with cancer of various organs, the most frequent pain was of medium intensity (NRS =4-6), namely in lung (69%), gastrointestinal tract (69.1%) and breast (44.7%) cancers. A similar trend was established in the current treatment process. Moderate and severe pain was common in lung (94.9%), breast (80.6%) and gastrointestinal tract (74.5%) cancers.

Depending on the type of treatment, the frequency of pain differed: 47.9% had pain during 119 neoadjuvant chemotherapy, 39.3% during 28 neo-/adjuvant radiation therapy, 124 during palliative chemotherapy - 82.3%, 82.6% of 46 palliative chemo-radiotherapy had pain, 24 during neo-/adjuvant chemo-radiation therapy - 62.5%.

The odds of pain were significantly higher for neoadjuvant chemotherapy (OR=3.4, 95%CI=2.1-5.4, $p < 0.001$), palliative chemotherapy (OR=3.4, 95%CI=2.0-5.7, $p < 0.001$) and palliative chemo- in case of radiation treatment (OR=2.7, 95%CI=1.2-5.9, $p = 0.016$). 86 (49.1%) had pain during 175 radically performed chemo-radiation therapy for cancer; 55.8% of them experienced moderate (45.3%) and severe (10.5%) pain. 149 (83.2%) of 179 patients experienced pain during palliative treatment, during which 86.6% ($p < 0.001$) experienced moderate (65.1%) and severe (21.5%) pain. Thus, pain during palliative therapy is 1.7 times higher than during radical therapy (Chi-Square 21.72; $p < 0.001$).

The same trends were found in a prospective study. Out of 203 radical treatments, 93 (45.8%) patients had pain; Among them, moderate (43%) and severe (11.8%) pain was diagnosed in 54.8%. Out of 151 cases of palliative therapy, 129 (85.4%) patients had pain; A total of 87.6% of them had moderate (60.5%) and severe (27.1%) pain. Thus, pain during palliative therapy (85.4%) is 1.9 times higher than during radical therapy (45.8%) (Chi-Square 68.05; $p < 0.001$). 48% had pain during radical therapy - neo-adjuvant chemotherapy (Chi-Square 62.14; $p < 0.001$). Pain was most common during palliative chemotherapy - 3.7% (OR=4.1, 95%CI = 2.3-7.6, $p < 0.001$) and palliative radiation therapy - 97.1% (OR=23.7, 95%CI = 3.2-175.3, $p < 0.001$), during individual methods of palliative therapy, moderate/severe pain ranges from 85.3-88.9%.

Recently, long and aggressive chemotherapy transfusions have become more frequent. As a result, side effects, including pain, increased. It was determined that 81 or 34.5% (OR=2.5, 95%CI=1.6-3.9, $p < 0.001$) had no

pain in the background of medication and radiation therapy, while 154 (65.5%) patients had pain of varying intensity. Out of 154 patients, 63.3% had moderate pain (OR=2.4, 95%CI-1.5-4.0, $p<0.001$), severe - 11.0% (OR=2.4, 95%CI-1.5-4.0, $p<0.001$). Thus, 81 patients or 34.5% had no pain during chemo-radiation therapy. The majority of patients had moderate pain - 63.3% (OR=2.4, 95%CI-1.5-4.0, $p<0.001$). In total, 115 or 74.7% had moderate/severe pain.

It was determined that out of 154 patients with pain during chemotherapy started in 109 patients or 70.8% in the first 3 days (OR=1.8, 95%CI – 1.12-2.8, $p<0.001$), and in 44 patients or 28.6% before one week. (OR=1.9, 95%CI – 0.97-3.6, $p=0.065$). Thus, 70.8% of patients (OR=1.8, 95%CI-1.12-2.8, $p<0.001$) experienced pain within the first 3 days of chemotherapy.

It was also determined (Table 9) that out of 119 patients without pain before treatment, pain started in 39 patients or 32.8% (OR=1.8, 95%CI – 1.12-2.8, $p<0.001$) 1-3 days after the start of chemotherapy, and within 1 week - 13 patients or 10.9% (OR=1.9, 95%CI – 0.97-3.6, $p=0.065$). Thus, 52 patients or 43.7% developed pain within 1 week after the start of chemotherapy (Chi-Square 16.27; $p<0.001$). A survey of patients concerned with the side effects of chemotherapy - pain - did not consider the same for radiation therapy. However, such patients report mouth ulcers, pain while swallowing, etc. We were able to interview 25 patients after radiation therapy for head and neck and larynx cancer. Nineteen (76%) were found to have radiation therapy-related pain and difficulty swallowing. 13 out of 17 (76.5%) patients developed stomatitis, pain, difficulty swallowing and mucositis within 10-15 days after the end of radiation therapy. We think that the issue needs in-depth research.

It should be noted that despite the adequacy of the prescribed analgesics, the number of patients with pain decreased by 117 (49.8%) and those that remained - 118 (50.2%) 1 month after the end of the treatment. The reduction affected the pain of all levels. Such a decrease is due in part to the effect of chemo-radiation therapy and in part to pain management.

At the time of the survey of oncology patients, 28 (11.9%) of the 235 patients with pain died, 3 (2.5%) of the 119 patients without pain, i.e. 28 of the 31 deceased or 90% had pain (OR=5.2, 95%CI – 1.6- 17.6, $p=0.008$), which is why the pain syndrome is likely to predict disease progression, which requires further study;

It was noted that the pain management index was 36.9%. The question arises as to who is responsible for this result: patients, doctors, legislators or all together. All of them were interviewed. Patients were asked if they told their doctor about the pain. It was determined that 33.6% of 235 patients did not report pain, and 66.4% reported it by their own initiative (Chi-Square 258.32, $p<0.001$). Thus, 33.6% (OR=15.8, 95%CI-4.6-54.1; $p<0.001$) of patients have incomplete registration of pain by doctors, which is a barrier to timely detection of pain.

To the question: "Why didn't you tell the doctor about the pain?" Out of 235 cancer patients, 22.6% said that "it didn't hurt too much", 7.2% said that "the doctor didn't ask", 6.8% were afraid of "postponing treatment", 46.4% - "could bear the pain" (Chi-Square 284.26; $p < 0.001$). Thus, 17% ($p < 0.001$) voluntarily informed the doctor about the pain, while 83% did not have such a desire, because they did not know the possibilities of pain management.

Patients were asked: Would they take morphine when needed? 19.2% refused, 33.9% "don't know", 11.3% are afraid of getting used to it. 9.3% stated that they "don't have cancer". 73.7% of the total number of patients refrained from taking morphine, a little less than 66% of 235 patients with cancer pain.

To the question: "Does the family influence the management of pain with opioids" - 24.8% of 222 patients with pain confirmed such influence (OR=4.0; 2.0-8.2; $p < 0.001$), and only 7.6% of families of 132 patients without pain had such influence.

The conducted research identified barriers of pain management associated with doctors: incomplete (39%) registration of pain frequency (Chi-Square 17.19; $p < 0.001$) and often (41.3%) not determining its strength (OR=7.3, 95%CI-3.4-15.7, $p < 0.001$); Assessment of pain intensity based on personal perception (98.6%) and not on a numerical scale - 1.4%)g (Chi-Square 166.39; $p < 0.001$). Pain management based on personal opinion (98.6%) and not according to the WHO pain management scheme, which is why the pain management index is only 36.9%; Low patient awareness of pain management - 99.2% (Chi-Square 342.10; $p < 0.001$) and 21.7% of patients with pain did not ask about pain when taking anamnesis (OR=2.4, 95%CI - 1.5-3.8, $p < 0.001$).

According to the data obtained, it was determined that 2/3 of the patients had moderate/severe (NRS 4-10) pain during the cancer treatment process; Doctors did not prescribe opioids to manage them until they were incurable and terminal. 97.7% of oncologists (Chi2=322.72, $p < 0.001$) confirmed that such an approach derives from the indications of clinical groups. In particular, the prescription of opioids during cancer treatment is prohibited by the current regulation.

The existence of clinical groups is associated with suffering of many patients. Here's what a 54-year-old man with pain writes (p228): "During the pain relief from cancer surgery, the doctor probably made a mistake with the first prick, then the second one and it went numb.. After the operation, I started having such pains that I could see my entire skeleton in my eyes and every point hurt. I can't describe it, on a 10-point scale, these pains were probably twenty (!) I can't describe it any other way, they kept me in the clinic for 3-4 days with morphine... Then they discharged me, they didn't prescribe me morphine, because you don't have cancer anymore.. Every day, sometimes 2 times I called a paid ambulance to stop the terrible pain... I tried to commit suicide three times because of the pain. The emergency doctors advised me to go to the clinic to prescribe morphine... I went and they didn't prescribe me... This continued for 2 years, I had a hotel business and Bankruptcy, I paid more than 35,000 GEL to numb the pain. Finally, the bank sold my house, business, hotel and left me on the street with my five children and old mother. The oncologist finally got the hang of it and put me on morph because it was the only thing that stopped the excruciating pain, and now it's September 2022 and I'm still alive and still addicted

to morph. We have already buried 8-9 close people and relatives with the same diagnosis, who were found after me and are already dead, and thanks to Morph, I am still alive and it doesn't even seem that I am sick.”

Attention is drawn to the fact that in 14.5% of cases the clinical stage of cancer is unknown/not registered. In addition, 0.8% of cases registered no clinical stage, 0.2% indicated advanced stage.

It is noteworthy that the population registry of cancer does not register cases of pain syndrome in oncology patients, their quality, and does not provide follow-up monitoring. Clinical groups, according to which management of pain syndrome in oncology patients is produced in Georgia, are also not registered.

A study of restrictions on pain management in cancer care found that Georgia laws (2012) recognize the need for opioids for medical purposes to be made available by physicians on a continuum of service, while bylaws (2008) limit opioid prescribing to untreated patients, including those in the terminal phase of the disease (2018). The doctor can provide the service only during the last 6 months, if the terminal phase of the disease is confirmed. Therefore, pain management is tailored not to the medical indication, but to the clinical group and expected life expectancy.

Current regulations for medical opioid use need to harmonize the advice of the 1961 Uniform Convention on Narcotic Drugs (PPSG 2013) and international standards (Health Organization, 2011), with national laws based on medical indications for pain management.

In addition, the evidence from analysis of existing opioid control documents provides a foundation that works for human health.

Evidence-based based on research results Main conclusions:

1. Using standardized indicators, the structure of the incidence of malignant tumors and the ranking of 5 main locations from 2015-2019 in Georgia, in the regions and in Tbilisi among male and female populations were determined. According to the age-standardized ratio (ASR) in Georgia from 2015-2019, every 100,000 men were diagnosed with cancer every year 183. According to cancer locations, lung cancer ranked I (ASR=27.3; 95% CI ASR= 26.4-28.2), II - prostate (ASR=20.4; 95% CI ASR= 19.6-21.1), III - bladder (ASR=16.0; 95% CI ASR= 15.3-16.7), IV - Colorectum (ASR=15.8; 95% CI ASR= 15.1-16.5), V - skin cancer (ASR=14.8; 95% CI ASR= 14.1-15.4).

2. From 2015-2019, the structure of cancer incidence in the population of men living in the city of Tbilisi and its regions was determined by standardized indicators and the ranking place of each location: I and II ranking places as st. In Tbilisi, as well as in the regions, they had lung and prostate cancer, respectively. At the same time, the cancer incidence rates of these locations in Tbilisi were, respectively, 1.3 times and 1.9 times higher than the incidence rates registered in the regions; Urinary bladder cancer occupied the fourth place both in Tbilisi and in the regions; III and V places were respectively occupied by colorectal and skin cancer in Tbilisi, and on the contrary in the regions - by skin and colorectal cancer.

3. From 2015-2019, 29,303 cases of women's malignant tumors were registered in Georgia. During the 5-year study period, age-standardized

(ASR) rates were 197 for every 100,000 women annually. According to the location of cancer, the first place was occupied by breast cancer (ASR=63.2; 95% CI ASR= 61.8-64.5), II - by the thyroid gland (ASR=34.4; 95% CI ASR=33.3- 35.5), III - cervix (ASR=13.4; 95% CI ASR= 12.8-14.1), IV - body of the uterus (ASR=11.3; 95% CI ASR= 10.8- 11.9), V- colorectum (ASR=10.3; 95% CI ASR= 9.7-10.8) cancer.

4. According to age-standardized rates (ASR) in Georgia, Tbilisi and regions, breast cancer ranks 1st in the structure of cancer morbidity (ASR=63.2). Breast cancer also ranks first both in Tbilisi (ASR=85.3) and in the regions (ASR=54.0). At the same time, the ratio of standardized incidence rates (SRR) shows that the incidence rate of breast cancer in Tbilisi was 1.6 times higher (SRR=1.6) than the incidence rate of cancer in this location in the regions.

5. Compared to the same data of 2008, it was determined that despite the decrease in the population in the country, the morbidity rate for all types of cancer is increasing. The incidence of cancer per 100,000 inhabitants in Georgia in 2008 was 143.0‰, and in 2019, the number of registered cancer cases doubled and amounted to 277.9‰, which is mainly related to the creation of the population registry of cancer in Georgia.

6. From 2018-2019, on average, 46,591 deaths from all causes were registered annually in Georgia, including 4,255 (9%) from cancer, and 42,336 (91%) from all other causes. In 2018-2019 12,335 deaths from all causes are registered in Tbilisi every year, including 1,476 (12%) from cancer, and 10,859 (88%) from all other causes.

7. In 2015-2019, the diagnosis of cancer in the zero stage in Georgia was negligible (0.2%). More than 50% were diagnosed in stage III-IV. The high frequency of cancer verification in stage IV is noteworthy.

8. From 2015-2019, a total of 52,179 cases of cancer of 35 locations were registered in both sexes of the Georgian population, including 989 cases of unknown and poorly defined locations, of which 737 (74.5%) were in the IV clinical stage. Among cancer locations, the highest frequencies of diagnosis in IV clinical stage were observed in liver (64.8%), pancreas (61.6%), lung (61.2%), gallbladder (51.2%), stomach (43.8%), bone and joint system (43.5%), in small intestine (42.0%) and retroperitoneum (41.5%) cancers.

9. In 2015-2019, in both sexes of the population of Georgia, cancer was diagnosed in the 1st stage in 22.1% of cases, in the 2nd - in 18.5%, in the 3rd - in 19.7%, in the 4th in 24.1%. Among the regions of Georgia, cancer in the 4th stage was diagnosed with a high frequency in Guria (ASR=56.2‰; AAR=85.7‰; CR64=3.6; CR74= 6.4), Tbilisi (ASR=54.2‰; AAR=79.2‰; CR64=3.2; CR74= 6.5), in Adjara (ASR=54.2‰; AAR=79.2‰; CR64=3.4; CR74= 5.7), in Racha-Lechkhumi (ASR=46.2‰; AAR =75.5‰; CR64=2.9; CR74= 5.2) and Samegrelo-Zemo Svaneti (ASR=43.0‰; AAR=62.9.5‰; CR64=2.9; CR74= 5.1).

10. The population registry of cancer does not register the cases of pain in oncological patients, their intensity, and does not provide follow-up monitoring. Also, clinical groups are not registered, although in Georgia they provide treatment of oncological patients and management of pain syndrome.

11. In 44,119 oncology patients with stages III and IV, pain frequency modeling determined the minimum (19,000 cases, 43.1%) and maximum (29,000 cases, 65.7%) estimated amounts of pain syndrome.
12. In Georgia, cancer-related pain is experienced by patients during cancer treatment with a frequency of 62.7-66.4% of cases ($p<0.001$); During the treatment of cancer patients, 73.9%-75.3% of patients had moderate to severe pain, which required opioid management according to the WHO pain management recommendation.
13. In the process of treatment of patients with cancer, there was pain both in early/intermediate stages - 43.7%, and in stage IV - 56.3%; In early/intermediate stages, pain was more frequent in women (50.5%) than in men (37.8%), and in IV stage - on the contrary, pain was more frequent in men (62.2%) than in women (49.5%);
14. During the treatment, pain is most common in lung (92.5%), gastrointestinal (78.5%) and urogenital tract complaints ($p<0.001$).
15. The frequency of pain syndrome during palliative chemo-radiation therapy is 1.7 times higher than during radical therapy ($p<0.001$). During palliative treatment, 87.6% of patients had pain of medium and strong intensity ($p<0.001$).
16. Opioid is prescribed only in 9.6% - 14.6% of patients with moderate/severe pain during cancer treatment ($p<0.001$). Because of this, patients experience suffering, a decrease in the quality of life and the effectiveness of treatment.
17. In patients with cancer pain, pain was relieved by analgesia in 23%-46.8% of cases ($p<0.001$), the index of pain management was 29.4%-36.9%, that is, the treatment was low effective; For moderate/severe pain, opioid was prescribed to 13.7% of patients; All these patients were considered incurable-terminal, transferred to the IV clinical group and special treatment was stopped.
18. 43.7% of pain ($p<0.001$) was associated with chemotherapy. During chemotherapy, 75.3% of patients had moderate and severe pain. During chemotherapy, pain syndrome lasts up to 1 week in 65.1% of patients ($OR=1.8$, $95\%CI - 1.12-2.8$, $p<0.001$), which is why opioid premedication was indicated; 10-15 days after radiation therapy, pain of various intensity develops, including severe. The issue needs further study.
19. The frequency of cancer pain in 1 month decreased by 49.8% and amounted to 50.2% of the initial amount; The lethality of patients with pain syndrome in 1 month was 11.9%, and among those without - 2.5% ($p<0.001$); 90% of the 31 patients who died had pain of moderate/severe intensity, which is why the pain syndrome is likely to be a predictor of disease progression, which requires further study;
20. Classification of patients according to clinical groups ($p<0.001$) is the main barrier to prescribing opioids during moderate/severe pain syndrome in 97.7% of cases, which is not used anywhere except in post-Soviet hospitals.

Practical recommendations:

As a result of the research, based on new evidence-based knowledge, the following recommendations were developed:

1. In order to advocate for the health of oncology patients, it is recommended that the division into clinical groups be removed from cancer management practices, guidelines, pain syndrome management legislation and subordinate regulatory acts.

1.1 Classification of oncological diagnoses worldwide is carried out by classifications of clinical stages and the TNM system. Division of oncology patients into clinical groups (Soviet know-how) was used only in the Soviet Union and, as a remnant, is still used today in less developed post-Soviet countries, including Georgia. To date, moderate/severe cancer pain has not been managed with opioids (97.7%) due to the use of clinical teams in patient management, as the bylaw allows opioid prescribing for medical purposes for treatment-naïve patients in the terminal phase within the last 6 months.

1.2 Division of oncology patients into clinical groups and management of pain syndrome according to it reduces the effectiveness of treatment, deprives patients of the chances of survival and life extension, sacrifices them for suffering and torture, is inhumane and violates the constitutional rights and freedoms of a person, including the patient.

1.3 In order to overcome the negative practices established in the management of pain inherited from the Soviet Union, which is related to the prescription of opioids according to "clinical groups", which is not based on the physiology of pain, the principles of its management and violates the fundamental human rights, it should be removed from the practice. Moreover, it operates only in a few former Soviet countries and nowhere else in the world.

1.4 Revision of legislation and removal of unreasonable restrictions and obstacles, elimination of contradictions, as well as consolidation of opioid pain management regulatory acts to avoid duplication of norms.

1.5 Facilitating the implementation of updated regulations in practice and providing information to doctors, clinic administrations and controlling bodies; The mentioned regulations should be placed on the website of the Ministry of Labor, Health and Social Protection of Georgia, which will make them more accessible.

2. A column should be included in the medical cards to record the intensity of pain; Doctors should inform patients about the principles of cancer pain management when receiving informed consent (form N IV-300-12/a) for medical services;

3. It is possible to solve the problem by implementing the World Health Organization (WHO, Geneva, 13, 1387) three-step scheme of pain management in the process of treatment of oncological patients, thereby achieving adequate pain management and reducing suffering in the treatment of cancer patients.

4. A pain management program should be introduced in graduate courses in medical schools, as well as support for basic pain management education for general practitioners. General practice doctors have to expand their knowledge through training in cancer control advocacy, cancer screening of key locations, early and timely diagnosis, classification-registration of cases according to clinical stages and TNM systems, active follow-up observation of patients, monitoring of ECOG status and pain syndrome.