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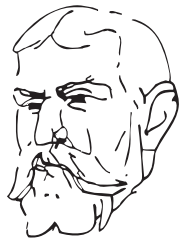

Memory of
dr Władysław
Biegański

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ORIGINAL ARTICLE

PREGNANCY AND BIRTH OUTCOMES IN FEMALE WITH AND WITHOUT ASSISTED REPRODUCTIVE TECHNOLOGY IN UKRAINE

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ABSTRACT

The aim: To assess and compare the risk of maternal/perinatal complications and adverse outcomes in pregnancy and childbirth conceived by ART with those conceived naturally in Ukraine.

Materials and Methods: We conducted a retrospective multicenter cohort study from January 1st, 2019 to December 31st, 2021. This study included pregnant women who delivered at 14 Women's Hospitals from 8 regions of Ukraine.

Results: A total of 21,162 pregnancies were included. Of these, there were 19,801 natural pregnancies and 1,361 pregnancies after ART. The proportion of ART pregnancies has increased every year in during study period, peaking in 2021 (6.7%). Data analysis showed that the risks of gestational diabetes, preeclampsia, moderate or severe anemia, liver-related diseases, thyroid-related diseases, preterm birth, placenta previa, postpartum hemorrhage, and cesarean section were significantly increased in ART pregnancy. For neonatal outcomes, women conceived by ART were more likely to have twins. The effects of ART on the risk of premature rupture of membrane, cord entanglement, intrapartum fever, and cesarean section were more pronounced in singletons pregnancies.

Conclusions: Women conceived by ART were at increased risks of several adverse pregnancy outcomes compared with women conceived naturally. Therefore, prenatal and intrapartum monitoring should be strengthened, and neonatal outcomes should be closely observed for ART pregnancy.

KEY WORDS: assisted reproductive technology (ART); pregnancy outcomes; pregnancy complications; perinatal complications; neonatal complications; Ukraine

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INTRODUCTION

Infertility is a global socio-economic, demographic, reproductive health and clinical issue affecting millions of people of reproductive age worldwide. Literature suggests that infertility affects approximately 15% of couples worldwide, accounting for 48.5 million couples [1], and 186 million individuals [2]. The estimated prevalence of infertility in Ukraine were 25,4% [3]. This applies to both primary and secondary infertility of married women. In the last three decades, the population of Ukraine has been rapidly shrinking due to low birth rates. Within 30 years, its population declined by 10.4 million, from a high of 51.9 million in 1991 to 41.5 million in 2020. One of the reasons for the low birth rate is the infertility among married population. According to national statistical reports, the prevalence of current infertility has increased in 3.0 times for the last five years (2016-2020) in Ukraine [3].

One of the effective methods of infertility treatment is assisted reproductive technologies (ART). Since the birth of the first test-tube baby in 1978, ART has become an effective treatment for infertility. With the progress of technology and provision of services, an increasing number of infants are born following ART therapy. In developed countries, ART pregnancies account for 1.5–5.9% of all births [4-7].

With the progress of assisted reproductive technology (ART) and the increasing number of ART pregnancy, its safety has become the focus of attention [8]. ART is used worldwide, at increasing rates, and data show that some adverse outcomes occur more frequently than following spontaneous conception [9]. Some researchers believe that the increased risks of adverse outcomes after ART conception are mainly related to ART manipulation factors [10], which is due to the addition of many non-physiological operations by ART. Other studies have pointed out that different methods of ART may lead to different types of adverse pregnancy outcomes [11]. However, other studies have concluded ART pregnancies do not have increased risks of adverse perinatal outcomes [12, 13]. At present, opinions are too far apart to reach a consensus.

However, current studies and evidence cannot fully elucidate the mechanism by which ART increases the risk of adverse pregnancy outcomes, and the specific mechanism needs further research. Similar studies have not been conducted in Ukraine. Although pregnancies conceived by ART have a higher risk of maternal/perinatal complications, the overall risk of adverse outcomes necessitating advanced obstetric care has not been closely examined. The challenge of a contemporary evaluation of birth outcomes after assisted conception in Ukraine is the lack of national databases.

THE AIM

To assess and compare the risk of maternal/perinatal complications and adverse outcomes in pregnancy and childbirth conceived by ART with those conceived naturally in Ukraine.

MATERIALS AND METHODS

STUDY DESIGN, SETTING, AND POPULATION

This retrospective multicenter cohort study included pregnant women who delivered at 14 Ukrainian Women's Hospitals in 2019–2021. After excluding women who had early abortions (≤12 weeks), or women who were discharged from care during pregnancy, a total of 21,160 pregnancies were included in the data analysis. Two cohorts were created: women who conceived by either intracytoplasmic sperm injection (ICSI), in vitro fertilization (IVF), ovulation induction (OI), gamete intra-fallopian transfer (GIFT), or artificial insemination (AI), were defined as group of ART pregnancy, and women who conceived naturally without ART, were considered as group of naturally pregnancy.

DATA COLLECTION

Data were collected from standardized clinical forms and hospital records after maternity discharge to form the research database. Maternal characteristics of all pregnancies were firstly extracted, including maternal age (year), intrapartum weight (kg), parity, birthplace, menstrual cycle (21–35 days, 36 days- or irregularity), abnormal pregnancy history and history of uterine fibroids. Maternal age was divided into five groups: <25, 25–29, 30–34, 35–39, ≥40 years. Intrapartum body mass index (BMI, kg/m2) was calculated as maternal intrapartum weight divided by the square of height, and classified into four groups: <25, 25–29.9, 30–34.9, ≥35 kg/m2. Parity did not include this pregnancy and was divided into 0 (nulliparae) and ≥1 (multiparae). Abnormal pregnancy history refers to a history of early abortion (≥2 times), intermediate and late abortion, abnormal development, or ectopic pregnancy. In this study we also used the standardized clinical forms and hospital records to obtain data on pregnancy complications, perinatal complications and neonatal outcomes. Data on pregnancy complications included gestational diabetes (fasting glucose concentrations ≥ 5.5 mmol/l or 2-h plasma glucose concentrations ≥ 8.0 mmol/l), preeclampsia (hypertension from 20 weeks' gestation and proteinuria; severe preeclampsia was defined as preeclampsia with either a diastolic blood pressure ≥ 110 mmHg or proteinuria ≥ 5 g/day or both), anemia (hemoglobin < 100 g/l and hematocrit < 0.30; moderate or severe anemia was defined as hemoglobin < 90 g/l or 60 g/l), liver-related diseases (cholestasis, hepatitis, liver function damage, etc.) and thyroid-related diseases (hyperthyroidism, hypothyroidism, thyroiditis, etc.). Data on perinatal complications included hospitalization time (day), preterm birth (<37 weeks' gestation), premature rupture of membrane, amniotic fluid pollution (clear as 0°, I°, II°, or III°), polyhydramnios (>2,000 ml in the third trimester), oligohydramnios (<300 ml in the third trimester), cord entanglement, torsion of cord, intrapartum fever (intrapartum temperature > 38°C), placenta previa, antepartum hemorrhage, postpartum hemorrhage (measured blood loss ≥ 500 ml) and delivery mode (spontaneous labor or cesarean section). And data on neonatal outcomes included gestational weeks in birth, offspring gender, birth weight (g), macrosomia (birth weight ≥ 4,000 g), twins or multiples, fetal distress, stillbirth or abnormal development (fetal malformation).

ETHICS

Ethical clearance for this study was obtained from the ethics committee of the Shupyk National Healthcare University of Ukraine. This study was performed in line with the principles of the Declaration of Helsinki. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Table I. Patient characteristics between naturally pregnancy (n=19,801) and assisted reproductive technology (ART) pregnancy (n=1,361) in Ukraine (2019-2021).

Variables	All pregnancy n=21,162	Naturally pregnancy	ART pregnancy	p-value
	n (%)	n (%)	n (%)	
Maternal age (year)	29.6±3.9	29.5±3.9	31.6±3.9	0.054
<25	1,327(6.3)	1,316(6.6)	11(0,8)	0.056
26-29	10,462(49.4)	10,105(51.0)	357(26.3)	
30-34	6,904(32.6)	6,358(32.1)	546(40.1)	
35-39	2,112(10.0)	1,813(9.2)	299(22.0)	
≥40	355(1.7)	208(1.1)	147(10.8)	
Intrapartum weight (kg)	70.6±9.1	70.5±9.0	72.8±9.9	0.025
Intrapartum BMI (kg/m^2)	26.8±3.1	26.7±3.2	22.9±3.4	0.03
Parity				0.034
Nulliparae	16,133(76.2)	14,929(75.4)	1,204(88.5)	
Multiparae	5,027(23.8)	4,871(24.6)	156(11.5)	
Birthplace				0.003
Kyiv region	8,412(38.8)	7,730(39.0)	682(50.1)	
Odesa region	3,684(17.4)	3,367(17.1)	317(23.3)	
Lviv region	2,437(11.5)	2,259(11.4)	178(13.1)	
Other regions	6,627(31.3)	6,444(32.5)	183(13.5)	
Menstrual cycle (day)				0.024
21-35	18,101(91.6)	16,995(92.1)	1,106(84.8)	
36 - or Irregularity	1,649(8.4)	1,452(7.9)	197(15.2)	
Abnormal pregnancy history	2,255(11.2)	1,868(9.9)	387(29.1)	0.052
Early abortion (≥2 times)	1,718(8.5)	1,449(7.7)	268(20.2)	0.036
Intermediate and late abortion or abnormal development	420(2.1)	346(1.8)	74(5.6)	0.021
Ectopic pregnancy	323(1.6)	211(1.1)	112(8.4)	0.034
With uterine fibroids	1,129(5.3)	1,016(5.1)	113(8.3)	0.012

Note: ART, assisted reproductive technology; BMI, body mass index

STATISTICAL ANALYSIS

All clinical data were entered in an Excel (Microsoft Corp., Redmond, WA, USA) database for statistical analysis. Results are expressed as median (range), mean ± standard deviation for continuous variables, and number and corresponding percentage for qualitative variables. We compared maternal characteristics and pregnancy outcomes between group of ART pregnancy and group of naturally pregnancy. Continuous variables were described as mean and standard deviation, and categorical variables were displayed as frequency (percentage). All comparisons between groups were conducted using standardized differences, which are not influenced by sample size and have been frequently used in previous large cohort studies. The association between ART using and pregnancy outcomes were evaluated by logistic regression analysis. The crude and adjusted odds ratio (OR) with 95% confidence intervals (95%CI) for pregnancy outcomes were calculated. Adjusted values were adjusted for maternal age, intrapartum BMI, parity, birth plurality and abnormal pregnancy history. All statistical analyses were two-sided and significance was set at $P < 0.05$.

RESULTS

A total of 21,162 women were included in this retrospective cohort study, of whom 1,361 women conceived by ART as group of ART pregnancy, and 19,801 women conceived naturally without ART as group of naturally pregnancy. During study period (2019-2021), the proportion of ART pregnancy has increased each year, reaching a peak in 2021 (6.7%). Of the ART pregnancy, the proportion of pregnant

Table II. The incidence of pregnancy complications between naturally pregnancy (n=19,801) and ART pregnancy (n=1,361) in Ukraine (2019-2021).

Pregnancy complications	All pregnancy (n=21,162)		Naturally pregnancy		ART pregnancy		*p*-value
	n	%	n	%	n	%	
Gestational diabetes	3,884	18.4	3,473	17.5	411	30.2	0.0239
Preeclampsia	805	3.8	673	3.4	132	9.7	0.0169
Severe preeclampsia	267	1.3	216	1.1	51	3.7	0.0114
Anemia	4,683	22.1	4,317	21.8	366	26.9	0.0092
Moderate or severe anemia	747	3.5	677	3.5	70	5.1	0.0079
Liver-related diseases [a]	807	3.8	734	3.7	73	5.4	0.0068
Thyroid-related diseases [b]	1,890	8.9	1,702	8.6	188	13.8	0.0154

[a] included intrahepatic cholestasis, hepatitis, liver dysfunction, liver damage etc.
[b] included hyperthyroidism, hypothyroidism, thyroiditis, thyroid tumor, etc.
ART, assisted reproductive technology

Table III. The incidence of perinatal complications between naturally pregnancy (n=19,801) and ART pregnancy (n=1,361) in Ukraine (2019-2021).

Perinatal complications	All pregnancy (n=21,162)		Naturally pregnancy		ART pregnancy		*p*-value
	n	%	n	%	n	%	
Hospitalization time (day)	4.9±2.3		4.9±2.3		6.8±2.7		0.026
Preterm birth	1,616	7.6	1,327	6.7	289	20.4	0.041
Premature rupture of membrane	5,879	27.7	5,581	28.1	298	21.7	0.013
Amniotic fluid pollution							0.015
Clear (0°)	17,357	82.0	16,154	81.6	1,203	88.4	
I°	1,125	5.3	1,064	5.4	61	4.5	
II°	1,173	5.5	1,127	5.7	46	3.4	
III°	1,488	7.0	1,437	7.3	51	3.7	
Polyhydramnios	571	2.7	524	2.6	47	3.5	0.004
Oligohydramnios	1,374	6.5	1,276	6.4	98	7.2	0.002
Cord entanglement	7,610	36.0	7,143	36.1	467	34.3	0.004
Torsion of cord	662	3.1	617	3.1	45	3.3	0.001
Intrapartum fever	2,376	11.2	2,248	11.4	128	9.4	0.006
Placenta previa	1,138	5.4	1,021	5.2	117	8.6	0.012
Antepartum hemorrhage	74	0.3	68	0.3	6	0.4	0.001
Postpartum hemorrhage	2,272	10.7	2,009	10.1	263	19.3	0.024
Cesarean section	9,041	42.7	8,017	40.5	1,024	75.2	0.075

Note: ART, assisted reproductive technology

women over 35 years old and multiparae increased mildly. In addition, the proportion of women with abnormal pregnancy history in ART pregnancy decreased sharply, and then increased rapidly. Patient characteristics between ART and naturally pregnancy is summarized in Table I.

In this study the mean maternal age and intrapartum BMI of women conceived by ART were significantly higher than those of women conceived naturally. Women conceived by ART were more likely to be nulliparae, more likely to have a long or irregular menstrual cycle and an abnormal pregnancy history (including early abortion, intermediate and late abortion, abnormal development, or ectopic pregnancy), and more likely to have uterine fibroids.

The incidence of pregnancy and perinatal complications in ART and natural pregnancy in Ukraine is presented in Table II, III. In this study statistically significant increases were noted in gestational diabetes (30.2%), preeclampsia (9.7%), thyroid-related diseases (13.8%), preterm birth (20.4%), placenta previa (8.6%), postpartum hemorrhage (19.3%) and cesarean section (75.2%) in ART pregnancy, compared to

Table IV. Neonatal outcomes between naturally pregnancy (n=19,801) and ART pregnancy (n=1,361) in Ukraine (2019-2021).

Neonatal complications	All pregnancy (n=21,162)		Naturally pregnancy		ART pregnancy		*p*-value
	n	%	n	%	n	%	
Gestational weeks	38.8±1.9		38.7±1.8		37.8±2.3		0.051
Birth weight (g)	3,317±506.8		3,331.5±494.5		3,138.5±631.7		0.034
Macrosomia	1,517	7.2	1,437	7.3	80	5.9	0.005
Twins or multiples	526	2.5	244	1.2	282	20.8	0.065
Fetal distress	1,442	6.8	1,367	6.9	75	5.5	0.005
Stillbirth or abdominal development	233	1.1	188	0.9	45	3.4	0.016

Note: ART, assisted reproductive technology

naturally pregnancy. The occurring rates of anemia (26.9%), liver-related diseases (5.4%), polyhydramnios (3.5%), oligohydramnios (7.2%) and torsion of cord (3.3%) were also elevated in ART pregnancy, but with no significant difference (Table III). However, there was a decline in the incidences of premature rupture of membrane (21.7%) and amniotic fluid pollution (I°: 4.5%, II°: 3.4%, III°: 3.7%) in ART pregnancy.

Results of the data analysis of neonatal outcomes between natural pregnancy and pregnancy after ART in Ukraine is presented in Table IV. Data analysis showed that the average birth weight in ART pregnancy was significantly lower than in natural pregnancy. In this study significant rises of incidence were observed in twins or multiples (20.8%) and stillbirth or abnormal development (3.4%) in ART pregnancy. No significant difference was noted in macrosomia and fetal distress between the two groups.

Multivariable logistic regression analysis showed that the association between ART and pregnancy outcomes were significant. All the pregnancy complication listed, including gestational diabetes, preeclampsia, moderate or severe anemia, liver-related diseases, and thyroid-related diseases, were more likely to occur among women conceived by ART.

In this study (risk for perinatal complications), the risk of preterm birth, placenta previa, postpartum hemorrhage, and cesarean section were significantly increased, while the risk of premature rupture of membrane, amniotic fluid pollution, cord entanglement, and intrapartum fever were significantly decreased in ART pregnancy as compared with naturally pregnancy. For neonatal outcomes, women conceived by ART were more likely to have twins or multiples, and the risk of stillbirth or abnormal development was also significantly increased. Moreover, the risk of macrosomia and fetal distress were significantly decreased in ART pregnancy.

This study showed that when restriction to singletons, the risks of adverse pregnancy outcomes were reduced. The effects of ART on the risk of premature rupture of membrane, cord entanglement, intrapartum fever, cesarean section, and stillbirth or abnormal development were more pronounced among singleton pregnancies compared with that among pregnancies of twins or multiples, while the effect of ART on the risk of polyhydramnios was more prominent among pregnancies of twins or multiples.

DISCUSSION

To our knowledge, this is the first epidemiological study that focuses on pregnancy and birth outcomes in female with and without assisted reproductive technology in Ukraine. The present retrospective cohort study was conducted to compare maternal and neonatal outcomes between ART and naturally pregnancies, and in addition to explore the association of ART with adverse pregnancy outcomes by stratifying on birth plurality and maternal age in Ukraine. A total of 21,162 pregnancies were included. Of these, there were 19,801 natural pregnancies and 1,361 pregnancies after ART. The proportion of ART pregnancies has increased every year in during study period, peaking in 2021 (6.7%). Data analysis showed that the risks of gestational diabetes, preeclampsia, moderate or severe anemia, liver-related diseases, thyroid-related diseases, preterm birth, placenta previa, postpartum hemorrhage, and cesarean section were significantly increased in ART pregnancy. For neonatal outcomes, women conceived by ART were more likely to have twins. The effects of ART on the risk of premature rupture of membrane, cord entanglement, intrapartum fever, and cesarean section were more pronounced in singletons pregnancies. We found a increase in the incidence of multiple births in ART pregnancies compared to naturally pregnancies. In the present study, the increased risks were found in ART pregnancy compared with naturally pregnancy: gestational diabetes, preeclampsia, moderate or severe anemia, liver-related diseases, thyroid-related diseases, preterm birth, placenta previa, postpartum hemorrhage, cesarean section, and stillbirth or abnormal development, which were largely consistent with the findings of previous studies [8, 14, 15].

The International Committee for Monitoring Assisted Reproductive Technologies (ICMART) annual world report series provides an important instrument for tracking trends in ART treatment and for providing clinical and public health data to ART professionals, health authorities, patients and the general public. ART is increasingly influencing the fertility trends of high-income countries characterized by a pattern of delayed childbearing. However, research on the impact of ART on completed fertility is limited and the extent to which delayed births are realized later in life through ART is not well understood. ART includes all infertility treatments to achieve conception; IVF is the process by which an oocyte is fertilized by semen outside the body; non-IVF ART treatments include ovulation induction, artificial insemination, and intrauterine insemination. IVF represents only a small portion of all infertility treatment used in Ukraine. It is well established that both IVF and subfertility, independent of treatment, are associated with compromised maternal and infant perinatal outcomes. As these and other reproductive technologies expand, leading to a substantial number of successful pregnancies and births, it is critical for prospective parents to understand the maternal and neonatal outcomes associated with ART. Several studies have shown that ART pregnancies have an increased risk of multiple pregnancy and adverse pregnancy outcomes, including gestational diabetes, gestational hypertension, placenta previa, preterm birth, operative delivery, low birth weight, birth defects and perinatal mortality [8, 16-18]. However, other studies have concluded ART pregnancies do not have increased risks of adverse perinatal outcomes [4, 7, 12, 13, 19]. The incidences of small for gestational age, preterm birth and cesarean section are similar between ART and naturally pregnancies. It is not clear whether the increased risk of adverse pregnancy outcomes is due to ART itself, multiple births, or potential infertility.

Infertility affects one in seven couples, and many of these need ART. To date, more than 8 million children have been conceived after ART globally [20], and up to 6% (range between 0.2% and 6.4%) of the European birth cohorts is conceived by ART [4]. ART is widely practiced throughout the world but continues to be characterized by significant disparities in utilization, practice, effectiveness and safety. ART involves standard in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI). In literature there is increasing evidence that infertility or subfertility is an independent risk factor for obstetrical complications and adverse perinatal outcomes, even without the addition of assisted human reproduction. Multiple pregnancy is the most powerful predictive factor for adverse maternal, obstetrical, and perinatal outcomes. Couples should be thoroughly counselled about the significant risks of multiple pregnancies associated with all assisted human reproductive treatments. Among singleton pregnancies, assisted reproductive technology is associated with increased risks of preterm birth and low birth weight infants, and ovulation induction is associated with an increased risk of low-birth-weight infants. Until sufficient research has clarified the independent roles of infertility and treatment for infertility, couples should be counselled about the risks associated with treatment. Women and couples considering assisted human reproduction and concerned about perinatal outcomes in singleton pregnancies should be advised that (1) intracytoplasmic sperm injection does not appear to confer increased adverse perinatal or maternal risk over standard in vitro fertilization, and (2) the use of donor oocytes increases successful pregnancy rates in selected women, but even when accounting for maternal age, can increase the risks of low birth weight and preeclampsia. Any ART procedure should be prefaced by a discussion of fetal outcomes and the slight increase in the risk of congenital structural abnormalities, with emphasis on known confounding factors such as infertility and body mass index. In pregnancies achieved by artificial reproductive technology, routine anatomic ultrasound for congenital structural abnormalities is recommended between 18 and 22 weeks.

Despite the continuous technological improvements, ART cannot fully compensate for the age-related decline in female reproductive performance because the effectiveness of ART also declines with age [21. 22]. The total number of ART births is directly influenced by ART treatment and success rates and indirectly shaped by further childbearing postponement, which leads to a higher proportion of women seeking to have children at older ages when their reproductive potential diminishes. However, alternative treatment options such as oocyte cryopreservation (egg freezing) or the use of third-party eggs from younger donors are expanding women's reproductive potential. Our prognosis suggest that increases in ART fertility rates will be mainly driven by an increase in the demand for infertility treatment. However, the diffusion of alternative treatment options, such as egg freezing and the use of third-party donor eggs, may lead to a sharp rise in ART success rates and alter these dynamics in the future.

STRENGTHS AND LIMITATION

This study has several strengths. First, this is the first multicenter cohort study was aimed to assess and compare the risk of maternal/perinatal complications and adverse outcomes in pregnancy and childbirth conceived by ART with those conceived naturally in Ukraine. Second, large size of the sample and the fact that it is population-based, which allowed us to conduct further subgroup analysis with enough power. Clinicians will be better informed about the adverse outcomes that have been documented in association with ART, including obstetrical complications, adverse perinatal

outcomes, multiple gestations, structural congenital abnormalities, chromosomal abnormalities, and imprinting disorders. However, there are some limitations in this study. The limitations of this study include its retrospective design and including 33.3% regions (8 from 24) in Ukraine. The results may not be representative of other regions of Ukraine. Therefore, we should be cautious in generalizing our findings to other Ukrainian regions. Second, we did not collect information on the ART form. Third, the retrospective design of this study could not assess a causal relationship between ART and adverse pregnancy outcomes. These limitations should be considered in future studies. However, this study provides valuable data as a first study for possible comparison with data from other countries.

CONCLUSIONS

This study showed the widespread application of ART in Ukraine, with the proportion of ART pregnancies increasing in the study period, and confirmed the increased risks of several adverse pregnancy outcomes in ART pregnancies. We found a increase in the incidence of multiple births in ART pregnancies compared to naturally pregnancies. In the present study, the increased risks were found in ART pregnancy compared with naturally pregnancy: gestational diabetes, preeclampsia, moderate or severe anemia, liver-related diseases, thyroid-related diseases, preterm birth, placenta previa, postpartum hemorrhage, cesarean section, and stillbirth or abnormal development, which were largely consistent with the findings of previous studies. Obstetricians should be aware of the increased risk of adverse outcomes among this population. Therefore, prenatal and intrapartum monitoring should be strengthened, and neonatal outcomes should be closely observed for ART pregnancy. More research should be conducted to further clarify whether the increased risk of adverse pregnancy outcomes is due to ART itself or other factors.

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ORIGINAL ARTICLE

PALLIATIVE SURGICAL TREATMENT OF PATIENTS WITH UNRESECTABLE CANCER OF THE HEAD OF THE PANCREAS COMPLICATED BY MECHANICAL JAUNDICE

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ABSTRACT

The aim: To improve the results of palliative surgical treatment of patients with unresectable cancer of the head of the pancreas, complicated by obstructive jaundice, disturbances of evacuation from the stomach, cancerous pancreatitis by improving surgical tactics and techniques of surgical interventions.

Materials and methods: There were 277 patients with unresectable cancer of the head of the pancreas participated in the study, who were divided into control (n=159) and main (n=118) groups depending on treatment tactics.

Results: The operation of choice in the surgical treatment of patients with unresectable cancer of the head of the pancreas, complicated by obturation of the biliary system and duodenum with a high surgical risk is endoscopic stenting of the bile ducts and duodenum with nitinol stents, which is accompanied by a decrease in the frequency of postoperative complications from 72.7 to 29.6% ($\chi2$=5.8, 95% CI 8.26-65.39, p=0.01), mortality from 36.4% to 0.0% ($\chi2$=10.69, 95% CI 11.8- 64.65, p=0.001). The patient's formation of biliodigestive and prophylactic gastrodigestive anastomosis is an effective and safe procedure, which, in comparison with only biliodigestive shunting, reduces the frequency of postoperative complications by 16.2% ($\chi2$=6.61, 95% CI 3.69-30.89, p=0.01), improves quality of life and prevents repeated surgical operations to restore evacuation from the stomach.

Conclusions: The use of the proposed surgical tactics and technique of surgical interventions in patients with unresectable cancer of the head of the pancreas, complicated by obstructive jaundice, disturbances of evacuation from the stomach, cancerous pancreatitis made it possible to reduce the frequency of complications by 9.3% ($\chi2$=3.94, 95% CI 0.09-17.86, p=0.04) and fatal cases by 5.8% ($\chi2$=4.5, 95% CI 0.42-12.72, p=0.03).

KEY WORDS: pancreatic head cancer, obstructive jaundice, cancerous pancreatitis

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INTRODUCTION

In the world, the incidence of pancreatic cancer is increasing, but at the time of diagnosis, more than 80% of cases are unresectable, and surgical interventions are aimed at eliminating such complications as obstructive jaundice, duodenal obstruction, pain syndrome [1]. At the same time, the necessary prerequisites for palliative chemotherapy in this category of patients are internal drainage of the biliary system and restoration of oral nutrition [2]. To solve this problem in practical surgery, there are two main approaches: performance of biliodigestive and gastrodigestive shunting by open surgical intervention and stenting of the bile ducts and duodenum [3]. According to literature data, when using surgical shunting, the frequency of complications reaches 25%, and the mortality rate is 15.7% [4]. In turn, endoscopic stenting of the biliary tract and duodenum is accompanied by a significantly lower number of complications, however, stents (especially endobiliary) are prone to infection, occlusion and migration, which requires repeated interventions with their reimplantation. In addition, in some cases, stenting is technically impossible, especially when the area of occlusion cannot be covered with an endoprosthesis [5].

The literature discusses the idea that the use of chemotherapy and the use of personalized approaches to cancer treatment increase the life expectancy of patients, while surgical bypass surgery is preferred because the need for repeated hospitalizations for stent replacement disappears [6]. At the same time, it remains relevant to clarify the tactics and techniques of palliative surgical treatment of patients with cancer of the head of the pancreas with a comparative analysis of the effectiveness of open and endoscopic surgical techniques to restore evacuation from the stomach, internal drainage of the biliary system, and in some cases, the pancreatic duct in order to improve results surgical treatment and quality of life of patients.

THE AIM

To improve the results of palliative surgical treatment of patients with unresectable cancer of the head of the pancreas, complicated by obstructive jaundice, disturbances of evacuation from the stomach, cancerous pancreatitis by improving surgical tactics and techniques of surgical interventions.

MATERIALS AND METHODS

There were treated 277 patients with unresectable cancer of the head of the pancreas, complicated by obstructive jaundice in the clinic of the Department of Surgery №2 of the Bogomolets National Medical University from 1997 to 2020. Depending on the treatment tactics, patients were divided into control (159 people) and main (118 people) groups. When compared, the patients of the studied groups did not differ in age, gender and level of hyperbilirubinemia at the time of hospitalization ($p>0.05$) (Table I).

At the first stage, the research design provided for the analysis of the results of palliative surgical treatment of control group patients (159 patients, of which 14 patients also had acute cancerous pancreatitis), who were treated in the surgical clinic during the period 1997-2006. Based on the results of the analysis, clarifications were formulated regarding the choice of tactics and surgical technique for the formation of biliodigestive, gastrodigestive and pancreatodigestive anastomoses. These innovations were used in the treatment of patients in the main group (118 patients), which were divided into 3 subgroups for the purpose of solving research tasks. The first subgroup was created by randomization and consisted of subgroups A and B (38 patients each) with the aim of studying the clinical effectiveness of supplementing biliodigestive shunting with prophylactic gastrodigestive (subgroup A underwent hepaticojejunoanastomosis with an extraperitoneal and isolated jejunal loop; subgroup B - hepaticojejunoanastomosis and gastrojejunoanastomosis). The second subgroup of the main group included 27 patients with cancer of the head of the pancreas, the course of which was complicated by mechanical jaundice, disturbances of evacuation from the stomach, severe comorbid and accompanying pathology and physical status of ASA III grading. In the course of a bidirectional, cohort study, the effectiveness of endoscopic stenting of the biliary system and duodenum with nitinol stents was studied in comparison with biliodigestive and gastrodigestive shunting. In the third subgroup of the main group, in a two-way cohort study with pancreatic head cancer complicated by mechanical jaundice and cancerous pancreatitis (15 patients), the effectiveness of two-stage treatment of patients with endoscopic transpapillary stenting of the biliary system in the first stage and one-moment biliodigestive decompression pancreatodigestive bypass was studied. The analysis of the results of the treatment of patients in the comparison groups was carried out.

Pancreatic head cancer was verified in accordance with the recommendations of the European Society for Medical Oncology (ESMO 2015, 2019), the National Comprehensive Cancer Network (NCCN, 2015-2020) and the classification of the American Joint Committee on Cancer (AJCC, editions VI, VII, VIII, 2002 -2017) [7]. Patients who suffered from stage III-IV pancreatic head cancer and whose cancer was identified as ductal adenocarcinoma (WHO, 2000) were included in the study. The decision on the unresectableness of tumors was made based on the conclusion of a multidisciplinary consensus of the clinic doctors by comparing the data of clinical, laboratory and radiological examination methods according to the recommendations of the NCCN (2015-2020) and ESMO (2015, 2019) [8]. The degree of impaired evacuation from the stomach was determined based on the results of radiography and fibrogastroduodenoscopy, and the statistical processing of the results was performed using the four-point GOOSS scale (Adler D.G., 2002) [9]. Liver dysfunction was determined by clinical and biochemical indicators recommended by the European Association for the Study of the Liver and Treatment of Acute Liver Failure (EASL) [10]. Acute cancerous pancreatitis was diagnosed according to the criteria proposed in Atlanta in 2012, treatment was carried out according to the protocol developed and approved in the clinic [11]. During endoscopic stenting of the biliary system, nitinol stents Boston Scientific WallSTENT Biliary Uncovered 10mm-60mm manufactured in the USA were used. HANAROSTENT Duodenum/Pylorus NDSL20-140-230 stents were used for stenting of the duodenum.

STATISTICS

The normality of data distribution was determined by the Shapiro-Wilk test. The difference between the groups was determined using Student's t test for independent samples in the case of parametric and Kruskal-Wallis test in the case of nonparametric data distribution. Differences in sample distribution were assessed using the $\chi 2$ test criterion. Differences between indicators were considered significant at $p<0.05$. Statistical analysis was performed using Statistica 10 (Serial Number: STA999K347150-W) and MEDCALC® (open access Internet resource, https://www.medcalc.org/calc/).

RESULTS

The types of surgical interventions used in patients of the control group, the frequency of complications and deaths are presented in Table II.

Table I. Demographic indicators and serum bilirubin content at the time of hospitalization in the studied groups

Indexes	Main group (n=118)	Comparison group (n=159)	p
Age, years	69±4,3	68±5,1	0,08
Sex men women	 72 (61%) 46 (39%)	 95 (59,7%) 64 (40,3%)	 0,82 0,82
Bilirubin content in blood serum, μmol/l	217,4±18,3	212±24,7	0,06

Table II. Operative interventions and frequency of complications in patients of the control group (n=159)

Type of surgical intervention	Number of patients	Complications	Fatal cases
Retrocolonic cholecystojejunostomy	117	18	8
Anterior colonic cholecystojejunostomy	4	3	1
Retrocolonic cholecystojejunostomy + gastrojejunostomy	10	5	3
Choledochoduodenostomy	4	2	1
Retrocolonic hepaticojejunostomy	14	4	4
External cholecystostomy; cholecystojejunostomy (in 2 stages)	7	3	-
Percutaneous external cholangiostomy; hepaticojejunostomy (in 2 stages)	2	-	-
Percutaneous, transhepatic, cholangioduodenostomy	1	-	-
Total:	159	35 (22%)	16 (10,1%)

Table III. Operative interventions and frequency of complications in patients of the main group (n=118)

Type of surgical intervention	Number of patients	Complications	Fatal cases
Retrocolonic hepaticojejunostomy	30	2	1
Endoscopic transpapillary stenting of the choledoch; hepaticojejunostomy (in 2 stages)	8	1	1
Retrocolonic hepaticojejunostomy + gastrojejunostomy	32	2	2
Endoscopic transpapillary stenting of the choledoch; hepaticojejunostomy + gastrojejunostomy (in 2 stages)	6	1	0
Endoscopic transpapillary stenting of the choledochus and duodenum with nitinol stents (in 2 stages)	24	6	0
Endoscopic transduodenal, transpapillary stenting of the choledochus and duodenum with nitinol stents (one-stage)	3	2	0
Retrocolonic cholecystojejunostomy	6	1	0
External cholecystostomy; retrocolonic hepaticojejunostomy (in 2 stages)	4	0	0
External cholecystostomy; hepaticojejunostomy + pancreaticojejunostomy (in 2 stages)	2	0	0
Endoscopic transpapillary stenting of the choledoch; hepaticojejunostomy + pancreaticojejunostomy (in 2 stages)	3	0	0
Total:	118	15 (12,7%)	4 (3,4%)

It should be noted that in the distant postoperative period, within 6 to 7 months after biliodigestive bypass, 18 (11.3%) patients of the control group had symptoms of progressive disturbances of evacuation from the stomach, therefore, 14 (8.8%) patients had a repeated surgical intervention was performed with a gastrojejunal anastomosis. A retrospective analysis of the results of treatment of patients in the control group showed that unsatisfactory results were obtained during surgical operations in elderly patients whose physical status corresponded to ASA III grading

(11 patients), in whom cancer of the head of the pancreas (T4N1M1) was complicated by jaundice, cholangitis, severe comorbid and concomitant pathology. Two-stage surgical treatment was accompanied by complications in 8 (72.7%) patients, 4 (36.4%) patients died.

The types of surgical interventions used in patients of the main group, the frequency of complications and deaths are presented in Table III.

When analyzing the results of treatment of the first subgroup of the main group in the period from 5 to 8 months after the surgical correction of jaundice in 6 (16.2%) people of subgroup A, the course of the disease was complicated by nausea, vomiting, a feeling of heaviness in the epigastrium, and the progression of cachexia. Based on the results of X-ray and fibrogastroscopy of the stomach, the patients were diagnosed with stenosis of the duodenum by a tumor, and these patients underwent repeated operations to undergo gastrojejunal anastomosis. In subgroup B patients, in the long postoperative period, there were no violations of the evacuation of gastric contents to the intestines in any case. There were also no phenomena of progressive cachexia. Thus, with the simultaneous application of hepaticojejunoanastomosis and gastrojejunoanastomosis in patients of subgroup B, a decrease in the frequency of complications was observed by 16.2% ($\chi2=6.61$, 95% CI 3.69-30.89, $p=0.01$) compared to patients subgroups A.

When analyzing the results of treatment of patients of the second subgroup of the main group, the specific weight of postoperative complications was 29.6% against 72.7% in the control group ($\chi2=5.8$, 95% CI 8.26-65.39, $p=0.01$) , there was no mortality, with 36.4% of deaths in the control group ($\chi2=10.69$, 95% CI 11.8-64.65, $p=0.001$). Endobiliary stents functioned effectively for the rest of the patients'lives. After duodenal stenting, oral intake of first liquid and then solid food began on the second day after the intervention. The degree of violations of oral nutrition, according to the GOOSS classification (D.G. Adler, 2002), at the time of hospitalization was 1.68±0.16 points, after correction - 2.5±0.21 points ($p<0.0001$). During further observation, it was established that obstruction of the endobiliary and duodenal stents did not occur and the patients were able to take food until the last days of life.

In the treatment of patients of the prospective cohort of the third subgroup of the main group, a two-stage tactic of surgical treatment was applied (in this subgroup, 10 (66.7%) patients were diagnosed with a mild course of cancerous pancreatitis, 5 (33.3%) with a moderate degree of severity). Thus, in patients with mild cancerous pancreatitis, internal biliodigestive bypass was performed after preoperative preparation. In patients with moderate severity of the disease at the first stage, external cholecystostomy was performed (two (13.3%) patients) and endoscopic transpapillary stenting of the hepaticocholedochus with a plastic stent (three (20%) patients). At the same time, according to the results of cultures of bile, its bacterial infection was confirmed in all patients: Escherichia Coli was cultured in three cases, Escherichia Coli and Klebsiella spp. in two. There were 10-12 days after the compensation of manifestations of multiple organ dysfunction, cholangitis patients underwent internal drainage of the biliary system to the jejunal loop isolated by Ru by means of hepaticojejunostomy with the imposition of a draining longitudinal pancreatojejunoanastomosis with the adduct loop of the jejunum.

Therefore, the use of the proposed surgical tactics and technique of operative interventions in patients of the main group made it possible to reduce the frequency of complications by 9.3% ($\chi2=3.94$, 95% CI 0.09-17?86, $p=0.04$) and fatal cases by 5.8% ($\chi2=4.5$, 95% CI 0.42-12?72, $p=0.03$).

DISCUSSION

Obstructive painless jaundice is most often caused by cancer of the head of the pancreas and is diagnosed, as a rule, at a late stage of the disease and is accompanied by impaired evacuation from the stomach, cancerous pancreatitis and distant metastases [12]. Five-year survival among patients with this pathology is 1-5%, while the frequency of postoperative complications reaches 25% [13]. In our study, when retrospectively analyzing the results of treatment of a control group of patients, the frequency of postoperative complications was 22%, and the mortality rate was 10.1%. Unsatisfactory results in the control group were primarily obtained during the surgical treatment of elderly patients in whom the course of the disease was complicated by jaundice, cholangitis, severe comorbid and accompanying pathology. According to current views, all patients with pancreatic head cancer should undergo palliative biliary drainage, especially in inoperable cases, before neoadjuvant chemotherapy, cholangitis, or severe symptomatic jaundice [14]. In our study, when performing endoscopic stenting of the biliary system and duodenum with nitinol stents in this category of patients, the specific weight of postoperative complications was 29.6% against 72.7% in the control group ($\chi2=5.8$, 95% CI 8.26-65 .39, $p=0.01$), there was no mortality, with 36.4% of deaths in the control group ($\chi2=10.69$, 95% CI 11.8-64.65, $p=0.001$). In patients with cancerous pancreatitis, a two-stage tactic of surgical treatment was proposed, which involved the performance of external cholecystostomy or endoscopic transpapillary stenting of the choledoch followed by hepaticojejunostomy and longitudinal pancreatojejunoanastomosis. Positive results were also obtained when supplementing the biliodigestive bypass

with prophylactic gastrodigestive bypass, namely with the simultaneous use of hepaticojejunoanastomosis and gastrojejunoanastomosis (a 16.2% decrease in the frequency of complications was observed ($\chi2$=6.61, 95% CI 3.69-30.89, p =0.01) in comparison with patients of subgroup A).

According to literature data, postoperative mortalityin this category of patients reaches 15.7% [15]. In our study, when using the proposed surgical tactics and technique of surgical interventions in patients of the main group, the frequency of postoperative complications was 12.7%, and the mortality rate was 4.3%. When compared with patients of the control group, the use of the proposed surgical tactics and technique of surgical interventions made it possible to reduce the frequency of complications by 9.3% ($\chi2$=3.94, 95% CI 0.09-17.86, p=0.04) and fatal cases by 5.8% ($\chi2$=4.5, 95% CI 0.42-12.72, p=0.03).

CONCLUSIONS

1. The operation of choice in the surgical treatment of patients with unresectable cancer of the head of the pancreas, complicated by obturation of the biliary system and duodenum with a high surgical risk is endoscopic stenting of the bile ducts and duodenum with nitinol stents, which is accompanied by a decrease in the frequency of postoperative complications from 72.7 to 29.6% ($\chi2$=5.8, 95% CI 8.26-65.39, p=0.01), mortality from 36.4% to 0.0% ($\chi2$=10.69, 95% CI 11.8- 64.65, p=0.001).
2. The patient's formation of biliodigestive and prophylactic gastrodigestive anastomosis is an effective and safe procedure, which, in comparison with only biliodigestive shunting, reduces the frequency of postoperative complications by 16.2% ($\chi2$=6.61, 95% CI 3.69-30.89, p=0 ,01), improves quality of life and prevents repeated surgical operations to restore evacuation from the stomach.
3. The use of the proposed surgical tactics and technique of surgical interventions in patients with unresectable cancer of the head of the pancreas, complicated by obstructive jaundice, impaired evacuation from the stomach, cancerous pancreatitis made it possible to reduce the frequency of complications by 9.3% ($\chi2$=3.94, 95% CI 0.09-17.86, p=0.04) and fatal cases by 5.8% ($\chi2$=4.5, 95% CI 0.42-12.72, p=0.03).

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ORIGINAL ARTICLE

RELATIONSHIP OF *HELICOBACTER PYLORI* CAGA AND VACA STATUS TO MORPHOLOGICAL CHANGES OF GASTRIC MUCOSA AND PRIMARY CLARITHROMYCIN RESISTANCE RATE IN PATIENTS WITH CHRONIC GASTRITIS: A CROSS-SECTIONAL STUDY

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ABSTRACT

The aim: To investigate the relation of *H. pylori* CagA and VacA status to morphological changes of gastric mucosa and primary clarithromycin resistance rate in patients with chronic gastritis.

Materials and methods: A cross-sectional study was conducted between May 2021 and January 2023, involving 64 patients with *H. pylori*-associated chronic gastritis. The patients were assigned to two groups according to the *H. pylori* virulence factors (CagA and VacA) status. The grades of inflammation, activity, atrophy, and metaplasia were determined according to the Houston-updated Sydney system. The identification of *H. pylori* genetic markers of antibiotic resistance and pathogenicity was performed by the polymerase chain reaction using paraffin stomach biopsies.

Results: Patients with CagA- and VacA-positive *H. pylori* strains had significantly higher grades of inflammation both in the antrum and in the corpus of the stomach, activity of gastritis in the antrum, higher incidence and grade of atrophy in the antrum. Primary resistance to clarithromycin was significantly more prevalent in patients with CagA- and VacA-negative *H. pylori* strains (58.3% vs. 11.5%, p=0.002).

Conclusions: Positive CagA and VacA status is related to more severe histopathological changes of gastric mucosa. In contrast, the rate of primary clarithromycin resistance is higher in patients CagA- and VacA-negative *H. pylori* strains.

KEY WORDS: *Helicobacter pylori*, CagA, VacA, gastritis, clarithromycin resistance

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INTRODUCTION

Gastric cancer (GC) is one of the leading causes of cancer mortality worldwide, with the highest incidence rates observed in the populations of Eastern Asia and Eastern Europe. According to the GLOBOCAN 2020 database, there were over 1 million new cases of GC and approximately 770,000 deaths attributed to it. If current trends persist, these figures are projected to double by 2040 [1].

One of the leading factors in the development of GC is *Helicobacter pylori* (*H. pylori*) infection, which induces a cascade of pathological changes in the gastric mucosa, including non-atrophic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, and cancer [2]. The risk of developing GC increases 18-fold with severe atrophic gastritis of the antrum, 90-fold with atrophy in the antrum and body, and 10-20-fold with intestinal metaplasia [3, 4]. However, it is worth noting that GC develops in only 1-2% of individuals infected with *H. pylori*, which is likely influenced by several factors, such as environmental factors, genetics, and the virulence of the *H. pylori* bacteria [2]. *H. pylori* virulence factors, such as those that express the cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA) proteins, may lead to a more severe grade of inflammation and impact the development of atrophy and metaplasia in the gastric mucosa [5].

Effective eradication of *H. pylori* significantly reduces the risk of developing GC, but one of the most important barriers to this is antibiotic resistance [6]. This necessitates research into the relation between virulent strains of *H. pylori* and the clarithromycin resistance [7].

The effect of *H. pylori* virulence factors on the clinical, endoscopic, and morphological manifestations of *H. pylori*-induced gastritis also remains poorly understood.

THE AIM

To investigate the relation of *H. pylori* CagA and VacA status to morphological changes of gastric mucosa and primary clarithromycin resistance rate in patients with chronic gastritis.

MATERIALS AND METHODS

A cross-sectional study was conducted between May 2021 and January 2023, involving 64 patients over 18 years old with *H. pylori*-associated chronic gastritis (CG), who gave informed consent to participate. The patients were assigned to two groups according to the *H. pylori* virulence factors status. Group 1 included 38 patients with CagA- and VacA-positive *H. pylori* strains, and Group 2 included 26 patients with CagA- and VacA-negative *H. pylori* strains. The study was approved by the Ethical Committee of the Bogomolets National Medical University (protocol №159) and performed in accordance with the principles of the Helsinki Declaration.

The exclusion criteria included patients with gastric and duodenal ulcers, malignant tumors of the stomach, or other conditions that could significantly affect the study results, as well as individuals who had used antibiotics within 30 days or proton pump inhibitors within 2 weeks prior to the visit.

The average age of participants in Group 1 was 48.4±5.7 years, and in Group 2 it was 45.8±5.4 years. There were no statistically significant differences in age or gender between the two groups.

The diagnosis of CG was established based on esophagogastroduodenoscopy with proximal jejunoscopy, chromoscopy using an Olympus Evis Exera III device with high resolution and magnification up to ×115, chromoscopy, and narrow-band imaging (NBI), followed by morphological examination of stomach and duodenal biopsies. During the endoscopic examination, the condition of the gastric mucosa was evaluated, including the presence of edema, hyperemia, atrophy, and metaplasia. Biopsies were taken from all the affected areas diagnosed using high-resolution and high magnification endoscopy, chromoscopy, and NBI.

The biopsy specimens were processed using a carousel-type histoprocessor STP-120. An EC-350 station was used to fill the paraffin blocks, an HM-340E series rotary microtome was used to cut the paraffin blocks, and a Robot-Stainer HMS-740 automated staining system (all devices from Carl Zeiss MicroImaging GmbH, Hamburg, Germany) was used to stain the histological samples with hematoxylin-eosin and alcian blue. We used for examination an Axioskop 40 microscope with an Axio Cam MRc5 camera (Carl Zeiss).

The grades of inflammation, activity, atrophy, and metaplasia were determined according to the Houston-updated Sydney system.

The identification of *H. pylori* genetic markers of antibiotic resistance and pathogenicity was performed by the polymerase chain reaction (PCR) using paraffin stomach biopsies. A2142G/C and A2143G point mutations of the 23S rRNA gene were analyzed using a sequencing regime that allows analysis of short sequences, while T2182C point mutation was analyzed in a single nucleotide polymorphism search mode.

Detection of serum IgA, IgG antibodies to CagA and VacA was carried out by solid-phase enzyme-linked immunoabsorbent assay (ELISA). A SUNRISE photometric reader (Tecan, Austria), an Elx50 automatic washer (BioTeck, USA), and incubator-shakers were used.

Statistical analysis has been performed using Stata 11 and Statistica 6 software packages. The frequency characteristics in two independent groups were compared by the chi-square (χ^2) test. All statistical methods of analysis and calculated indicators were compared at a predetermined level of type I error (α) not exceeding 5% - $p<0.05$.

RESULTS

Studying the effect of *H. pylori* virulence factors on gastric mucosa inflammation, we found that patients with CagA- and VacA-positive *H. pylori* strains had a significantly higher grade of inflammation both in the antrum and in the corpus of the stomach (Table I).

The degree of CG activity was determined based on the severity of infiltration of the lamina propria and epithelial layer with neutrophilic leukocytes.

Table II demonstrates data on the degree of gastritis activity depending on the presence of *H. pylori* virulence factors. Thus, an active inflammatory process in the antrum of the stomach was found in 35 patients (54.7%), of whom 26 (68.4%) were in Group 1, and 9 (34.6%) were in Group 2. An active inflammatory process in the corpus was observed in 18 patients (28.1%), of whom 14 (36.8%) were in Group 1, and 4 (15.4%) were in Group 2. The degree of inflammatory activity in the antrum was statistically higher in patients with CagA- and VacA-positive *H. pylori* strains ($p<0.05$), while there was no significant difference between the two groups in the corpus of the stomach.

We also compared in both groups the cases of gastric mucosa atrophy in the antrum and corpus (Table III). Mu-

Table I. Grade of mucosal inflammation in the antrum and corpus of the stomach in patients with CagA- and VacA-positive and -negative strains of *H. pylori*

Inflammation	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}
Localization	Antrum			Corpus		
Grade 1, n (%)	5 (13.1)	16 (61.5)	0.0001	12 (31.6)	26 (100)	0.0001
Grade 2, n (%)	27 (71.1)	10 (38.5)		6 (15.8)	0	
Grade 3, n (%)	6 (15.8)	0		20 (52.6)	0	

Table II. Degree of chronic gastritis activity in the antrum and corpus of the stomach in patients with CagA- and VacA-positive and -negative strains of *H. pylori*

Activity	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}
Localization	Antrum			Corpus		
Present, n (%)	26 (68.4)	9 (34.6)	0.008	14 (36.8)	4 (15.4)	0.061
Absent, n (%)	12 (31.6)	17 (65.3)		24 (63.1)	22 (84.6)	
Degree 1, n (%)	8 (30.8)	6 (66.7)	0.048	14 (100)	4 (100)	1.00
Degree 2, n (%)	16 (61.5)	3 (33.3)		0	0	
Degree 3, n (%)	2 (7.7)	0		0	0	

Table III. Grade of atrophy in the antrum and corpus of the stomach in patients with CagA- and VacA-positive and -negative strains of *H. pylori*

Atrophy	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}
Localization	Antrum			Corpus		
Present, n (%)	24 (63.1)	11 (42.3)	0.099	11 (28.9)	4 (15.4)	0.208
Absent, n (%)	14 (36.9)	15 (57.7)		27 (71.1)	22 (84.6)	
Grade 1, n (%)	11 (45.8)	10 (90.9)	0.012	11 (100)	4 (100)	1.00
Grade 2, n (%)	13 (54.2)	1 (11.1)		0	0	
Grade 3, n (%)	0	0		0	0	

Table IV. Presence of metaplasia and its type in the antrum and corpus of the stomach in patients with CagA- and VacA-positive and -negative strains of *H. pylori*

Metaplasia	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}	Group 1 (n = 38)	Group 2 (n = 26)	p_{1-2}
Localization	Antrum			Corpus		
Present, n (%)	15 (39.5)	8 (30.8)	0.476	7 (18.4)	1 (3.8)	0.083
Absent, n (%)	23 (60.5)	18 (69.2)		31 (81.6)	25 (96.1)	
Type						
Complete (small intestinal), n (%)	11 (73.3)	6 (75)	0.931	4 (57.1)	1 (100)	0.408
Incomplete (colonic), n (%)	4 (26.6)	2 (25)		3 (42.9)	0	

Table V. Primary clarithromycin resistance rates in patients with CagA- and VacA-positive and -negative strains of *H. pylori*

Point mutations	Group 1A (n = 26)	Group 2A (n = 12)	p
T2182C, n (%)	2 (7.7)	5 (41.7)	0.022
A2143G, n (%)	1 (3.8)	2 (16.7)	0.229
A2142G/C, n (%)	0	0	-
Total	3 (11.5)	7 (58.3)	0.002

cosal atrophy in the antrum was detected in 24 (63.1%) patients in Group 1, and 11 (42.3%) patients in Group 2. Atrophy in the corpus was observed in 11 (28.9%) patients with *H. pylori* virulence factors, and 4 (15.4%) patients with CagA- and VacA-negative *H. pylori* strains. We found a statistically significant difference in the grade of atrophy

in the antrum between the groups. Patients with CagA- and VacA-positive *H. pylori* strains had a greater grade of atrophy (p=0.012). There was no statistically significant difference in the frequency and grade of atrophy in the stomach corpus between both groups.

Table IV shows data on the presence of intestinal metaplasia in the corpus and antrum of the stomach in both groups. In patients with *H. pylori* virulence factors, intestinal metaplasia in the antrum was observed in 15 (39.5%) individuals, with 11 cases of small intestinal metaplasia, and 4 cases of colonic metaplasia. In 8 (30.8%) patients in Group 2, metaplasia was found in the antrum, with 6 (75%) cases of small intestinal metaplasia and 2 (25%) cases of colonic metaplasia. We found no statistically significant difference in the incidence and type of metaplasia in the gastric antrum between the groups (p>0.05).

In the stomach corpus, intestinal metaplasia was detected in 7 (18.4%) patients in Group 1, and 1 (3.8%) patient in Group 2. Of the 7 patients in Group 1, 4 (57.1%) had small intestinal metaplasia and 3 (42.9%) had colonic metaplasia. 1 patient in Group 2 had small intestinal metaplasia. The observed occurrence of metaplasia in the stomach corpus did not exhibit a statistically significant difference between the two groups (p>0.05).

We studied the presence of primary resistance to clarithromycin in 38 patients, comprising 26 patients with CagA- and VacA-positive *H. pylori* strains (Group 1A), and 12 patients with CagA- and VacA-negative *H. pylori* strains (Group 2A). The identification of A2143G, A2142G/C, and T2182C point mutations in the V domain of 23S rRNA was used to determine the primary resistance to clarithromycin. 10 (26.3%) patients exhibited A2143G and T2182C point mutations out of the total number studied, as shown in Table V. Among the Group 1A patients, the point mutations were found in 3 patients (11.5%), whereas they were detected in 7 patients (58.3%) in another group. The results indicated that primary resistance to clarithromycin was significantly more prevalent in patients with CagA- and VacA-negative *H. pylori* strains (p=0.002).

DISCUSSION

Our findings suggest that patients with CG and *H. pylori* virulence factors (i.e., CagA and VacA) are statistically more likely to exhibit higher grades of inflammation in both the antrum and corpus of the stomach. Other researchers have noted that adhesion of *H. pylori* to gastric epithelial cells is associated with activation of several types of protein kinases (ERK, p38, JNK), which regulate the inflammatory process. JNK is predominantly activated during infection with CagA-positive *H. pylori* strains, which leads to a more pronounced inflammatory process [8]. The cascade of inflammatory responses is initiated as a result of pro-inflammatory cytokines production such as IL-8 and neutrophil activation factor by epithelial cells. The expression of these cytokines is particularly high in cases of infection with CagA-positive *H. pylori* strains, thereby suggesting a probable association between the presence of CagA- and VacA-positive *H. pylori* strains and heightened inflammation [9]. S. A. Boukhris et al. found a significant association between the presence of the CagA gene and increased neutrophil infiltration in patients under the age of 50 years old and stomach cancer in the age group over 50 years old. A relation has also been established between *H. pylori* VacA s1m1 genotypes, metaplasia, and gastric cancer [10]. Based on the results of our study, patients infected with CagA- and VacA-positive *H. pylori* strains exhibit a statistically significant increase in the level of gastritis activity in the antrum of the stomach, which is indicative of heightened neutrophil infiltration into the gastric lamina propria and the epithelial layer of the antrum. However, no statistically significant difference was observed between the groups with respect to inflammation in the corpus of the stomach. N. Almeida et al. found a significant correlation between CagA and the grade of metaplasia, neutrophil activity, and chronic inflammation. In addition, CagA- and VacA-positive *H. pylori* strains were associated with an increased risk of gastric ulcers [11]. N. Kim et al. observed a link between the incidence of gastric cancer and the existence of CagA and VacA m1 in patients over the age of 61 years old [12]. However, no association was detected between virulence factors and precancerous changes in the gastric mucosa in the study conducted by M. Akar et al. [13]. Our study revealed that patients with *H. pylori* virulence factors exhibit a significantly greater grade of atrophy in the antrum, while no statistically significant difference was observed in the corpus of the stomach. However, there was no statistically significant difference in the presence of metaplasia in the antrum and corpus of the stomach between the two groups. V. Shetty et al. noted that the combination of CagA- and VacA-positive *H. pylori* strains leads to peptic ulcer and gastric cancer [14]. Variations in several genes, besides CagA and VacA genotypes, may also be associated with the risk of inflammation and carcinogenesis, the data on which remain uncertain [15]. Thus far, there is no systemic analysis that has investigated the effect of bacterial virulence factors on the onset and progression of gastroduodenal diseases.

The elimination of *H. pylori* is deemed to be a cost-effective approach to mitigate the risk of GC. According to the Maastricht VI/Florence Consensus, the choice of treatment regimen should be based on the rate of the resistance of *H. pylori* strains to clarithromycin in a particular region [16]. Multicenter studies have shown that the primary level of clarithromycin resistance is more than 15% in majority of European countries, which makes

eradication regimens with clarithromycin ineffective [17]. There is a possible link between virulence factors and antimicrobial resistance. D.E. Brennan et al. found that patients with CagA-negative and VacA S2-positive strains had a high rate of primary resistance to clarithromycin (50.5%) [18]. Another cohort study found an increased frequency of A2143G point mutations among less virulent VacA i2 strains, and an increased frequency of A2142G point mutations in more virulent VacA i1 strains [19]. M. Karbalaei et al. showed the lower rate of resistance to antibiotics in patients with less virulent (VacA s2m2) strains [7]. Conversely, M. Bachir et al. did not find a link between virulence factors and clarithromycin resistance, which is consistent with the data from our study [20].

The limitations of a study are small sample size, inability to study other genes associated with the Cag Pathogenicity Island, and the lack of analysis pertaining to the various subtypes of VacA strains.

CONCLUSIONS

Our study reveals that patients with CagA- and VacA-positive *H. pylori* strains demonstrate significantly higher grades of inflammation in both the antrum and corpus of the stomach, activity of gastritis in the antrum, higher incidence and grade of atrophy in the antrum. We also noted that T2182C and A2143G mutations in the V domain of the 23S rRNA gene were more frequently detected in patients with CG and CagA- and VacA- negative strains of *H. pylori*.

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ORIGINAL ARTICLE

ALGORITHM OF RADIOLOGICAL EXAMINATION OF PATIENTS IN THE PLANNING OF ORTHODONTIC TREATMENT OF INTERARCH RELATIONSHIP OF TEETH AND TEETH POSITION ANOMALIES

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ABSTRACT

The aim: To increase the efficiency of diagnosis and planning of orthodontic treatment of patients with interarch relationship of teeth and teeth position anomalies by developing an optimal algorithm for radiological research using cone-beam computed tomography (CBCT), teleroentgenography (TRG), orthopantomography (OPG).

Materials and methods: 1,460 patients with interarch relationship of teeth and teeth position anomalies were examined at the Department of Radiology of the P. L. Shupyk National Healthcare University of Ukraine. The cohort of 1460 examined patients was divided by gender: 600 men (41.1%) and 860 women (58.9%) aged 6 to 18 years and 18 to 44 years. Distribution of patients was held by the number of the primary pathology signs and the number of concomitant pathology signs.

Results: The choice of the optimal radiological examination of patients is influenced by the number of signs of the main and accompanying pathology. The risk of secondary examination of the patient with a mathematical method of choosing the optimal diagnostic technique is determined.The risk of secondary radiological examination of the patient was determined at a marginal probability of 88% (at a higher value, the model predicts a repeat visit).

Conclusions: The developed diagnostic model shows that when determining the Pr-coefficient of 0.79, it is recommended to carry out OPTG and TRG. With indicators of 0.88, the recommendation is to conduct CBCT in the age groups 6-18 and 18-44 years.

KEY WORDS: cone-beam computed tomography, teleroentgenography, orthopantomography, interarch relationship of teeth

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INTRODUCTION

The high prevalence of interarch relationship of teeth and teeth position anomalies explains the presence of a high percentage of patients requiring orthodontic, orthopedic or complex treatment. In the treatment of this pathology, radiological examination is used not only for the purpose of primary diagnosis, but also for comparison of the treatment plan and prognosis, studying of the treatment process dynamics [1-3].

Diagnostic radiology methods for patients with interarch relationship of teeth and teeth position anomalies are based on performing a pantomographic and cephalometric study of the skull in a lateral projection, to describe the morphology and growth of the facial skeleton in different age groups. Depending on the presence of concomitant pathology (presence of retained, dystopic, supernumerary teeth; temporomandibular joint dysfunction), it is necessary to use additional radiological methods [4-6].

Currently, there is an alternative method of examining patients with interarch relationship of teeth and teeth position anomalies. It is cone-beam computed tomography (CBCT) of the maxillofacial region. CBCT is the method of choice in various orthodontic cases, for example, in facial asymmetry, discernible open occlusion and other defects in the patient's facial skeleton development. The advantage of this diagnostic method is low radiation exposure, which is important for such a group of patients as children and adolescents, as well as its high informativeness [7, 8].

Delayed and incorrect diagnosis of interarch relationship of teeth and teeth position anomalies. leads to the appearance of a number of complications, which subsequently affects the choice of treatment and its duration. Thus, there is a need for a wider introduction of optimal and informative diagnostic radiology methods with a low patient exposure level into practice.

THE AIM

To increase the efficiency of diagnosis and planning of orthodontic treatment of patients with interarch relationship of teeth and teeth position anomalies by developing an optimal algorithm for radiological research using cone-beam computer tomography (CBCT), teleroentgenography (TRG), orthopantomography (OPG). We analyzed the statistical data of orthopantomography, teleroentgenography and cone-beam tomography diagnostic efficiency in groups of patients aged 6 to 18 years and 18 to 44 years with a combination of the primary and concomitant pathology signs and established the importance of mathematical calculation of the influence of the combination of the primary and concomitant pathology signs at recall radiological examination of patients. Impact was calculated using the Mann-Whitney U test.

MATERIALS AND METHODS

In the period 2016 to 2020, 1,460 patients with interarch relationship of teeth and teeth position anomalies were examined at the Department of Radiology of the P. L. Shupyk National Healthcare University of Ukraine. The formation of the group was carried out according to the medical documentation data, retrospectively and non-randomized according to the inclusion criteria.

Patient inclusion criteria: initial examination of patients with interarch relationship of teeth and teeth

Table I. Distribution of patients according to the primary pathology and research methods in the age group of 6-18 years

No	Primary pathology signs	Number of patients	%	Diagnostic methods at initial examination	Diagnostic methods at recall examination
1.	Teeth retention	83	5.7	OPG+TRG	CBCT
2.	Teeth dystopia	66	4.5	OPG+TRG	CBCT
3.	Teeth rotation	79	5.4	OPG+TRG	CBCT
4.	Distal occlusion	142	9.7	OPG+TRG	CBCT
5.	Mesial occlusion	73	5.0	OPG+TRG	CBCT
6.	Milk tooth with permanent occlusion	38	2.6	OPG+TRG	CBCT
7.	Edge-to-edge occlusion	83	5.7	OPG+TRG	CBCT

Table II. Distribution of patients according to the primary pathology and methods of examination in the age group of 18-44 years

No	Primary pathology signs	Number of patients	%	Diagnostic methods at initial examination	Diagnostic methods at recall examination
1.	Teeth retention	132	9.1	OPG+TRG	CBCT
2.	Teeth dystopia	105	11.7	OPG+TRG	CBCT
3.	Teeth rotation	125	7.2	OPG+TRG	CBCT
4.	Distal occlusion	226	15.5	OPG+TRG	CBCT
5.	Mesial occlusion	116	8.0	OPG+TRG	CBCT
6.	Milk tooth with permanent occlusion	60	4.2	OPG+TRG	CBCT
7.	Edge-to-edge occlusion	132	9.1	OPG+TRG	CBCT

Table III. Distribution of patients according to the concomitant pathology and methods of examination in the age group of 6-18 years

No	Concomitant pathology signs	Number of patients	%	Diagnostic methods at initial examination	Diagnostic methods at recall examination
1.	TMJ dysfunction	110	7.5	OPG+TRG	CBCT
2.	TMJ hypermobility	81	5.5	OPG+TRG	CBCT
3.	Inflammatory process of the tooth root	39	2.7	OPG+TRG	CBCT
4.	Inflammatory process of accessory nasal sinuses	62	4.3	OPG+TRG	CBCT
5.	Tooth decay	62	4.3	OPG+TRG	CBCT
6.	Tooth adentia	25	1.7	OPG+TRG	CBCT
7.	Decrease in the level of bone tissue	62	4.3	OPG+TRG	CBCT

Table IV. Distribution of patients according to the concomitant pathology and research methods in the age group of 18-44 years

No	Concomitant pathology signs	Number of patients	%	Diagnostic methods at initial examination	Diagnostic methods at recall examination
1.	TMJ dysfunction	177	8.8	OPG+TRG	CBCT
2.	TMJ hypermobility	129	8.0	OPG+TRG	CBCT
3.	Inflammatory process of the tooth root	263	18.0	OPG+TRG	CBCT
4.	Inflammatory process of accessory nasal sinuses	118	8.1	OPG+TRG	CBCT
5.	Tooth decay	146	10.0	OPG+TRG	CBCT
6.	Tooth adentia	62	4.3	OPG+TRG	CBCT
7.	Decrease in the level of bone tissue	73	5.0	OPG+TRG	CBCT

Table V. Distribution of patients aged 6 to 18 years into groups according to the number of the primary and concomitant pathologies signs

No	Group	Number of primary pathology signs	Number of concomitant pathology signs	Number	%
1.	1_0	Distal occlusion	–	29	5.2
2.	1_1	Mesial occlusion	Inflammatory process of accessory nasal sinuses	19	3.4
3.	1_3	Edge-to-edge occlusion	Inflammatory process of accessory nasal sinuses, tooth decay, TMJ hypermobility	34	6.2
4.	1_4	Mesial occlusion	Inflammatory process of accessory nasal sinuses, tooth decay, inflammatory process of the tooth root, TMJ dysfunction	31	5.5
5.	2_1	Rotation, retention	Inflammatory process of the tooth root	24	4.3
6.	2_2	Rotation, retention	Inflammatory process of the tooth root, tooth decay	58	10.4
7.	2_3	Mesial occlusion, retention	Inflammatory process of the tooth root, tooth decay, inflammatory process of accessory nasal sinuses	47	8.4
8.	3_0	Distal occlusion, dystopia, retention	–	24	4.3
9.	3_1	Dystopia, retention, rotation	TMJ hypermobility	25	4.5
10.	3_2	Mesial occlusion, retention, dystopia	Inflammatory process of the tooth root, TMJ hypermobility	47	8.4
11.	4_0	Distal occlusion, retention, dystopia, rotation	–	26	4.6
12.	4_1	Mesial occlusion, retention, dystopia, milk tooth	Inflammatory process of the tooth root	25	4.5
14.	4_2	Distal occlusion, retention, dystopia, rotation	TMJ hypermobility, tooth decay	67	12.0
15.	4_3	Distal occlusion, retention, dystopia, rotation	Inflammatory process of accessory nasal sinuses, inflammatory process of the tooth root, TMJ dysfunction	51	9.2
16.	5_0	Mesial occlusion, retention, rotation, dystopia, milk tooth	–	27	4.8
17.	5_1	Distal occlusion, retention, dystopia, rotation, milk tooth	Inflammatory process of the tooth root	26	4.6

position anomalies, retained and dystopic teeth, temporomandibular joint hypermobility and dysfunction, presence of a milk tooth with a permanent occlusion.

Exclusion criteria: patients after orthodontic treatment and those who had no history of interarch relationship of teeth and teeth position anomalies. Patients older than 44 years, who had interarch relationship of teeth and teeth position anomalies, were not included in the study, since, according to the attending doctor recommendations, they were to undergo orthopedic treatment (implant restoration, removable and fixed constructions). This choice of treatment is due to the complexity and

Table VI. Distribution of patients aged 18 to 44 years into groups according to the number of the primary and concomitant pathologies signs

No	Group	Number of primary pathology signs	Number of concomitant pathology signs	Number	%
1.	1_0	Distal occlusion	–	26	2.8
2.	1_1	Mesial occlusion	Inflammatory process of accessory nasal sinuses	38	4.3
3.	1_3	Edge-to-edge occlusion	Inflammatory process of accessory nasal sinuses, tooth decay, TMJ hypermobility	49	5.4
4.	1_4	Mesial occlusion	Inflammatory process of accessory nasal sinuses, tooth decay, inflammatory process of the tooth root, TMJ dysfunction	87	9.6
5.	2_1	Rotation, retention	Inflammatory process of the tooth root	106	11.7
6.	2_2	Rotation, retention	Inflammatory process of the tooth root, tooth decay	101	11.2
7.	2_3	Mesial occlusion, retention	Inflammatory process of the tooth root, tooth decay, inflammatory process of accessory nasal sinuses	100	11.1
8.	3_0	Distal occlusion, dystopia, retention	Inflammatory process of accessory nasal sinuses, tooth decay	47	5.2
9.	3_1	Dystopia, retention, rotation	TMJ hypermobility	69	7.6
10.	3_2	Mesial occlusion, retention, dystopia	Inflammatory process of the tooth root, TMJ hypermobility	75	8.3
11.	4_0	Distal occlusion, retention, dystopia, rotation	–	15	1.6
12.	4_1	Mesial occlusion, retention, dystopia, milk tooth	Inflammatory process of the tooth root	23	2.5
14.	4_2	Distal occlusion, retention, dystopia, rotation	TMJ hypermobility, tooth decay	44	4.8
15.	4_3	Distal occlusion, retention, dystopia, rotation	Inflammatory process of accessory nasal sinuses, inflammatory process of the tooth root, TMJ dysfunction	59	6.5
16.	5_0	Mesial occlusion, retention, rotation, dystopia, milk tooth	–	44	4.8
17.	5_1	Distal occlusion, retention, dystopia, rotation, milk tooth	Inflammatory process of the tooth root	17	1.8

Table VII. Radiodiagnostic predictors

Groups (of the primary pathology)	Groups (of the concomitant pathology)	Retention	Teeth rotation	Intercept
-1.54227	-0.32056	-2.71016	-0.63075	4.3477

duration of orthodontic treatment of patients of this age.

Radiological examination of patients was carried out on a Planmeca RroMax 3D cone-beam computed tomographic scanner with the SmartPan system. Patients underwent orthopantomography (OPG), frontal/lateral view teleroentgenography (TRG) and cone beam computed tomography **(C**BCT).

The cohort of 1460 examined patients was divided by gender: 600 men (41.1%) and 860 women (58.9%) aged 6 to 18 years and 18 to 44 years. The distribution of patients by the number of the primary pathology signs and the number of concomitant pathology signs is presented in Table I, II, III, IV.

The distribution of patients aged from 6 to 18 years according to the primary pathology allowed to determine that distal occlusion (142 (9.7%)) was in the first place in terms of frequency of detection. A milk tooth with the permanent occlusion was detected in 38 (2.6%) patients with interarch relationship of teeth and teeth position anomalies in the above-mentioned age group, which was determined the least often. Such an primary pathology sign occurred the most rarely (Table I).

When distributing patients according to the ptimary pathology, aged 18 to 44 years, it was found that distal occlusion (226 (15.5%)) was the most common. A milk tooth with permanent occlusion was found in a small number of 60 (4.2%) patients (Table II).

The distribution of patients aged from 6 to 18 years according to the primary pathology allowed to determine that distal occlusion (142 (9.7%)) was in the first

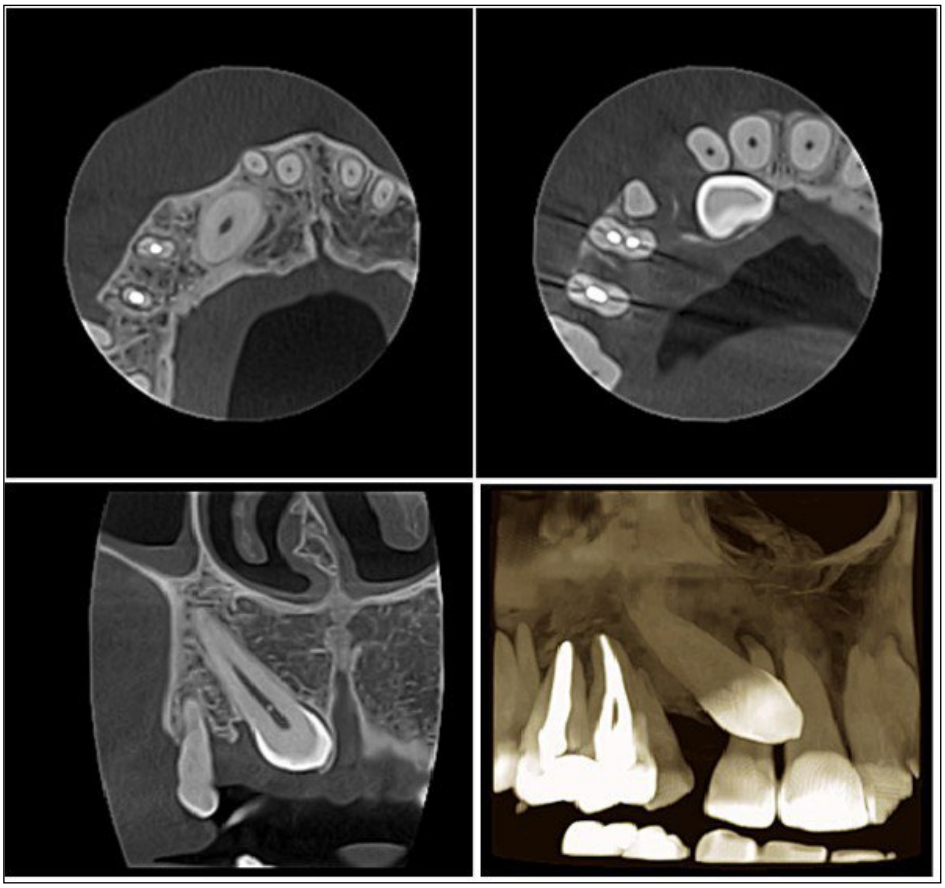

Fig. 1. Patient K., 18 years old. CBCT segment (80x80 cm) of teeth 1.5-2.1. Tooth 1.3. partial rotation, retention. Milk tooth 5.3 in the tooth row

Fig. 2. Patient K. 21 years old. CBCT at recall radiological examination. Coronal, sagittal slices. Tooth 2.3 displacement and rotation, 1.1, 1.2 teeth concretion, tooth 1.8 retention and dystopia, tooth 4.1

place in terms of frequency of detection. A milk tooth with a permanent occlusion was detected in 38 (2.6%) patients with interarch relationship of teeth and teeth position anomalies in the above age group. This sign of the primary pathology occurred most rarely (Table III).

In 263 (18.0%) patients aged 18-44 years, the inflammatory process of the tooth root was detected, which became the most common symptom of this group of patients. Tooth adentia (62 (4.3%)) had the lowest value and occurred rarely (Table IV).

STATISTICAL DATA PROCESSING

Data preparation for analysis was performed in Microsoft Excel, and statistical data analysis was carried out using STATISTICA 64 ver.10.0.1011.0 software by StatSoft Inc. Data analysis reports are presented directly from the specified software without any changes, which ensures their transparency and objectivity.

RESULTS

We analyzed the results of the examinations and made a statistical analysis of 560 (38.3%) patients with interarch relationship of teeth and teeth position anomalies, aged 6-18 years, who underwent orthopantomography and teleroentgenography (frontal or lateral views) during the initial radiological examination. Depending on the number of signs of the primary and concomitant pathologies, this group of patients was subjected to CBCT during recall radiological examination (Table V).

After dividing the patients into groups depending on

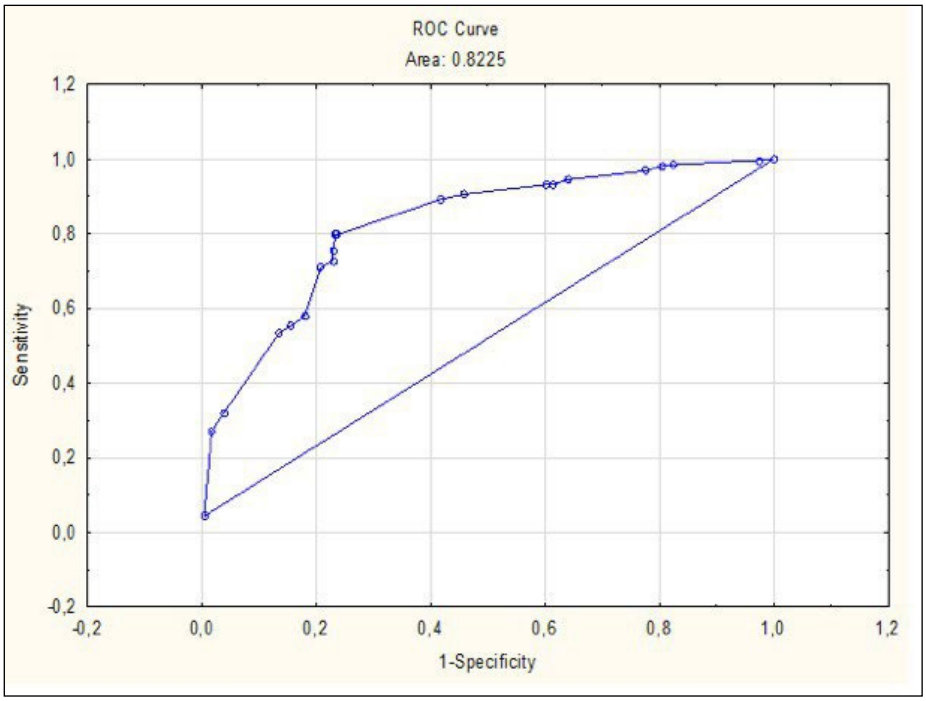

Fig. 3. ROC Curve Area

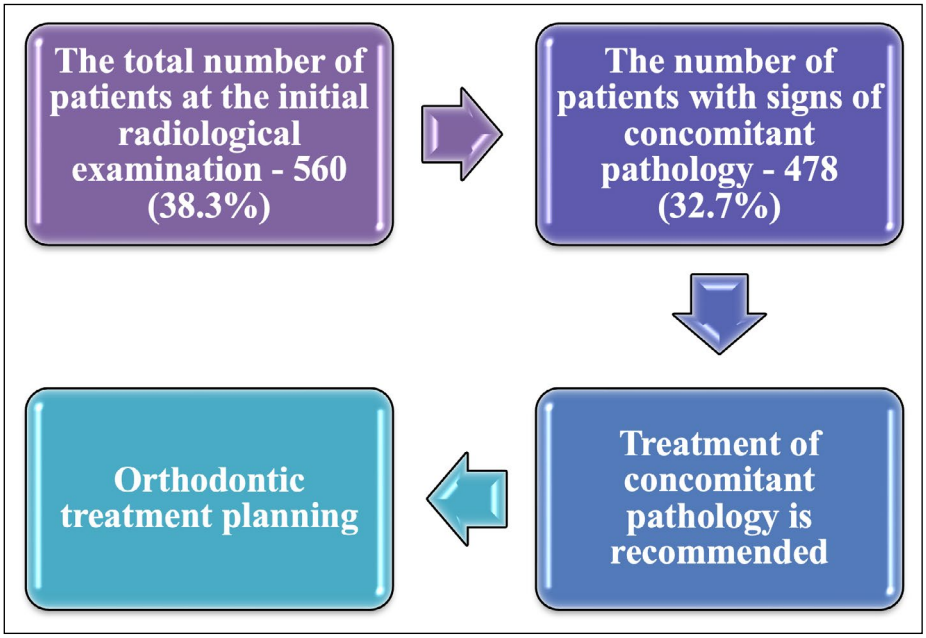

Fig. 4. Recommendations in orthodontic treatment planning based on radiological examination data with detected signs of concomitant pathology in the age group from 6 to 18 years.

the number of signs of the primary and concomitant pathologies, it was determined that 67 (12.0%) patients had a combination of such signs of the primary and concomitant pathologies as distal occlusion, retention, dystopia, rotation and hypermobility of the temporomandibular joint, tooth decay. In 19 (3.4%) patients, a combination of mesial occlusion and inflammatory process of nasal sinuses was determined, which became the smallest statistical value in the patient distribution table. When comparing the data of radiological examination methods of patients with a combination of signs of pathologies during the initial radiological examination, it was determined that the greater the number of signs of the primary and concomitant pathologies in the combination, the greater the risk of repeated scanning of patients.

We determined radiological signs of interarch relationship of teeth and teeth position anomalies on CBCT of the upper and lower jaws, segment, facial skeleton bones (Fig. 1).

We analyzed the results of examinations and conducted a statistical analysis of 900 (61.7%) patients aged 18 to 44 years, with interarch relationship of teeth and teeth position anomalies, who underwent orthopantomography and teleroentgenography (frontal or lateral views) during the initial radiological examina-

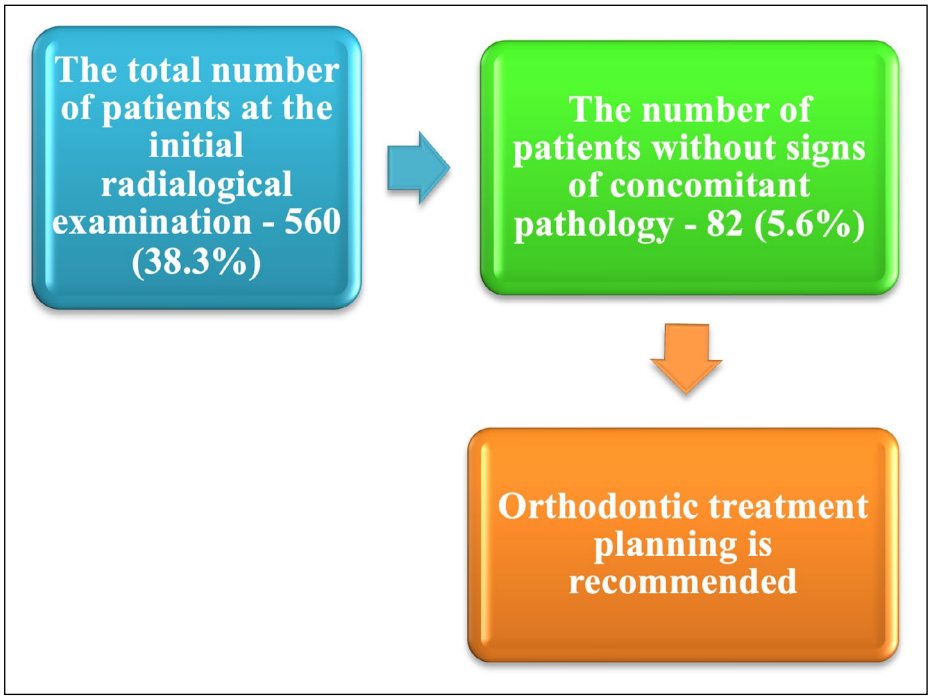

Fig. 5. Recommendations in orthodontic treatment planning based on radiological examination without signs of concomitant pathology in the age group from 6 to 18 years.

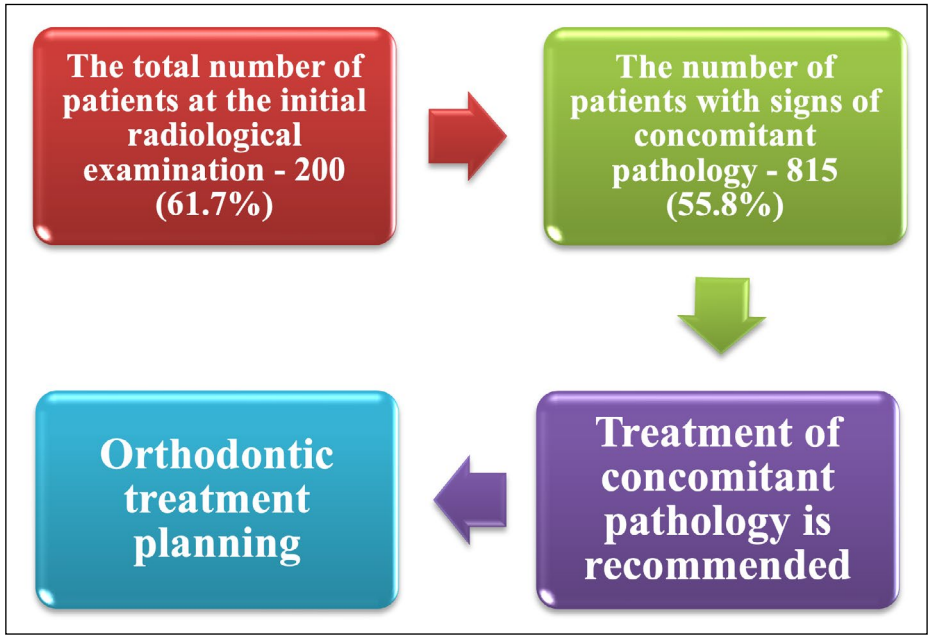

Fig. 6. Recommendations in orthodontic treatment planning based on radiological examination data with detected signs of concomitant pathology in the age group from 18 to 44 years.

tion. Depending on the number of the primary and concomitant pathologies signs**,** this group of patients was subjected to CBCT during recall radiological examination. The distribution of patients into groups is presented in (Table VI).

A demonstration of a case of a patient on KPKT with a repeated radiological examination is presented in (Fig. 2).

After conducting the analysis, we established that men aged 27 years (24.3%) and women aged 25 years (19.8%) with interarch relationship of teeth and teeth position anomalies apply for a recall radiological examination more often. This was explained by the fact that the patients showed signs of concomitant pathology at this age, but the direct influence of gender on recall radiological examination was not proven.

According to the research results, we determined the diagnostic efficiency of orthopantomography, teleroentgenography and cone-beam computed tomography in patients aged 6 to 18 years and 18 to 44 years with a combination of signs of the primary and concomitant pathology based on the calculation of sensitivity, specificity and accuracy. In groups of patients 1_0, 1_1, 1_3 aged 6 to 18 years with a small number of signs of the primary and concomitant pathology, the indicators of the diagnostic efficiency of OPG, TRG were: accuracy - 93.7%, sensitivity - 96.6%, specificity - 50%,

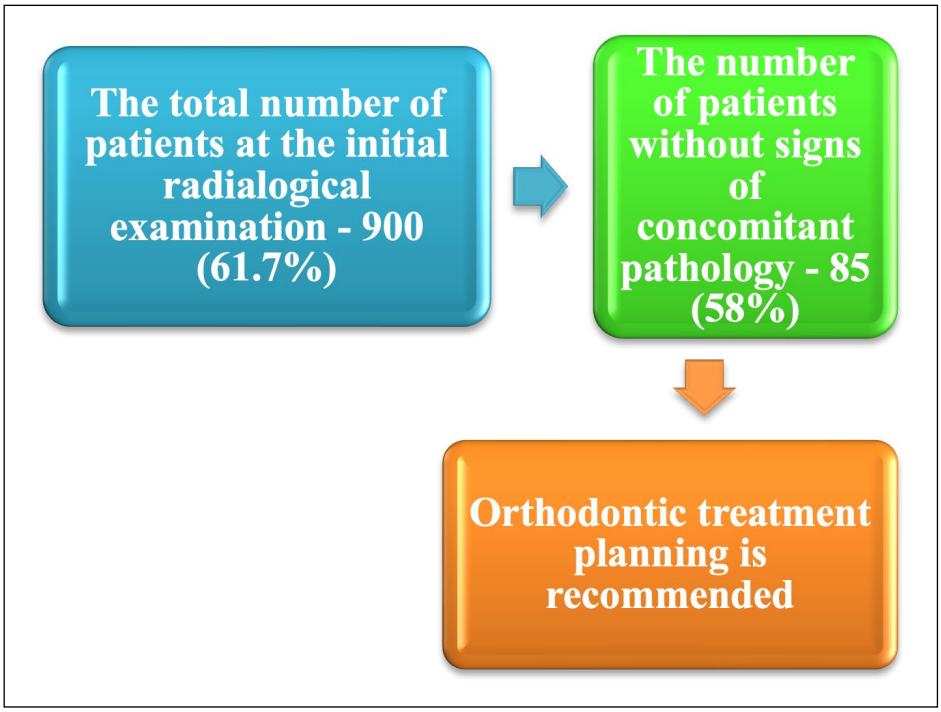

Fig. 7. Recommendations in orthodontic treatment planning based on radiological examination without signs of concomitant pathology in the age group from 18 to 44 years.

on the other hand with the increase in the quantitative indicators of the primary and concomitant pathology, the diagnostic efficiency of the methods decreased, so in groups 4_2, 4_3 it was: accuracy - 46.3%, sensitivity - 32.3%, specificity - 51.2%. At the same time, the indicators of the diagnostic effectiveness of cone-beam computed tomography remained high, so in groups 1_1, 5_0, the indicators were: accuracy - 93.7%, sensitivity - 96.6%, specificity - 50%. When analyzing the data in the age group from 14 to 18 years, similar dynamics of decreasing indicators of the diagnostic efficiency of orthopantomography and teleroentgenography were observed. So, in the group 1_0, 1_1, the indicators were: accuracy – 92.3%, sensitivity – 95.8%, specificity – 50.0%; in group 5_0, 5_1: accuracy – 52.2%, sensitivity – 44.0%, specificity – 45.0%.

Instead, the diagnostic efficiency remained high. In group 1_3, the indicators were: accuracy - 96.0%, sensitivity - 95.6%, specificity - 66.6%, in group 5_1: accuracy - 89.0%, sensitivity - 93.3%, specificity - 50.0% . The decrease in the specificity of CBCT in the groups is due to the selective scanning of the jaw segment and the temporomandibular joint area (8x8).

We analyzed the statistical data of the diagnostic efficiency of orthopantomography, teleroentgenography and cone-beam tomography in patients aged 6 to 18 years and 18 to 44 years with a combination of the primary and concomitant pathology and established the importance of mathematical calculation of the influence of the combination of signs of the primary and concomitant pathology on the recall radiological examination of patients. Impact was calculated using the Mann-Whitney U test. The test has shown that the H0 hypothesis about the absence of influence should be rejected and the alternative hypothesis should be accepted, about the registered significance of the influence of the combination of signs of the primary and concomitant pathology on the probability of recall examination of the patient ($p<0.005$).

With the use of radiodiagnostic predictors, we developed a diagnostic model for predicting the risk of the occurrence of patient recall after the initial diagnostic examination.

$$Pr = 1 - \frac{1}{1 + \exp(-\sum_{j=1}^{4} Param_j \, A_j - intercept)},$$

where is probability of recall;

– coefficients from (Table VII) corresponding to predictors of influence on the outcome of treatment, such as:

- groups (of the primary pathology) - the number of the primary pathology signs;
- groups (of the concomitant pathology) – the number the concomitant pathology signs;
- retention;
- teeth rotation.

The model is characterized by statistically significant coefficient estimates and a high ROC Curve Area for biostatistical research: 0.82 (Fig.3).

In terms of risk of recall, the marginal probability value is set at 88% (if the estimated probability of recall *Pr* is higher, the model predicts recall and vice versa).

Based on the indicators of the diagnostic effective-

ness of radiological diagnostic methods in the case of a combination of signs of the primary and concomitant pathology we have proposed recommendations for orthodontic treatment of patients aged 6 to 18 and 18 to 44 years planning.

According to the results of OPG, TRH, CBCT examinations of 560 (38.3%) patients in the age category from 6 to 18 years, it was determined that 478 (32.7%) had signs of concomitant pathology, therefore they were recommended to consult doctors of related specialties, concomitant pathology correction and only after that, orthodontic treatment planning. In 82 (5.6%) patients, signs of concomitant pathology were not determined, so they were recommended to plan orthodontic treatment. The graphic visualization of the algorithm is presented in (Fig. 4, 5).

The cohort of 1460 examined patients was divided by gender: 600 men (41.1%) and 860 women (58.9%) aged 6 to 18 years and 18 to 44 years. The distribution of patients by the number of the primary pathology signs and the number of concomitant pathology signs is presented in Table I, II, III, IV, V, VI.

According to the results of the examinations, in the age group of patients from 18 to 44 years (900 (61.7%)), number of patients with signs of concomitant pathology was 815 (55.8%). These patients are recommended to adjust the plan of orthodontic treatment in order to eliminate signs of concomitant pathology. 85 (5.8%) patients had no signs of concomitant pathology and were recommended further planning of orthodontic treatment. The graphic visualization of the algorithm is presented in (Fig 6, 7).

DISCUSSION

At the first stage of the study, the frequency of abnormalities in the ratio of dental arches and the position of teeth in patients was determined based on the analysis of orthopantomogram, teleroentgenogram, and cone-beam computed tomography data. Determination of the effectiveness of orthopantomogram, teleroentgenogram in direct and lateral projections, cone-beam computer tomogram in the case of anomalies of the ratio of dental arches and the position of teeth. Correlations between age, gender and the risk of re-visiting a patient with abnormalities in the ratio of dental arches and tooth position were found out [9, 10]. We evaluated patients aged 6-18 years and patients aged 18-44 years who underwent orthopantomography and teleradiography at the initial visit. During the secondary examination, CPCT was performed on the patients. Semiotically, in patients aged 6-18 during the initial radiological examination, signs of the main pathology were revealed: retention of teeth, dystopia of teeth, rotation of teeth, distal bite, mesial bite, milk tooth with permanent bite, direct bite and and signs of accompanying pathology: TMJ dysfunction, TMJ hypermobility, tooth root inflammatory process, PPN inflammatory process, tooth caries, tooth adentia, decreased bone tissue level. The total number of patients with signs of concomitant pathology was. These patients are recommended to adjust the plan of orthodontic treatment in order to eliminate signs of concomitant pathology. Based on the results of the radiological examination, patients were recommended for further planning of orthodontic treatment. In patients aged 18-44 semiotically, during the initial radiological examination, signs of the main pathology were revealed: retention of teeth, dystopia of teeth , rotation of teeth, distal bite, mesial bite, milk tooth with permanent bite, direct bite and signs of concomitant pathology TMJ dysfunction, TMJ hypermobility, tooth root inflammatory process, PPN inflammatory process, tooth caries, tooth adentia, decreased bone tissue level. The total number of patients with signs of concomitant pathology was. The total number of patients with signs of concomitant pathology was. These patients are recommended to adjust the plan of orthodontic treatment in order to eliminate signs of concomitant pathology. According to the results of radiological examination, further planning of orthodontic treatment was recommended for patients. The next stage was the determination of radiological predictors affecting the repeated radiological examination of patients with anomalies of the ratio of dental arches and the position of teeth. In order to build a prognostic model, as a result of the analysis, influence predictors were selected, which turned out to be statistically significant: groups - the number of signs of the main pathology, groups - the number of signs of accompanying pathology, retention, tooth rotation. The connection of these indicators with the index of repeated treatment was studied using the logit model. The model is characterized by statistically significant coefficient estimates and a high ROC Curve Area for biostatistical research. The interpretation of the statistical characteristics of the method is similar to the one given above. At the same time, the Cutoff Probability Point is the probability of no repeat appeal, which separates cases where there is a repeat appeal from those where it is not expected by the model. Thus, they independently developed a mtaermatic model for the optimal choice of radiological examination of patients.

CONCLUSIONS

It was established that men aged 27 (24.3%) and women aged 25 (19.8%) with interarch relationship of teeth

and teeth position anomalies require recall radiological examination for the identification of concomitant pathology signs (21 .2% and 10.8%). There was no evidence of influence of gender on recall radiological examination. The frequency of interarch relationship of teeth and teeth position anomalies was determined and specified. In 38.4% of patients (aged 6-18 years), according to the results of the initial OPG and TRG examination, distal occlusion was most often detected as the primary pathology (9.7%), and the presence of a milk tooth was detected only in 2.6% of patients. TMJ dysfunction was detected more often (7.5%), tooth adentia was detected rarely (1.7%). In the age group from 18 to 44 years, distal occlusion was the most frequent primary pathology (15.5%), and a milk tooth was the least common (in 4.2% of patients). TMJ dysfunction was the most frequent sign of concomitant pathology (8.8%), and tooth adentia was less common (in 4.3% of patients). The analysis of the frequency of interarch relationship of teeth and teeth position anomalies according to the results of OPG, TRG, CBCT has shown that in the age group from 6 to 18 years, signs of concomitant pathology were detected in 32.7% of patients, and in the group from 18 to 44 years those were detected in 55.8% of patients. Meanwhile, signs of the primary pathology were detected in 5.6% and 5.8% of patients in two age categories. It has been proven that the recall radiological examination of patients in the age category from 6 to 18 years is due to the primary pathology signs in 38.6% of patients, and concomitant pathology in 30.3%. It was determined that in the age group from 18 to 44 years, the recall was caused by the primary pathology in 64.8%, and concomitant pathology in 62.2%. During the recall examination, CBCT was performed in 38.4% of patients in the age group of 6 - 18 years and in 61.6% of patients in the age group of 18 - 44 years. A relationship between the frequency of the primary and concomitant pathologies signs in the case of interarch relationship of teeth and teeth position anomalies and the indicators of the diagnostic efficiency of OPG, TRG, CBCT was statistically proven: aged from 6 to 18 years in the group with one sign of the primary pathology, the indicators at OPG were: accuracy -93.7%, sensitivity - 96.6%, specificity - 50%. However, in the presence of 4 signs of the primary and concomitant pathologies, indicators of diagnostic efficiency at OPG were: accuracy - 51.0%, sensitivity - 57.6%, specificity - 37%; at TRG: accuracy - 47.3%, sensitivity - 37.0%, specificity - 47.2%; at CBCT accuracy - 89.0%, sensitivity - 95.8%, specificity - 50.0%. In patients aged 18 to 44 years, the diagnostic efficiency of OPG, TRG, CBCT were: in the group with one sign of the primary pathology, the indicators at OPG were: accuracy - 92.3%, sensitivity - 95.8%, specificity - 50.0%; at TRG: accuracy - 92.1%, sensitivity - 95.8%, specificity - 50.0%. However, in the presence of 4 signs of the primary and concomitant pathologies, indicators of diagnostic efficiency at OPG were: accuracy - 49.5%, sensitivity - 48.3%, specificity - 38.5%; at TRG: accuracy - 44.1%, sensitivity - 40.0%, specificity - 39.3%; at CBCT: accuracy - 89.0%, sensitivity - 95.8%, specificity - 50.0%. A diagnostic model has been developed for predicting the risk of patients recall, with a mathematical method for choosing the optimal diagnostic method. The risk of recall was determined at a marginal probability of 88% (at a higher value, the model predicts a recall). With a determined Pr-coefficient of 0.79, OPG and TRH examinations are recommended; with coefficient of 0.85, CBCT is recommended in both age groups. An algorithm of radiological examination of patients for planning orthodontic treatment of interarch relationship of teeth and teeth position anomalies, based on the use of a diagnostic model has been improved. It was determined that the treatment of concomitant pathology was recommended to 32.7% of patients aged 6-18 years. 5.6% of patients, with only the primary pathology detected, were directed to orthodontic treatment planning.

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ORIGINAL ARTICLE

ANALYSIS OF MAIN TRENDS OF DEVELOPMENT OF HEALTH CARE IN UKRAINE

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ABSTRACT

The aim: To substantiate the conceptual approaches of building a cluster model of primary medical care at the level of the hospital district in terms of the development of family medicine, in particular, the consolidation of health care institutions as the main providers of medical services in the provision of primary medical care in the hospital district and improving its efficiency.

Materials and methods: Methods of structural and logical analysis, bibliosemantic, abstraction and generalization were used in this work.

Results: The analysis of the legal framework in the field of health care of Ukraine demonstrated multiple attempts to reform it in order to increase the availability and efficiency of medical and pharmaceutical services. The practical implementation of any innovative project becomes much more difficult or even impossible without a carefully developed plan. Today in Ukraine there are 1,469 united territorial communities, 136 districts, so more than one thousand primary health care centers (further written as PHCCs) have been created against, a possible 136. A comparative analysis indicates the economic validity and possibility of such changes - the creation of a single health care facility at the level of a hospital cluster to provide primary medical care. For example, the Bucha district of the Kyiv region consists of twelve territorial communities, and 11 primary health care centers (PHCCs), the latter have separate subdivisions under their control in the form of: general practice-family medicine dispensary (GPFMD), group practice dispensary (GPD), paramedic and midwifery points (PMP), paramedic points (PP).

Conclusions: The implementation of a cluster model of providing primary medical care in the form of the creation of a single health care facility at the level of a hospital cluster has a number of advantages in the short term. For the patient, it is the availability and timeliness of medical care, at least at the level of the district, not the community; cancellation of paid medical services during the provision of primary medical care regardless of the place of its provision. For the subject of governance (the state) – cost reduction during the provision of medical services.

KEY WORDS: hospital district, cluster model, primary medical care, quality indicator, patient

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INTRODUCTION

Improving the efficiency of providing medical care is one of the key priorities of the health care system at all stages of providing medical care. As a general rule, the patient's initial application as a subject of receiving medical services is made to a health care institution that provides primary medical care, i.e. through a general practitioner-family medicine doctor. The change in legislation in the field of health care allows to optimize the provision of medical care at hospital level. The authors propose a cluster model of primary medical care as an element of the functioning of the hospital district.

THE AIM

The purpose of this work is to substantiate the conceptual approaches of building a cluster model of primary medical care at the level of the hospital district at the stage of development of family medicine. In particular, the enlargement of health care institutions as the main providers of medical services while providing primary medical care in the hospital district and improving its efficiency.

MATERIALS AND METHODS

Methods of structural and logical analysis, bibliosemantic, abstraction and generalization were used in this work.

RESULTS

The question of reforming the health care system appeared on the agenda almost immediately after Ukraine

gained independence. The socio-economic crisis of the 1990s seriously affected the resource provision of the health care sector, which continued to work according to the Soviet system in new market conditions. The primary conceptual approaches of that time were focused on finding additional sources of funding without attempting to change the organizational infrastructure of the industry. At the specified stage, solving such a task was possible by expanding the scope of paid medical services, as well as by introducing mandatory medical insurance. The format of mutual settlement between health care institutions was introduced into practice in the case of providing assistance to patients not registered at the service address of this institution.

Adopted in 1996, the Constitution of Ukraine [1] suspended the implementation of market mechanisms in health care. Soon, the "Fundamentals of the Legislation of Ukraine on Mandatory State Social Insurance" [2] was developed and adopted, which significantly reduced the flexibility and adaptability of the nascent medical insurance. Insurance companies lost interest in participating in health insurance, as the adopted legal framework created an opportunity only for a monopolistic model with the creation of a semi-state insurance fund. The approval of the government resolution in September 1996, in accordance with the then-current norm-setting trend, "List of paid services provided in state and community health care institutions and higher medical educational institutions" [3] narrowed the scope of attracting extrabudgetary funds to finance the activities of health care institutions.

The preservation of legislative and economic mechanisms for health care financing against the background of hyperinflation led to stagnation in the industry and a noticeable deterioration in the state of health care in the late 1990s. This led to an intensification of the search for ways out of the current situation, which was facilitated, in particular, by the decision of the Constitutional Court of Ukraine adopted on May 29, 2002 No. 10-рп/2002 regarding the interpretation of the provisions of the third part of Article 49 of the Constitution of Ukraine (provision of free medical care by state and community healthcare institutions). This decision determined that medical services may go beyond medical care and in this case be provided on a paid basis [4]. At the same time, the list of paid medical services should be established by the laws of Ukraine. This decision was not implemented for a long time, since the above-mentioned government list was not canceled and continued to be applied, and when developing concepts for the development of the health care sector, only norms were proposed for co-payment of services by citizens, which did not fully correspond to the content of the decision of the Constitutional Court.

At the same time, on June 21, 2001, the first Budget Code of Ukraine was adopted, which was valid until January 1, 2011. For the first time, it regulated the state financial system and clearly outlined the rules of budget financing, in particular, the sphere of health care [5].

In December 2000, the Decree of the President of Ukraine approved the Concept of Health Care Development of the Population of Ukraine [6]. It provided, in particular, that "the reform of the economic foundations of the health care system will be aimed at creating transparent financial and economic mechanisms for targeted accumulation and targeted use of funds necessary for the full implementation of citizens' constitutional rights to health care, medical assistance and medical insurance . In order to achieve the appropriate level of health of the population, the state will maintain control over the mechanisms for ensuring the volume and quality of medical care, which will gradually increase due to budgetary funding and attracting additional sources of funding" [6]. The concept also defined that "the state-communal model provides for the creation of two sectors of medical care: the sector of publicly available medical care and the sector of additional opportunities in the field of health care. The sector of publicly available medical care will ensure the protection, strengthening and restoration of the population's health using technologies determined by the basic standard of quality of publicly available medical care, supply of the most necessary medicines and medical products to the population, stay in a hospital. Within the sector, universal medical care sufficient to ensure a basic standard of quality will be provided to all categories of the population for all types of diseases, injuries, during pregnancy and childbirth. The sector of additional opportunities will contribute to meeting the needs of citizens in health care, which involves the use of technologies, the level of which exceeds the generally available standards. At the same time, the provision of medical care within the framework of the sector of additional opportunities will not replace the care that is provided" [6].

In addition, the Concept provided for the division of medical care into primary, secondary and tertiary levels. The document stated that "Medical care at the primary level will include preventive measures, outpatient treatment and inpatient care in the main specialties, at the secondary level - specialized, technologically more complex, at the tertiary level - high-tech care and treatment of the most complex and rare diseases. At the same time, it is assumed that the main part of medical services to the population should be provided at the primary level. The financial and economic mechanism of providing medical care at the primary, secondary and tertiary levels can differ significantly. The demarcation of different levels

will be determined by the medical and technological standards of providing medical care. State control over compliance with the specified standards will be carried out at each level" [6].

In the organizational-structural part of this Concept regarding the services of providing specialized medical care, the following goals were defined:

"arrangement of the network of centers of specialized medical care;

provision based on multi-channel financing of the operation of a network of medical and preventive facilities for providing free medical and social assistance to chronic patients who need long-term treatment and care, the disabled, the elderly, etc.;

rationalization of the use of the bed fund based on the improvement of the resource-normative base of treatment and prevention facilities, the introduction of modern resource-saving medical technologies, standards of diagnosis and treatment, differentiated depending on the level of the treatment-diagnostic process and the stage of providing medical care;

improving the quality of inpatient and specialized medical care in medical and preventive facilities of various forms of ownership.

Medical care, which replaces hospitalization, will develop by expanding the network of cost-effective organizational forms of medical care: day hospitals, inpatients at home, ambulatory surgery centers, etc.; expansion of the range of such medical services and improvement of the resource-normative base in the context of the reorganization of the provision of primary medical care and its transition to the principles of general medical practice (family medicine); wider application of the specified forms for the prevention and diagnosis of diseases, treatment and rehabilitation of patients".

In order to implement the above-mentioned Decree, the Measures for the Implementation of the Concept of the Development of Health Care of the Population of Ukraine [7] were approved, where the relevant central bodies of the executive power were instructed "during the formation of budgets of all levels to provide for a gradual increase in budgetary allocations for health care based on the available budgetary resources and ensure their effective use. To prepare proposals for amendments to legislative acts and to develop new laws on the creation of legal, economic and management mechanisms for the implementation of the constitutional rights of citizens to health care, social protection of patients and medical workers, ensuring sanitary and epidemic well-being and meeting the population's needs for necessary medicines and medical products".

In July 2002, the Government Program for providing citizens with state-guaranteed free medical care was approved [8]. This document established a list of types of free medical care, defined the indicators on the basis of which the amounts of such medical care were to be calculated. In particular, the indicator of the volume of outpatient polyclinic care is determined according to the number of visits per 1,000 patients, and the indicator of the volume of inpatient care is determined by the number of bed days and the number of hospitalizations per 1,000 patients, as well as the average length of stay of one patient in a hospital. According to this Program, the scope of submission and calculations of indicators of the cost of medical care must be performed in accordance with methodological recommendations [8].

In December 2005, the Decree of the President of Ukraine "On urgent measures to reform the public health care system" was issued [9].

The basis of the reforms in that period, in addition to the definition of the guaranteed part of the aid financed exclusively from budget funds, was also the strengthening of the role of the family doctor, the change in the proportions of the distribution of financial funds in favor of the primary level, and the strengthening of the organizational, legal and financial independence of health care institutions . Since the second half of the 2000s, such innovations have also been added, such as the transition of medical institutions to the status of community enterprises, the creation of hospital districts, the system of financing primary care according to the capitation method, financing the services themselves, and not the facilities (beds, heating radiators, etc.). The issue of mandatory health insurance has not lost its relevance. But, despite the large number of conceptual approaches and ideas, unfortunately, none of the concepts was implemented. In some regions, a number of experiments were carried out on the creation of community enterprises, the introduction of procurement of medical services, and other innovations, but there was no systemic reform at the state level.

At the same time, non-state-controlled processes of commercialization of the activities of state and community health care institutions were actively growing in the industry itself. At hospitals, so-called charitable funds and cash registers were massively created, to which almost every patient seeking medical care was forced to pay for services. Complex types of treatment, in particular, surgical interventions, became paid by more than 60-70%. The order of purchase and distribution of medicines did not provide a transparent mechanism for their accounting and control of their intended use. The social and political demand for the settlement of this situation grew.

The next conceptual direction of reforming the health care system was determined and agreed upon by ex-

perts and systematized in the government resolution "Some issues of improving the health care system" adopted on February 17, 2010 No. 208 [10]. The following were determined, in particular:

- Clear distribution of institutions according to the level of assistance and transition of most of them to the status of community enterprises;
- Introduction of contractual relations in the provision of medical services;
- Determination of the guaranteed volume and resolution of the issue of paid services at the legal level;
- Financing of primary care on the basis of standards of costs per person, and secondary care - through the conclusion of contracts between the customer and the provider of medical services based on the principle of payment for the services actually provided, taking into account the needs of the population;
- Development of public-private partnership;
- Implementation of specialization of healthcare facilities, i.e. formation of hospital districts [10].

In June 2010, the Committee on Economic Reforms under the President of Ukraine approved the Program of Economic Reforms for 2010-2014 "Prosperous Society, Competitive Economy, Effective State" [11].

In the "Medical service reform" section of this program, the main goal was defined ("improving the health of the population, ensuring equal and fair access of all members of society to medical services of appropriate quality") and set the following tasks:

– improve the quality of medical services;
– increase the availability of medical services;
– to improve the efficiency of state financing;
– to create incentives for a healthy lifestyle of the population and healthy working conditions [11].

The document also determined that "the implementation of reforms in the budgetary model of financing healthcare of Ukraine will allow to prepare the conditions for the transition to the insurance model (social health insurance)" [11].

The implementation of the medical reform was envisaged in three stages. At the first stage (until the end of 2010), it was planned to integrate funds for the provision of primary health care at the level of districts and cities, for the provision of secondary (specialized) and emergency medical care at the level of the region, for the provision of tertiary (highly specialized, high-tech) care - at the regional and state levels, as well as redistribute funds in favor of financing primary health care and preventive medicine, as well as move to contract financing of community and state health care institutions.

At the second stage (by the end of 2012), it was planned to test the proposed changes in the pilot regions, optimize the territorial network of medical facilities, create hospital districts, and introduce the remuneration of medical personnel, based on the assessment of the volume and quality of the work performed.

At the third stage (by the end of 2014), it was planned to transfer all medical institutions to the system of contractual relations between the customer and the provider of medical services, to introduce a unified methodology for calculating the cost of medical services paid by the state and, ultimately, to ensure preparation for the introduction of mandatory social medical insurance [11].

In order to implement this Program, the National Action Plans for the implementation of the Program of Economic Reforms for 2010-2014 "Prosperous Society, Competitive Economy, Effective State" for 2011, 2012 and 2013 were approved by the Decrees of the President of Ukraine [12, 13, 14]. In accordance to them, a number of normative legal acts were adopted, in particular, changes to the "Basics of Ukrainian legislation on health care", on the basis of a special law, a pilot project was launched to reform the health care system in Vinnytsia, Dnipro, Donetsk regions and the city of Kyiv [15], acts of the Cabinet of Ministers and the Ministry of Health of Ukraine determined the procedure for providing assistance at various levels, established primary health care centers in most regions of Ukraine, developed basic criteria for the selection of health care facilities for the creation of intensive care hospitals, prepared a draft resolution on hospital districts .

This reform process was stopped for an audit of its results in 2014 after the Revolution of Dignity. A separate law introduced a moratorium on the liquidation and reorganization of health care institutions of state and community forms of ownership [16], which became invalid only in January 2015. At the same time, the need to determine the further development vector of the health care system, which was in the process of several years of reform, prompted the development of updated conceptual and strategic documents and their implementation.

In accordance with the order of the Ministry of Health of Ukraine adopted on 24.07.2014 No. 522, the Strategic Advisory Group on Reforming the Health Care System in Ukraine (SAG) was formed [17], which developed the National Strategy for Reforming the Health Care System in Ukraine for the period 2015-2020 [18]. This document did not receive regulatory approval, but on its basis, two conceptual documents of the Cabinet of Ministers of Ukraine were adopted in November 2016: Concept of reform of the financing of the health care system [19] and Concept of development of the public health system [20]. These government decisions were

designed to contribute to increasing the availability of quality medical care by transitioning to health care financing based on mandatory state health insurance for citizens. For this, it is planned to accumulate funds directly in the state budget. The Concept also envisages the introduction of a state-guaranteed package of medical care, the creation of a single national customer of medical services - the National Health Service of Ukraine, which was also entrusted with the functions of quality management of medical services. The providers of medical services were to become autonomized (reorganized into community non-commercial enterprises) health care institutions. The second Concept defined the principles of building a holistic public health system, which was responsible for the implementation of ten operational functions of public health, from participation in the formation of policies in health care to the promotion of a healthy lifestyle and communications in health care.

In September 2016, by order of the Ministry of Health of Ukraine, restrictions on the staffing structure of institutions were removed [21]. Another prerequisite for the implementation of the concept of health care system financing reform was the Law of Ukraine "On Amendments to Certain Legislative Acts of Ukraine Regarding the Improvement of Legislation on the Activities of Health Care Institutions", adopted in April 2017, which was supposed to solve two main tasks: change in the organizational and legal status of state and community health care institutions and their financing. The law also defined a number of incentives, including financial ones, for the reorganization of health care institutions - state and community institutions into treasury enterprises and community non-commercial enterprises, and a simplified procedure for the reorganization of health care institutions was established. Also, the definitions of "medical service" and "medical care" were introduced for the first time, which now means "the activities of health care institutions and natural persons - entrepreneurs, who are registered and received the appropriate license in accordance with the procedure established by law, in the field of health care, which is not necessarily limited to medical care, but is directly related to its provision" [22].

The Law of Ukraine "On State Financial Guarantees of Medical Services of the Population" adopted in June 2017 became the main legislative basis for the implementation of the said Concept [23].

The purpose of the Law was "to create an effective mechanism for financing the provision of medical services and medicines at the expense of budget funds to ensure the preservation and restoration of the health of the population of Ukraine. It is also determined that the amount of medical services and medicines, the cost of which is covered by state guarantees and the degree of coverage, is fixed at the level of the law in the state-guaranteed package, within which the state will guarantee full payment from the state budget for the necessary medical services and medicines in an emergency, at the palliative and primary level, and partially at the secondary (specialized) and tertiary (highly specialized) levels, provided by health care providers. At the same time, the medical care component at all levels will always be fully paid for by the state.

To ensure the ability to forecast the amount of health care costs, the Cabinet of Ministers of Ukraine annually approves a specific list of services and medicines that are included in the guaranteed package" [23].

The law also stipulates that medical services and medicines can be obtained at the expense of the state budget in health care institutions of any form of ownership and from individual entrepreneurs who have concluded contracts for medical care of the population with the National Health Service of Ukraine. It was determined that the financing of the provided medical services and medicines is carried out according to the unified approved tariffs.

It is expected that the result of the implementation of the new health care financing model will be the principle of "money follows the patient", which means directing budgetary funds to pay for certain medical services and medicines provided directly to patients, and not to the priority maintenance of the infrastructure of medical facilities.

The new financing mechanism began to be implemented gradually, at the primary level, starting in 2018. Its implementation at the secondary and tertiary levels, which was initially planned to be carried out by 2020, began to be implemented only in March 2021.

Thus, the reform of the national health care system, aimed at ensuring the constitutional rights of citizens to health care, led to a number of organizational changes in the system of providing assistance, its financing, management, resource management, including human resources. The emergence of new structures, new forms of medical care, the redistribution of functions between them, actualized the problems of optimizing various types of medical care, substantiating the principles of its functioning in new financial, economic and organizational-management conditions.

The modern vector of development of the health care system in Ukraine was received by the Verkhovna Rada of Ukraine on July 1, 2022, when the Verkhovna Rada of Ukraine adopted the Law of Ukraine "On Amendments to Certain Legislative Acts of Ukraine on Improving the Provision of Medical Care" [24], which updated the basic law - Fundamentals of Ukrainian legislation on

health care health, and the Laws of Ukraine "On State Financial Guarantees of Medical Services of the Population", "On Rehabilitation in the Field of Health Care", "On Remuneration", "On Protection of Personal Data", Civil Code of Ukraine.

The adopted Law provides a new definition of the term "hospital district", which now means the territory within which the provision of high-quality, comprehensive, continuous and patient-oriented medical and rehabilitation care is ensured through the organization of a capable network of health care institutions [24].

The creation of hospital districts in the course of reforming specialized medical care was also foreseen in its previous models.

For the first time at the legislative level, the concept of a hospital district was defined in the Law of Ukraine "On the procedure for reforming the health care system in Vinnytsia, Dnipro, Donetsk regions and the city of Kyiv" as "an organizational and functional association of health care institutions of the pilot region, which satisfy the need of the population of one or more administrative-territorial units of such a region for secondary (specialized) medical care" [15]. In accordance with this law, in October 2012, the Procedure for the establishment of hospital districts in Vinnytsia, Dnipro, Donetsk regions and the city of Kyiv was approved. It provided for the creation of hospital districts at the rate of one such district "for one or more administrative-territorial units of the pilot region with a population of 150 to 350 thousand people, taking into account the density of settlement and the sex-age structure of the population, the state of transport communications, their geographical location, prospects of socio-economic development, as well as the positions of territorial communities" [25]. Within each hospital district, on the basis of existing health care facilities, the following types of facilities were to be created, such as a multidisciplinary intensive care hospital of the first or second level, a multidisciplinary children's intensive care hospital, a planned treatment hospital, a restorative (rehabilitation) treatment hospital, a medical consultation center and diagnostics (consultative and diagnostic center), specialized medical center, hospice.

In the Procedure for the establishment of hospital districts, adopted by Resolution No. 932 of the Cabinet of Ministers of Ukraine on November 30, 2016, it was determined that a hospital district is a functional association of health care facilities located in the relevant territory, which ensures the provision of secondary (specialized) medical assistance to the population of such territory. On the territory of each oblast there could be from one to several hospital districts. This procedure provided for the creation of hospital districts around multidisciplinary intensive care hospitals of the first or second level. The boundaries of the hospital district were determined according to the principle: "The service area of the hospital district is determined by the timeliness of arrival at multidisciplinary intensive care hospitals, which should not exceed 60 minutes, and should be equivalent to the radius of the service area of 60 kilometers, provided there are paved roads" [26]. The Order of the Ministry of Health of Ukraine adopted on February 20, 2017 No. 165 approved the Model Regulation on the Hospital District, which provided for the creation of a hospital council in each district "to identify problematic issues, coordinate actions, develop proposals and recommendations for the implementation of state policy in the field of health care at the level of the hospital district as well as regarding the organization and functioning of medical care in the hospital district", the planning and financing of the development of the district was determined [27]. However, this order was not registered with the Ministry of Justice of Ukraine, which limited its implementation.

In December 2019, the Law of Ukraine "On Amendments to Certain Legislative Acts of Ukraine Regarding Emergency Measures in the Field of Health Care" determined that "a hospital district is an aggregate of health care facilities and natural persons - entrepreneurs, registered in the established by the law of order and received a license for the right to carry out economic activities in the field of medical practice, providing medical services to the population of the relevant territory" [28]. The new Procedure for the creation of hospital districts provided for the creation of only one hospital district within the Autonomous Republic of Crimea, region, cities of Kyiv and Sevastopol and determined that "within the hospital district, a capable network of the hospital district is being formed, which consists of basic health care facilities and other health care facilities, including multidisciplinary children's hospitals, perinatal centers, specialized centers and health care facilities of health, which provide medical assistance for oncological, infectious diseases, tuberculosis and other socially significant diseases" [29].

The implementation of the changes outlined in the Law of Ukraine "On Amendments to Certain Legislative Acts of Ukraine Regarding the Improvement of Medical Assistance" adopted on July 1, 2022, provides for the development of health care institutions through the prism of the cluster model. The hospital district is defined as the basis for ensuring the territorial accessibility of quality medical and rehabilitation care to the population, and the hospital district, in turn, is divided into hospital clusters, within which comprehensive access of the population to inpatient medical care is

organized. The boundaries of hospital districts and hospital clusters, the procedure for their definition and functioning, as well as the procedure for determining cluster, super-cluster and other types of health care institutions that are part of the capable network of health care institutions of the hospital district, are determined by the Cabinet of Ministers of Ukraine based on the needs of the population in medical care and providing comprehensive medical and rehabilitation care.

The legislator singled out such types of health care institutions as a general health care institution - a multidisciplinary hospital that provides medical and rehabilitation assistance to the population of a territorial community or several communities and provides basic areas of inpatient medical care in accordance with the list determined by the Cabinet of Ministers of Ukraine, stabilization of the patient's condition and his routing to cluster and supra-cluster health care institutions; cluster – a multidisciplinary hospital facility capable of meeting the population's need for medical and rehabilitation assistance in the area of the hospital cluster for the most common diseases and conditions in the areas of inpatient medical care in accordance with the list determined by the Cabinet of Ministers of Ukraine; supercluster – a multidisciplinary hospital facility that has available resources and technologies aimed at providing medical care in the most complex and/or rare cases of diseases to the population of the entire hospital district in the areas of inpatient medical care in accordance with the list determined by the Cabinet of Ministers of Ukraine.

This approach made it possible to combine secondary (specialized) and tertiary (highly specialized) medical care [30] into specialized medical care. Thus, the Law of Ukraine "On Amendments to Certain Legislative Acts of Ukraine Regarding the Improvement of the Provision of Medical Care" Article 35 2 of the Fundamentals of the Health Care Legislation of Ukraine is set out in a new version, which regulates the general principles of providing specialized medical care and gives it the following definition: Specialized medical care - medical care provided in outpatient or inpatient settings by doctors of the appropriate specialization (except general practitioners - family doctors) in a planned manner or in emergency cases and includes consultation, diagnosis, treatment and prevention of diseases, injuries, poisoning, pathological and physiological (during pregnancy and childbirth) conditions, including with the use of high-tech equipment and/or highly specialized medical procedures of high complexity; referral of a patient in accordance with medical indications for the provision of specialized medical care from another specialization" [24].

Such legislative changes provide for the following division of medical care by type: emergency, primary, specialized, palliative care. It is also determined where medical assistance can be provided, in particular by the location, residence (stay) of the patient, in outpatient settings, in day hospital settings, in inpatient settings [24].

These transformative processes will affect the procedure for providing medical care, patient routes, and coordination between types of medical care and relevant health care facilities. Each type of medical care has its own peculiarities of its provision, in most of the legal acts that regulate a certain type of medical care, there are references to norms that do not correspond with each other. A unified approach and the same understanding of the health care system, the principles of its construction, the procedure for providing medical care in the relationship: "health care institution - doctor - patient" is a prerequisite for the development and adoption of a single unified regulatory act. For comparison: in Ukraine, in 2010, tax legal relations were normalized for this purpose and in this way, and the Tax Code of Ukraine [30] was adopted, which unified and codified tax regulatory acts [32].

Thus, the resolution of the Verkhovna Rada of Ukraine adopted on July 17, 2020 No. 3650 "On the formation and liquidation of districts" formed a sub-regional level of the administrative-territorial system of Ukraine, according to which 136 enlarged districts were formed, against 490 [33]

In our opinion, the boundaries of the hospital district should coincide with the boundaries of the oblast as an administrative-territorial unit, and the hospital cluster should be determined by the territory of the district of the corresponding hospital district, for example, the Kyiv region consists of seven districts, accordingly, the network of the hospital district of the Kyiv region may have the following hospital cluster model (Fig. 1).

In the cluster model of the Law of Ukraine "On Amendments to Certain Legislative Acts of Ukraine Regarding the Improvement of Medical Care" [24], primary medical care was left out of consideration, and therefore we offer the following model of primary medical care.

Thus, in accordance to the Procedure for the establishment of hospital districts, which was approved by the Cabinet of Ministers of Ukraine Resolution No. 1074 adopted on 27.11.2019 "Some issues of the establishment of hospital districts", the establishment of hospital districts is carried out on the basis of a combination of the following principles, in particular:

- safety and quality of medical care based on evidence-based medicine;
- timeliness of access to medical care;
- economic efficiency, which consists in ensuring the highest possible quality of medical care under the condition of rational and economical use of resources. [29]

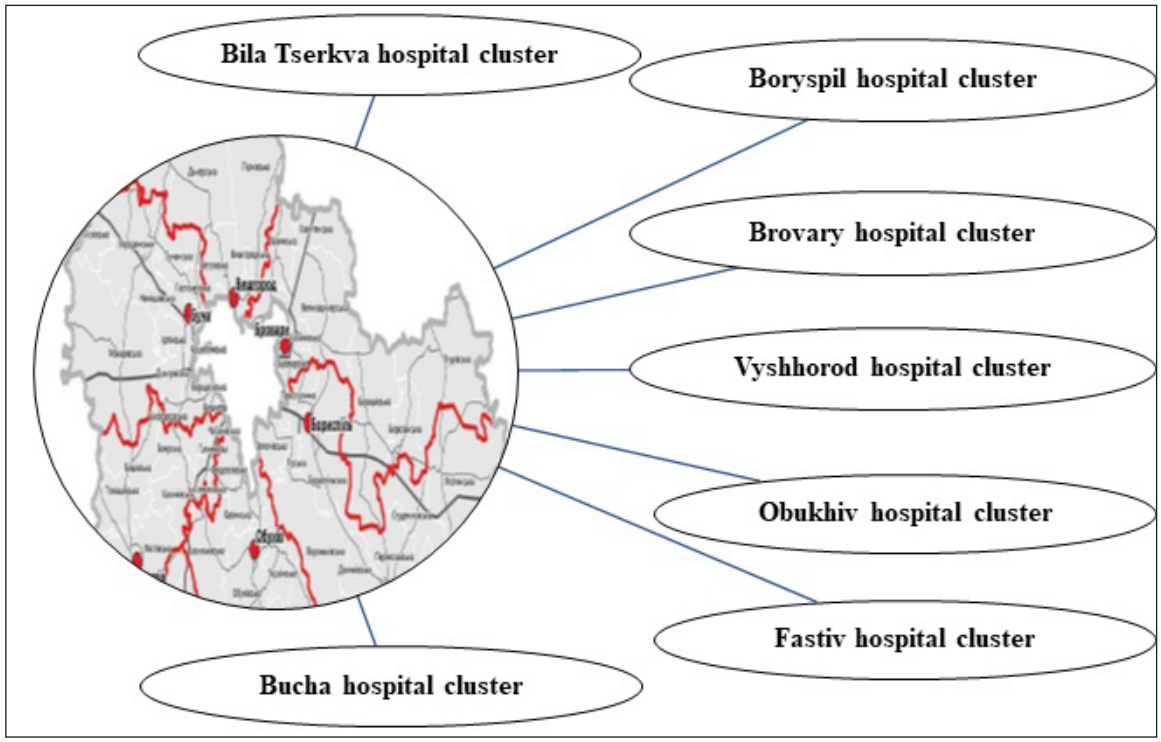

Fig. 1. A cluster model at the level of a hospital district

Table I. Number of communities with distribution by regions

Number of communities/ Region	City community	Urban villages community	Village community	Altogether
Odesa region	19	25	47	**91**
Dnipro region	20	25	41	**86**
Rivne region	11	13	40	**64**
Cherkasy region	16	10	40	**66**
Zaporizhzhia region	14	17	36	**67**
Uzhhorod region	11	18	35	**64**
Chernivtsi region	11	7	34	**52**
Zhytomyr region	12	22	32	**66**
Mykolaiv region	9	14	29	**52**
Lutsk region	11	18	25	**54**
Khmelnytskyi region	13	22	25	**60**
Ivano-Frankivsk region	15	23	24	**62**
Poltava region	16	20	24	**60**
Vinnytsia region	18	22	23	**63**
Kherson region	9	17	23	**49**
Kyiv region	24	23	22	**69**
Kropyvnytskyi region	12	16	21	**49**
Sumy region	15	15	21	**51**
Ternopil region	18	16	21	**55**
Lviv region	39	16	18	**73**
Chernihiv region	16	24	17	**57**
Kharkiv region	17	26	13	**56**
Donetsk region	43	14	9	**66**
Luhansk region	20	12	5	**37**
IN TOTAL	**409**	**435**	**625**	**1469**

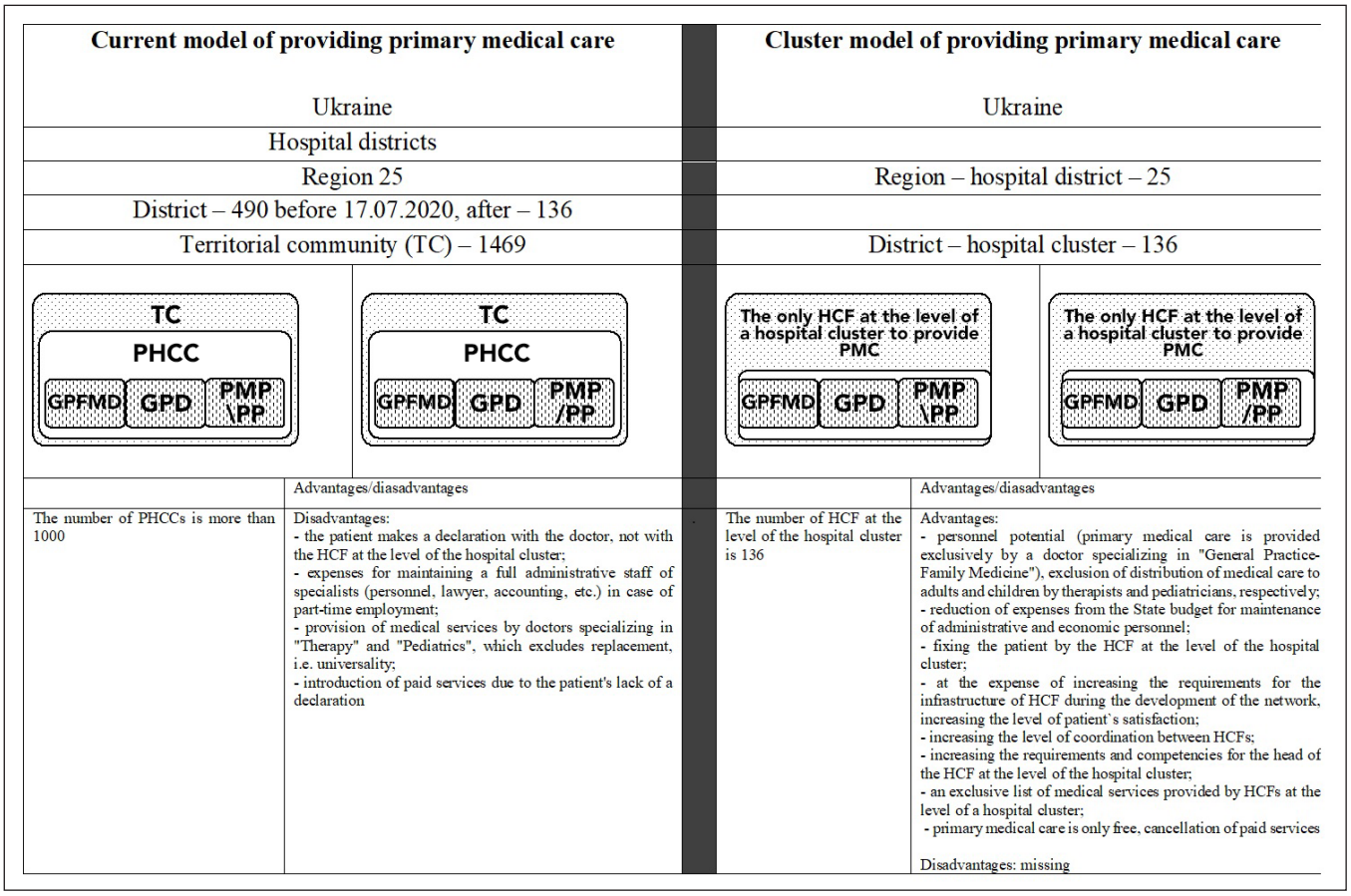

Fig. 2. Comparison of the current model of providing primary medical care and the proposed cluster model of providing primary medical care

The development of a cluster model of providing primary medical care can be cost-effective under the condition of creating a single health care facility at the level of a hospital cluster in the form of a state non-profit enterprise.

Today in Ukraine there are 1,469 united territorial communities [34] (table I), 136 districts [33], so more than one thousand primary health care centers (further written as PHCCs) have been created against [35], a possible 136.

A comparative analysis indicates the economic validity and possibility of such changes - the creation of a single health care facility at the level of a hospital cluster to provide primary medical care. For example, the Bucha district of the Kyiv region [36] consists of twelve territorial communities, and 11 primary health care centers (PHCCs), the latter have separate subdivisions under their control in the form of: general practice-family medicine dispensary (GPFMD), group practice dispensary (GPD), paramedic and midwifery points (PMP), paramedic points (PP). The creation of a single health care facility at the level of a hospital cluster, i.e. the consolidation of facilities, will reduce the burden not only on the state budget under the medical guarantee program, but also on the budget of the PHCCs due to the combination of personnel and legal services, will eliminate the duplication of functions of administrative and economic personnel, and will naturally increase the requirements for the head of the health care facility as a manager of the district scale in the field of health care, and not within the community (Fig. 2).

DISCUSSION

The cluster model of providing primary medical care in the form of the creation of a single health care facility at the level of a hospital cluster, implies a change in the approach to the organization and provision of primary medical care. Thus, today the order of the Ministry of Health of Ukraine No. 504 adopted on 19.03.2018 "On approval of the Procedure for providing primary medical care" (hereinafter the order of the Ministry of Health No. 504) [37] establishes that the patient chooses a doctor with whom he makes a declaration, that is, the doctor forms the practice of primary medical care, however, in our opinion, it is expedient to establish that the patient makes the declaration not with the PMC doctor, but with the health care facility (HCF). The advantages are obvious, firstly, the dismissal of a doctor from HCF will in no way affect the availability and timeliness of

medical assistance; secondly, the new doctor will not waste time on concluding a new declaration; thirdly, the patient can receive a medical service within a single health care facility at the level of a hospital cluster; fourthly, the institution will not lose funds due to staff turnover.

In addition, in our opinion, the state should continue the vector of development of family medicine and limit the transitional stage (up to 5 years), when primary medical care can be provided by doctors of other specialties than the specialty "General Practice-Family Medicine". Thus, Clause 4 of Section II (List of PMC services and organization of their provision) of the Procedure for providing primary medical care, approved by order of the Ministry of Health No. 504, stipulates that the optimal volume of PMD practice is: 1,800 people per general practitioner - family doctor; 2,000 people per therapist; 900 people for one pediatrician" [37]. Also, the order of the Ministry of Health No. 504 stipulates that the scope of practice may differ from the optimal one depending on socio-demographic, infrastructural and other features of the territory within which the persons belonging to the relevant practice live" [37]. The provision of primary medical care by doctors of various specialties requires additional costs, both from the HCF budget (for example, arranging the workplace, medical equipment), and from the state budget (training a larger number of specialists of various specialties at higher educational institutions), and most importantly, there is a risk of not providing medical assistance to the patient due to the absence of a doctor of the relevant specialty (illness, vacation and other reasons).

An equally important element of this model is the requirement for the material and technical base of each structural unit, as a provider of primary medical care. Yes, we believe that the GPFMD and/or the GPD, depending on the category of the settlement: city - settlement - village, should have in their staff at least 12 - 8 - 2 doctors exclusively in the specialty "General practice-family medicine". That is, for full and timely provision of primary medical care, structural units must be formed according to the principles of universality and interchangeability (personnel potential); accessibility (in the sense of location in the settlement) is also a priority, but of the second level. Taking into account such changes, the state standards/requirements regarding the premises in which primary medical care will be provided are also subject to revision.

The key figure of this model is the patient, because we believe that primary medical care should consist of an exclusive list of medical services, and be completely free of charge for the patient, and the introduction of such paid services of primary health care centers by territorial communities does not comply with the principle of accessibility.

At the same time, such a concept of building a cluster model of primary medical care will contribute to the introduction of health insurance. After all, it will partly be its adaptation and unification of standards and indicators of the quality of medical care in a single health care institution at the level of a hospital cluster for the provision of primary medical care, which in the future will ensure the full performance of the functions of insurance medicine at the state level and the transition to the model insurance medicine.

CONCLUSIONS

The implementation of a cluster model of providing primary medical care in the form of the creation of a single health care facility at the level of a hospital cluster has a number of advantages in the short term. For the patient, the availability and timeliness of medical care, at least at the level of the district, not the community; cancellation of paid medical services during the provision of primary medical care regardless of the place of its provision. For the governing body (the state) it leads to cost reduction in the provision of medical services.

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ORIGINAL ARTICLE

ASSESSMENT OF AMBIENT AIR POLLUTION BY PARTICULATE MATTER (PM_{10}, $PM_{2.5}$) AND RISK FOR HUMAN HEALTH CAUSED BY WAR ACTIONS

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ABSTRACT

The aim: To assess pollution level of ambient air (PM_{10}, $PM_{2.5}$), related to war actions on the territory of Kyiv city and the region for prioritization of medical and environmental problems hazard assessments for the human health.

Materials and methods: Physical and chemical methods of analysis (PM_{10}, $PM_{2.5}$ – gas analyzers APDA–371, APDA-372 HORIBA); human health risk assessment; statistical data processing methods (StatSoft STATISTICA 10.0 portable, Microsoft® Excel 2019).

Results: There were found unusually high average daily levels of ambient air pollution: PM_{10} – in March (125.5 μg/m^3) and August (99.3 μg/m^3); $PM_{2.5}$ – in March (108.2 μg/m^3), May (23.3 μg/m^3), June (24.6 μg/m^3) and August (27.1 μg/m^3), which were primarily due to the conduct of active war actions and their consequences (fires, rocket attacks) and intensified in the spring-summer period adverse weather conditions. Possible social losses of the population in the form of additional deaths due to inhalation of PM_{10} and $PM_{2.5}$, the maximum could be in the range of eight cases per 10,000 people to seven cases per 100 people.

Conclusions: Conducted research can be used to assess the determination of damage and losses caused to the ambient air and the human health of Ukraine as a result of military actions; justification of the adaptation measures choice (environmental protection and preventive direction) and reducing health-related costs.

KEY WORDS: air pollution, PM_{10}, $PM_{2.5}$, war actions, risk assessment

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INTRODUCTION

According to the World Health Organization (WHO), air pollution is one of the leading risk factors associated with 4.2 million deaths per year, which is about 7.6 % of additional deaths worldwide [1]. This issue is especially relevant in the conditions of active war actions (missile attacks, shell explosions, destruction and fires in ecosystems, residential and non-residential premises, etc.) associated with the russian federation's aggression on the territory of Ukraine. This leads to emissions of a large number of pollutants into the ambient air, namely (main): particulate matter (PM_{10} and $PM_{2.5}$), nitrogen compounds (NOx), carbon monoxide (CO), sulfur dioxide (SO_2), ozone, non-methane volatile organic compounds (NMVOCs), etc. Pollutants with the most convincing evidence of their negative impact on human health include particulate matter (PM_{10}, $PM_{2.5}$) [2]. Numerous epidemiological studies show a clear connection between ambient air pollution by particulate matter (PM_{10}, $PM_{2.5}$) and the development or exacerbation of respiratory diseases (bronchial asthma, lung cancer, chronic bronchitis, chronic obstructive pulmonary disease, emphysema) and cardiovascular system (ischemic heart disease, arrhythmias, heart failure, sudden cardiac arrest), cerebrovascular diseases, diseases of peripheral arteries, venous thromboembolism, etc. [3,4]. Thus, war actions on the territory of Ukraine create not only an additional contribution to ambient air pollution, but also cause increased human health risk which leads to significant health-related costs.

THE AIM

Assessing of the air pollution level (PM_{10}, $PM_{2.5}$), related to war actions on Kyiv city and the region territory for prioritization medical and ecological problems of assessing the danger to human health.

MATERIALS AND METHODS

In accordance with the assigned tasks, field studies of chemical pollution of ambient air PM_{10}, $PM_{2.5}$ in the surface layer of the atmosphere (SLA) were conducted in mode (round the clock, continuously) at three

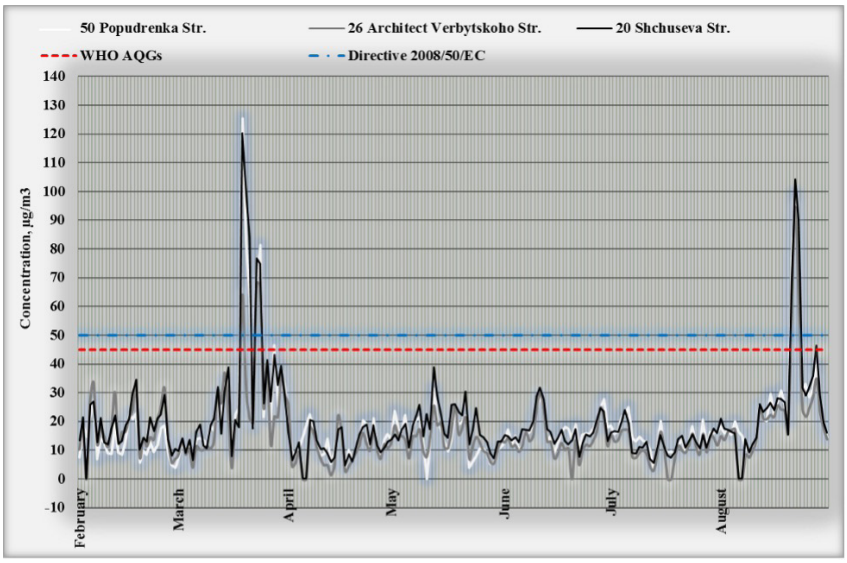

Fig. 1. Average daily mass concentrations of PM_{10} in ambient air according to the data of three AQMS in Kyiv city (February-August 2022), µg/m^3

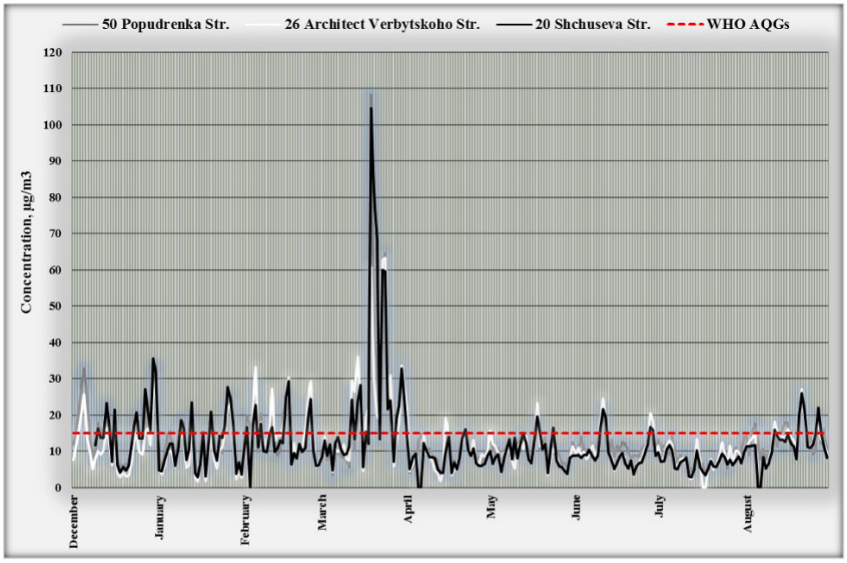

Fig. 2. Average daily mass concentrations of $PM_{2.5}$ in ambient air according to the data of three AQMS in Kyiv city (February-August 2022), µg/m^3

air quality monitoring stations (AQMS), which are located in Kyiv city: 50 Popudrenka Str.; 26 Architect Verbytskoho Str. (left bank of the Dnipro River) and 20 Shchuseva Str. (right bank of the Dnipro). Instrumental measurements of PM_{10} and $PM_{2.5}$ concentration levels were made using gas analyzers APDA-371 and APDA-372 (Air Pollution Dust Analyzer, Horiba), which use the industry-certified principle of the beta-ray attenuation method [5], [6]. Beta Source – ^{14}C (carbon-14), 60 µCi ± 15 µCi (< 2.22 X 106 Beq), Half-Life 5730 years; Beta Detector Type – photomultiplier tube with scintillator. Range – 0-1 000 µg/m^3 (standard), 0-100, 200, 250, 500, 2000, 5000, 10.000µg/m^3(special application); Lowest Detection Limit (2σ) (1 hour) – < 4.8µg/m^3 (less than 4.0 µg/m^3 typical); Lowest Detection Limit (2σ) (24 hour) – < 1.0µg/m^3. Measurement accuracy of the method is ± 5 %. Operation Temperature – 0° to +50°C; ambient temperature – -40° to +55°C (standard); ambient humidity – 0 to 90 % RH, non-condensing.

The assessment methods meet the requirements of Directive 2008/50/EC, Resolutions of the Cabinet of Ministers of Ukraine № 827 date 14.08.2019 and the order of the Ministry of Internal Affairs of Ukraine №300 date 21.04.2021 [7-9]. Measurement of mass concentration levels PM_{10} (15799 measurements of one-hour concentrations) i $PM_{2.5}$ (15801 measurements) performed in the time intervals from February to August 2022 and a compare between 2022 (during active military operations around Kyiv city) and 2021 (pre-war period).

Assessments of human health hazards associated with ambient air pollution PM_{10}, $PM_{2.5}$, due to the lack of hygienic standards approved in Ukraine, conducted on the basis of comparison with the limit values (air quality standards) recommended by Directive 2008/50/EC and WHO recommendations. [1, 7].

Calculations of risk levels (individual risks of mortality – IRM) for the health of the exposed population was carried out using the general procedure of the

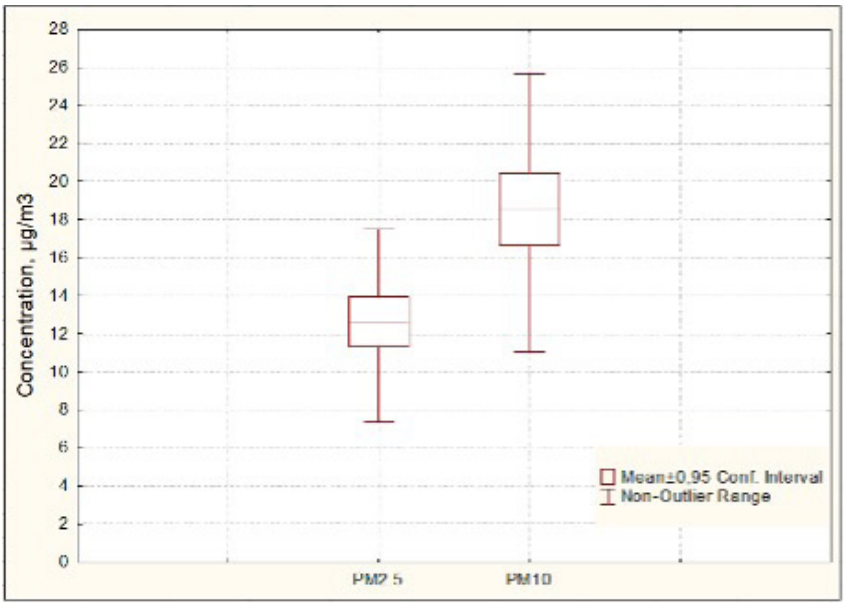

Fig. 3. Diagram of the average mass concentrations of $PM_{2.5}$ and PM_{10} in the ambient air of Kyiv city (February-August 2022), µg/m³

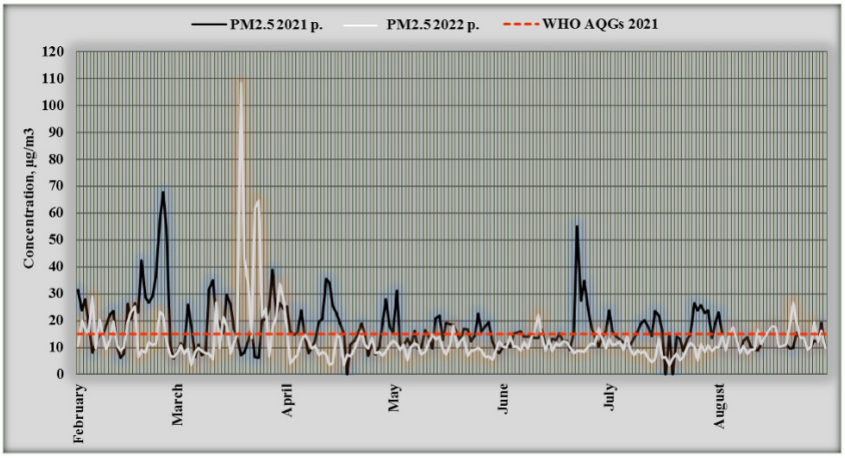

Fig. 4. Comparative analysis of average daily mass concentrations of PM_{10} in ambient air according to the data of AQMS on the 50 Popudrenka Str. in Kyiv city (February - August 2021-2022), µg/m³

human health risk assessment methodology (HHRA), developed and recommended by the US Environmental Protection Agency and WHO.

Statistical data processing – using software tools «Microsoft® Excel 2019» and STATISTICA 10.0 (with the calculation of the minimum (min) and maximum (max) values, average value (M), mean square deviation (σ)).

RESULTS

On the basis of the conducted studies, it was determined that during the war period of observation (from February to August 2022), the average daily concentrations of PM_{10} and $PM_{2.5}$ vary at three AQMS, respectively, in the range from 1.3 µg/m³ to 125.5 µg/m³ and from 1.7 µg/m³ to 108.2 µg/m³ (Fig. 1, 2).

At the same time, an analysis of mass concentrations of particulate matter was carried out, obtained during the entire study period and averaged over Kyiv city (according to three AQMS) showed that the average values (min-max; M±m) were at the same level (3.8 µg/m³ – 103.3 µg/m³; 18.5±0.95 µg/m³) for PM_{10} and (3.2 µg/m³ – 91.2 µg/m³; 12.6±0.66 µg/m³) – $PM_{2.5}$. At the same time, 25 % and 75 % of the results were within the limits: PM_{10} (11.4÷20.5 µg/m³) and $PM_{2.5}$ (7.9÷13.6 µg/m³) (Fig. 3).

The conducted studies demonstrate almost homogeneity of the measured mass concentrations values at the studied monitoring AQMS, although they are located in different areas of the city and at great distances from each other (more than 10 km, left and right banks of the Dnipro River), which indicates the absence of influence of physical and geographical factors in the conditions of microclimate of the city on the geospatial distribution of pollutants in the SLA.

During the comparisons of PM_{10} average daily concentrations of studies received in different months (Table I) it was found that they've exceeded the recommended limit values in March and August 2022 according to WHO recommendations (2.8 and 2.3) times and Directive 2008/50/EC (2.5-2.1) times, respectively.

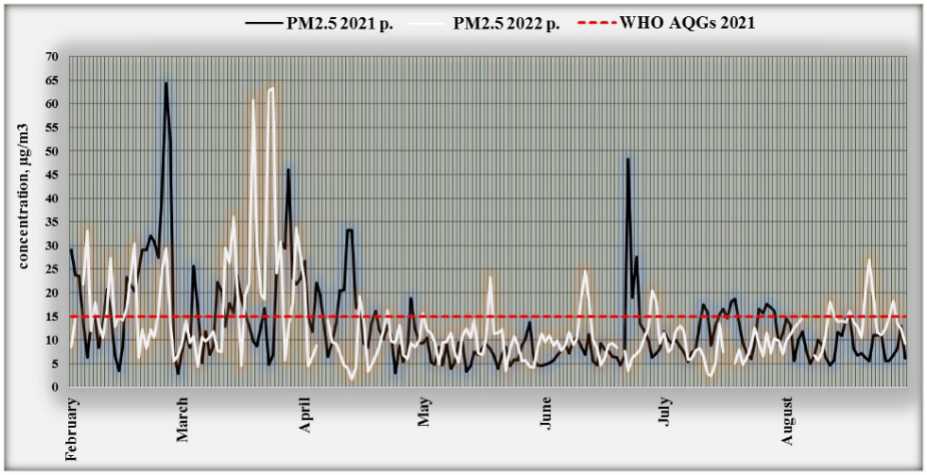

Fig. 5. Comparative analysis of average daily mass concentrations of $PM_{2.5}$ in ambient air according to the data of AQMS on the 26 Architect Verbytskoho Str. in Kyiv city (February - August 2021-2022), µg/m^3

Table I. Average daily mass concentrations of PM10 averaged for a month at three AQMS in Kyiv city (February-August 2022), µg/m3

Averaging period, month	Air quality monitoring stations								
	26 Verbytskogo Str.			26 Architect Verbytskoho Str.			26 Verbytskogo Str.		
	M	min	max	M	min	max	M	min	max
February	13.2	3.9	27.7	17.8	5.8	33.6	18.3	8.2	34.4
March	31.2	4.5	125.5	23.7	3.8	68.2	33.0	6.6	120.2
April	13.0	4.0	22.4	10.5	1.3	25.4	12.4	4.7	20.5
May	14.8	3.9	31.3	13.9	5.5	25.6	18.8	7.1	38.9
June	16.9	8.9	28.9	14.1	4.9	30.1	17.0	7.7	31.9
July	14.1	3.7	25.0	11.4	3.0	17.2	13.1	5.6	24.1
August	28.2	10.0	99.3	25.0	7.5	94.7	29.6	9.3	104.3

Table II. Average daily mass concentrations of $PM_{2.5}$ averaged for a month at three AQMS of Kyiv city (February-August 2022), µg/m^3

Averaging period, month	Air quality monitoring stations								
	26 Verbytskogo Str.			26 Architect Verbytskoho Str.			26 Verbytskogo Str.		
	M	min	max	M	min	max	M	min	max
February	14.5	6.4	28.9	16.1	5.6	33.1	13.7	6.1	29.2
March	21.8	3.5	108.2	21.7	4.4	63.3	25.0	4.7	104.5
April	9.5	3.6	16.4	9.1	1.7	21.9	8.5	4.0	16.2
May	10.3	5.3	18.1	9.6	3.4	23.3	9.6	3.9	19.6
June	11.5	7.9	22.0	10.6	3.4	24.6	9.6	3.6	21.6
July	8.8	3.6	14.3	8.2	2.4	13.4	7.0	2.9	11.6
August	13.6	7.8	26.8	13.5	5.6	27.1	12.9	5.2	25.9

As for average daily mass concentrations $PM_{2.5}$ for different months of the current military period under investigation, they've exceeded the recommended standards, according to WHO recommendations, by (1.1-7.2) times during almost the entire observation period, with the exception of July 2022. (Table II)

Such a wide range of PM mass concentrations indicates significant pollution variability, which can be conditioned a combination of factors such as meteorological elements SLA (wind speed and direction, atmospheric pressure, etc.), stability of the atmosphere, time of year, as well as conducting active war actions (air strikes, missile attacks, fires) on the territory of Kyiv city and the Kyiv region, which were most active until the end of March.

Analyzing the foregoing, studies have been conducted to assess the possible impact of particulate matter on human health. Estimated calculations showed that the levels of individual risk of mortality (IRM) during the studied period can vary for PM_{10} within – $IRM=7.9\times10^{-6}\div7.7\times10^{-4}$. At the same time, in March and August, the risk values were observed at the level ($ICR_{total} \geq 10^{-4}$), which are unacceptable for the population according to WHO recommendations, and possible social losses of the population in the

form of additional deaths, can be up to eight cases per 10,000 people. As for $PM_{2.5}$, the risk levels ranged from – IRM=$1.2\times10^{-3}\div7.3\times10^{-2}$ and in March, June, August could lead from 1 to 7 additional deaths per 100 people.

DISCUSSION

Comparing the pre-war monitoring data with the data obtained during the studied period, it was determined (Fig. 4), that a significant increase PM_{10} pollution in ambient air is atypical for March and most likely related to active war actions during this period, as the impact of industrial emission sources and motor vehicles (reduction of traffic, introduction of curfews) was minimal. Ambient air pollution by PM_{10} in August was similar to last year, but somewhat exacerbated by fires around the city caused by rocket strikes.

According to the previous studies of pre-war period, a high level of PM_{10} was usually observed in April-June and August and was mainly associated with unfavorable metrological conditions (surface temperature inversion → absence of convection (intense mixing of air masses) → formation of fog, smog (aerosols), etc); and strengthening from the side of aero-biological pollution, seasonal mass fires, disposal (burning) of organic waste by local residents and dust storms in the city. The foregoing is also confirmed by the results of monitoring studies conducted over the past five years, but characterized by higher concentrations levels, which were created by the industrial enterprises emissions (maximum technological capacity) and intensive traffic and the number of motor vehicles [10-12].

As for $PM_{2.5}$, high levels were observed throughout the studied period (Fig. 5), except for July. The largest number of days with exceeding the average daily mass $PM_{2.5}$ concentration (recommended by WHO) was determined in March (16 days) and February (11 days).

According to the previous studies, in pre-war period, the high level of $PM_{2.5}$ during February-March was associated with work of heating energy facilities. But taking into account the fact that in 2022 the heating period in Kyiv city was completed earlier (at the end of March), and the maximum daily average values of ambient air pollution $PM_{2.5}$ were at the level (max – 108.2 μg/m³), which in 1.6 – 2.8 times exceeds the indicators of previous years, it is possible to assert that the high level of $PM_{2.5}$ pollution most likely resulted from active war actions. High mass concentrations of $PM_{2.5}$ recorded in May are also uncharacteristic (max – 23.3 μg/m³), June (max – 24.6 μg/m³), August (max – 27.1 μg/m³) of 2022 and were caused by fires due to rocket attacks, that provoked fires in the territories of garbage dumps and burning peatlands and forests in the Chernobyl Exclusion Zone.

The performed calculations on probabilistic estimates showed the need for additional epidemiological studies for the implementation and development of preventive programs (in particular through information campaigns, alerts) with the aim of preventing additional deaths among the population. Because of available global data indicate that acute exposure PM_{10} in 24 hours leads to an increase in daily mortality from 0.5 to 1.6 % for each 10 μg/m³, and when the average daily concentration increases by 10 μg/m³, the frequency of pathological symptoms from the respiratory organs increases on 2.4 %. At the same time, the increase in the level of $PM_{2.5}$ by 10 μg/m³ increases the risk of myocardial infarction on 2.5 % and the number of people hospitalized with cardiovascular diseases on 1.28 % [13].

CONCLUSIONS

Conducted research allowed to evaluate the level of ambient air pollution (PM_{10}, $PM_{2.5}$) and risk for human health, related to war actions as a result of the russian federation's military aggression and the following results were obtained.

1. It was determined that the average daily mass concentrations (according to three AQMS data) in 2022 vary in the range for: PM_{10} (from 1.3 μg/m³ to 125.5 μg/m³) and $PM_{2.5}$ (from 1.7 μg/m³ to 108.2 μg/m³) and the lack of influence on their geospatial distribution was found in SLA physical and geographical factors in the city's microclimate.
2. Exceeding the average daily concentrations, according to the recommended air quality standards, was established for: PM_{10} in March and August 2022, in accordance with WHO recommendations (2.8 and 2.3) times and Directive 2008/50/EC (2,5-2,1) times; $PM_{2.5}$ (1.1-7.2) times during almost the entire observation period (except of July), according to WHO recommendations.
3. Uncharacteristically high average daily levels of ambient air pollution with particulate matter were revealed: PM_{10} – March (125.5 μg/m³) and August (99.3 μg/m³); $PM_{2.5}$ – March (108.2 μg/m³), May (23.3 μg/m³), June (24.6 μg/m³) and August (27.1 μg/m³), which were primarily caused by the conduct of active war actions and their consequences (fires, rocket attacks), intensified in the spring-summer period by unfavorable meteorological conditions.
4. Levels of individual risk of mortality were calculated (IRM), which can vary for PM_{10} within – IRM=$7.9\times10^{-6}\div7.7\times10^{-4}$ and $PM_{2.5}$ – IRM=$1.2\times10^{-3}\div7,3\times10^{-2}$, which according to WHO recommendations ($ICR_{total} \geq 10^{-4}$) are inadmissible for the population. It was estimated that possible social losses of the population in the form of additional

deaths, caused by inhalation exposure to PM_{10} and $PM_{2.5}$, can be as high as eight cases per 10,000 people to seven cases per 100 people.

Analyzing the above, conducted research can be used to assess the determination of damage and losses, caused by ambient air and human health of Ukraine, as a result of the russian federation's armed aggression for reparations in international courts; justification of the choice of adaptation measures (environmental protection and preventive direction) aimed at reducing the human health risk (especially for sensitive population groups: children, the elderly and pregnant women) in wartime conditions.

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ORIGINAL ARTICLE

GLOBAL BURDEN OF DISEASE DUE TO AMBULATORY CARE SENSITIVE CONDITIONS, 1990-2019

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ABSTRACT

The aim: To evaluate the long-term dynamics of health losses caused by ambulatory care sensitive conditions (ACSCs) to justify the priorities of public policy regarding this group of diseases.

Materials and methods: The data used were obtained from the Institute of Health Metrics and Evaluation, the European database "Health for All", for 1990-2019. The study was conducted using bibliosemantic, historical and epidemiological study methods.

Results: Disability-adjusted life years (DALYs) due to ACSC over 30 years in Ukraine averaged 5145.4 years per 100,000 population (95% CI 4731.1 -5559.7), which is approximately 14% of DALYs of all reasons without a clear trend of change - compound annual growth rate (CARG) of 0.14%. These five causes – angina pectoris, chronic obstructive pulmonary diseases (COPD), lower respiratory infections, diabetes, and tuberculosis – account for 90% of the disease burden associated with ACSCs. There was an increasing trend in DALYs (CARG varied for different ACSCs in the range of 0.59-1.88%), except for COPD, where the decrease in CARG reached -3.16%.

Conclusions: This longitudinal study found a small trend toward increased DALYs due to ACSCs. State measures to influence modified risk factors to reduce the burden of losses from ACSCs proved to be ineffective. To significantly reduce DALYs, a more clear and more systematic healthcare policy regarding ACSCs is needed, which includes a set of primary prevention measures, and organizational and economic strengthening of the primary health care.

KEY WORDS: disability-adjusted life years, public policy, primary health care

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INTRODUCTION

The concept of Ambulatory care sensitive conditions (ACSCs) provides for the possibility of hospitalization prevention of patients with a certain group of diseases through a timely and effective provision of outpatient, and first of all, primary health care (PHC) [1]. Hospitalization occurs when a course of these diseases is exacerbated due to the ineffectiveness of outpatient treatment. This leads to worse outcomes (a disability or death) and financial losses, especially in countries of the world with the lowest level of healthcare expenses. In Ukraine, the group of ACSCs for the adult population include 16 chronic, acute, and vaccine-managed diseases with a total volume of preventable hospitalization of about 50% [2]. At the same time in European countries, for the most significant ACSCs, this indicator can reach 80% with some variation [1].

Generalized information on the quantification of health losses due to mortality and disability is provided by the Global Burden of Disease (GBD), which combines years of life lost due that premature mortality and years of life lost due to that time lived in states of less than full health - Disability-adjusted life years (DALYs) [3]. Data on GBD are used to evaluate the effectiveness and efficiency of healthcare initiatives [4]. The study of health loss due to diseases, injuries, and risk factors is coordinated by the Institute for Health Metrics and Evaluation (IHME) which is an independent global center for health research at the University of Washington in Seattle (USA). However, a separate study of the burden of disease caused by ACSCs has not been conducted in Ukraine.

THE AIM

To assess the long-term dynamics of health losses caused by ACSCs to substantiate the priorities of public policy regarding this group of diseases.

MATERIALS AND METHODS

The database IHME was used to study DALYs associated with ACSCs [5] which covers information on premature death and disability from diseases and injuries in 195

countries throughout the 1990 to 2019 period, the information on age-standardized DALYs per 100,000 population of relevant or closely related ACSCs in Ukraine was selected. For a detailed description of the situation, the profile of Ukraine regarding GBD was also analyzed. Additional research information was obtained using materials from WHO Europe "HFA-DB" database [6].

Bibliosemantic, historical and epidemiological methods were used in the study. Statistical processing of the results was carried out using the software program STATISTICA 6.1 (StatSoftInc., serial number AGAR909E-415822FA) and Excel-2010 using methods of parametric and non-parametric statistics, analysis of dynamics series; arithmetic means (M), 95% confidence interval (CI), Spearman correlation coefficients (r_s) were calculated. The critical value of the level of statistical significance was accepted at the level of $p<0.05$ (5%).

Compliance with the principles of bioethics and medical deontology was confirmed in the conclusion of the biomedical ethics commission of the Dnipro State Medical University (protocol No. 6 dated 15.02.2023).

RESULTS

Age-standardized DALYs rates in patients with ACSCs for the period 1990-2019 in Ukraine ranged from 4,578.4 to 5,826.3 years per 100,000 population; the average level over 30 years of follow-up was 5145.4 years per 100,000 population (95% CI 4731.1-5559.7) (Fig. 1).

In general, the dynamics of DALYs due to ACSCs did not reveal a clear tendency to change - the compound annual growth rate (CAGR) was 0.14%. Significant changes in the indicator ($p<0.01$) with a CAGR of 5.28% took place in the period 1990-1995, and subsequently, multidirectional fluctuations without significant deviations were observed. The forecast age-standardized DALYs rates calculated by the method of exponential smoothing shows that in the absence of intensive interventions, DALYs rates due to ACSCs during the next 10 years will virtually not change and will amount to 4859.1-4921.1 per 100,000 population in 2024-2029, respectively.

A strong direct relationship between DALYs rates due to ACSCs and DALYs due to all causes was revealed ($r_s=0.89$; $p<=0.01$). During the observation period, the share of losses by ACSCs was quite stable and on average was 13.56% (95% CI 12.97-14.14) of losses from all causes.

In the structure of GBD associated with ACSCs, during the entire observation period (Fig.2), almost half of all DALYs are due to angina pectoris (AP) - 50.7% (95% CI 46.1-55.3). The second and third places are shared due to chronic obstructive pulmonary disease (COPD) and lower respiratory infections (LRI) - 13.7% (95% CI 8.2-19.2) and 11.2% (95% CI 10.2-12.2) respectively. The fourth and fifth places belong to diabetes type II (7.9%; 95% CI 7.4-8.4) and tuberculosis (6.5%; 95% CI 5.1-7.9). Together, these 5 diseases account for 90% of all DALYs due to ACSCs. The contribution of other ACSCs (hypertensive heart disease - HHD, asthma, upper respiratory infections - URI, iron-deficiency anemia - IDA, peptic ulcer disease - PUD, bacterial skin disease - BSD) was insignificant and together amounted to about 10%.

The dynamics of DALYs rates due to individual ACSCs had a multidirectional character (Fig.3, Table I). During the entire period of observation, the highest DALYs were due to AP (2643.0 per 100,000 population; 95% CI 2323.2-2962.7). The maximum CAGR was found in 1990-

Table I. Compound annual growth rate of DALYs are ACSCs-related for the period 1990-2019 (in %)

ACSC	1990-1995	1995-2000	2000-2005	2005-2010	2010-2015	2015-2019	1990-2019
AP	6.77	0.60	2.03	-3.46	0.89	-1.21	0.93
HD	3.02	-0.46	1.25	-1.37	2.45	-0.86	0.66
COPD	2.49	-4.91	-5.90	-8.14	-2.19	0.10	-3.16
LRI	5.83	0.73	-1.11	-5.97	7,11	-1.97	0.67
ULI	0	0.02	0	-0.22	0.40	-0.32	-0.02
Asthma	0.53	-3.63	-4.14	-3.26	-1.09	1.94	-1.63
Tuberculosis	12,12	5.90	3.55	-8.75	2.49	-2.74	1.88
Diabetes	4.99	-0.66	-0.14	-1.28	0.25	0.48	0.59
IDA	1.90	-2.02	-2.23	-3.96	-0.47	-0.37	-1.21
PUD	6.23	-3.90	-0.30	-2.96	6.49	-2.23	0.47
BSD	1.48	-0.87	1.30	1.22	9.51	-1.02	1.88

Note. See markings Fig. 2.

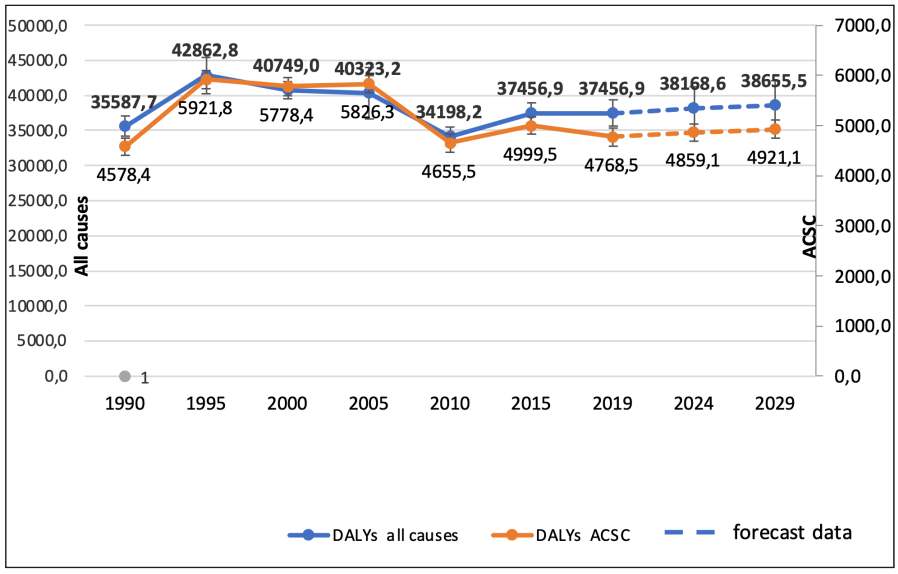

Fig. 1. The dynamics of age-standardized DALYs in Ukraine due to all causes and due to ACSCs (1990-2019 per 100,000 population) with a forecast of their scale for a 10-year period (until 2029).
Source: Calculated according to [5].

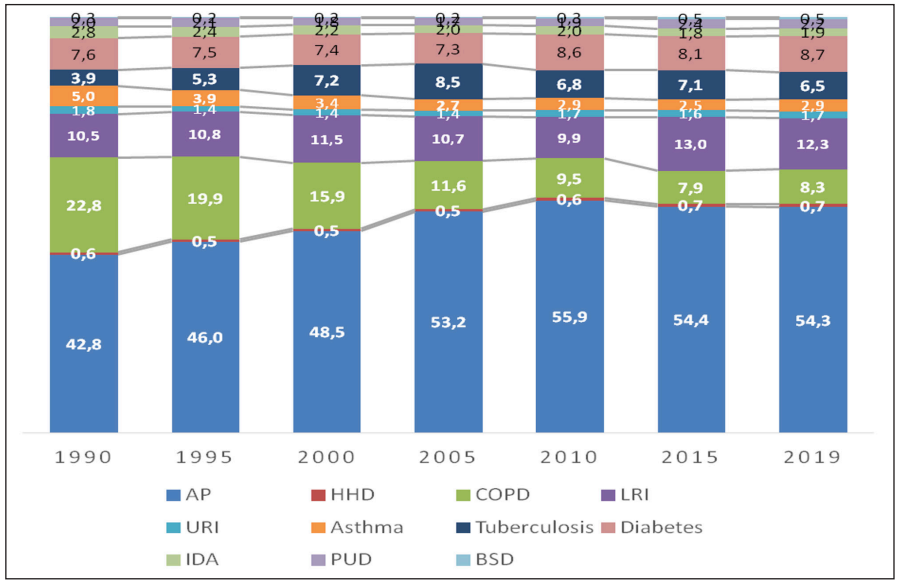

Fig. 2. The structure of the burden of diseases caused by various ACSCs in Ukraine during 1990-2019 (in %)
Note. HHD - hypertensive heart disease, AP - angina pectoris; COPD – Chronic obstructive pulmonary disease; IDA - Iron deficiency anemia; LRI - Lover respiratory infection; URI - Upper respiratory infection; BSD - Bacterial skin disease; PUD - Peptic ulcer disease

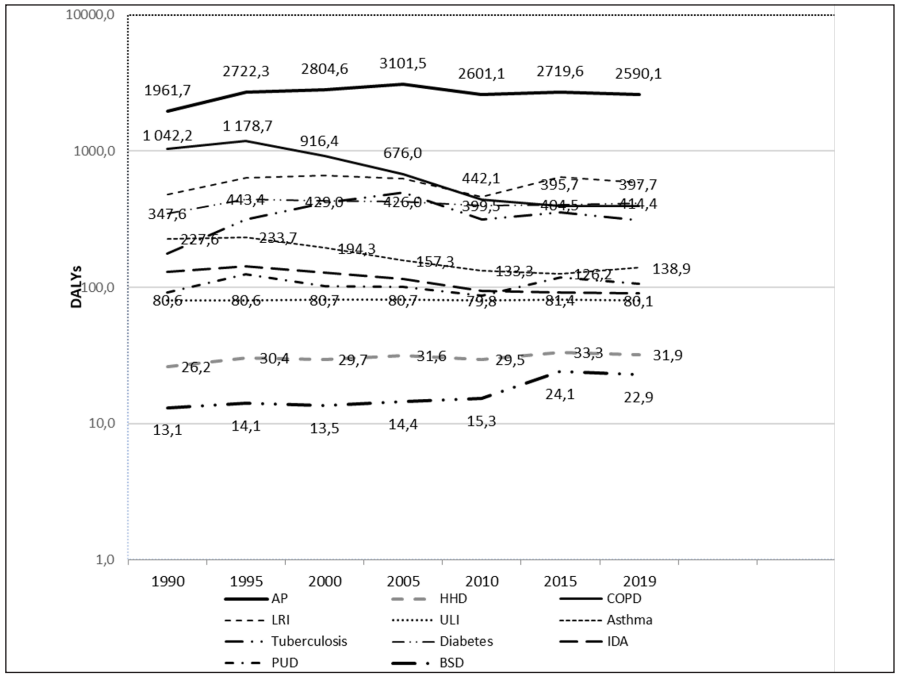

Fig. 3. Dynamics of DALYs due to various ACSCs in Ukraine for 1990-2019 (logarithmic graph per 100,000 population)
Note: see markings Fig. 2.

1995 (6.77%), and the increase in the level of losses in patients with AP albeit at a lower rate continued until 2005 with multidirectional fluctuations in subsequent periods and a total CAGR of 0.93%.

A significantly lower DALYs rates were COPD-related (721.2; 95% CI 419.0 - 1023.5), LRI (586.3; 95% CI 509.9-662.7), diabetes mellitus type II (409.2; 95% CI 380.5-437.9) and tuberculosis (341.1; 95% CI 248.6 - 433.5) with different change trends. In patients with COPD after the year 1995 DALYs rates declined with an overall negative CAGR of -3.16% for 1990- 2019. DALYs rates attributable to LRI had a slight overall upward trend (CAGR 0.67%) with sharp increases in 1990-1995 and 2010-2015 (CAGR 5.83% and 7.11%, respectively) and a sharp drop in 2005-2010 (-5.97%), which could be due to the consequences of the influenza epidemic situation in Ukraine at the time. After rising in 1990-1995 with a CAGR of 4.99%, the DALYs due to diabetes showed no clear dynamics; overall CAGR was 0.59%. The highest CAGR of age-standardized DALYs due to tuberculosis was registered in 1990-1995 (12.12%), growth at a lower rate continued until 2005, after which a long-term trend towards a decrease in losses from this disease was observed (CAGR for the period 2005-2019 was -3.11%), although in 2019 the DALYs rates due to tuberculosis were still higher than in 1990. Among other ACSCs with relatively small average DALYs rates due to asthma (173, 0; 95% CI 131.2-214.9) and IDA (112.8; 95% CI 93.1-132.6) show a steady downward trend: CAGR for 1990-2019 -1.63% and -1.21%, respectively; DALYs rates due to HHD and PUD in the presence of ups and downs in different years essentially did not change during the entire observation period and DALYs rates due to BSD (16.8; 95% CI 12.5 – 21.1) increased with a CAGR of 1.88%.

DISCUSSION

For the first time, a longitudinal 30-year study (1990-2019) of the burden of disease caused by ACSCs that are significant for Ukraine was conducted. Two key findings emerged from this study: 1) DALYs due to ACSCs were significant; 2) improving the efficiency of outpatient care for patients with ACSCs could reduce the level of hospitalization for these diseases and also prevent more negative consequences (such as mortality and disability) and ineffective financial losses, which is especially relevant during the crisis periods of the COVID-19 pandemic, the war of the Russian Federation against Ukraine and the post-war period.

The results of the study show that in Ukraine the DALYs share due to ACSCs averaged at around 14%, and the levels of age-standardized DALYs due to ACSCs as well as the GBD from all causes had a very small trend to growth during the observation period (CAGR 0.14% and 0.17% respectively), which is close to the growth rates of DALYs due to all causes in the same period in Eastern Europe – 0.13% [5].

The greatest DALYs rates due to ACSCs fall on AP with a certain tendency towards its growth. A moderate downward trend was shown by DALYs due to COPD and asthma. No clear changes in DALYs of diabetes-related are noted. A turning point in the negative dynamics of tuberculosis-related DALYs was achieved only in the middle of the first decade of the 21st century, but their rates remain significantly higher compared to 1990 [7]. DALYs due to other ACSCs despite the multidirectional trends of changes in individual diseases remained insignificant during the entire observation period.

Positive changes in the scope of DALYs due to ACSCs can be achieved by affecting the risk factors that shape them. In Ukraine, the leading risk factors associated with global DALYs throughout the observation period remained: 1) metabolic factors: high systolic blood pressure (attributable risk in 2019 was 21.1%); high LDL (low-density lipoprotein) cholesterol (14.4%); high body-mass index - (13.4%); high fasting plasma glucose (6.9%) and 2) behavioral factors: dietary risks (17.3%); tobacco (14.7%); alcohol use (9.8%), which corresponds to similar characteristics for the countries of Eastern Europe overall [8] and are risk factors for ACSCs with the highest DALYs. So, for example, the attributive risk of high blood pressure, which is defined in Ukraine as DALYs due to ischemic heart disease (IHD)/ AP, is 57.6%; high LDL cholesterol - 49.7%, tobacco -26.1%, which practically coincides with the data on the impact of these factors on DALYs of IHD worldwide [9] Attributable risk of smoking, which is considered the main risk of mortality worldwide [10], for DALYs due to COPD accounted for 55.0%, asthma - 13.4%, tuberculosis - 36.1% [5].

All of these risk factors are amenable to some correction through lifestyle modification and pharmacotherapy if necessary. It has been proven that the widespread use of antihypertensive medications makes it possible to keep the global average blood pressure at a stable level [10].

In Ukraine, separate measures are aimed at reduction of the impact of modifiable risk factors. Since 2005, the state policy has been actively implemented in the fight against smoking [11], the result of which can be considered a decrease in the age-standardized prevalence of tobacco use from 37.7% in 2000 to 26.2% in 2019 [6], however, this did not have a significant impact on the amount of ACSCs-related DALYs. The high cost of medications for outpatient treatment of the population is an obstacle to effective treatment and further reduction of ACSCs- related DALYs DALYs. The state program "Affordable Medicines" [12], which has been operating

in Ukraine since 2017, aims to increase the accessibility and to a certain extent the continuity of treatment at the level of primary health care. It provides for the cost reimbursement of a specified list of medications prescribed for patients with cardiovascular diseases (primarily antihypertensive drugs and drugs for dyslipoproteinemia, diabetes type II, and asthma. The short period of implementation of the program does not provide an opportunity to assess the effectiveness of its impact on the outcome. However, it has already been established at this stage that without reinforcement by systemic organizational measures, it will be difficult to expect a good result. For example, due to the poor organization of health screening and monitoring of compliance with drugs, 33.6% of people do not know that they have hypertension, and only 14.4% manage and control it effectively [13].

The inadequacy of measures to reduce DALYs due to ACSCs is indirectly evidenced by the materials of a global study of the index of effective coverage of health services [14], which for Ukraine in 2019 was equal to 57% with average annual changes for 1990-2019 of 0.2% (95% CI 0.4-0.6), which is lower compared to both Eastern European countries and global world data (66.5% and 60.3% respectively; average annual rates of change during 1990-2019 were 0.7- 0.9%). Attention is drawn to the catastrophically low (only 2%) coverage index for patients with ischemic heart disease.

OUR STUDY HAS SEVERAL LIMITATIONS, INCLUDING THE FOLLOWING:

1) Data on GBD by ACSCs in Ukraine may have certain deviations from the true values due to differences in the classification used by the IHME and the International Classification of Diseases of the 10th revision. In the study, DALYs due to LRI were estimated as mainly caused by pneumonia, URI - by influenza; AP - as 35.5% of IHD [15].
2) ACSCs in Ukraine are defined for adults, while the work used age-standardized DALYs for the entire population. It should be noted that the shift in the obtained data was insignificant since the highest DALY rates are caused by diseases that the vast majority of adults suffer from - AP, COPD, diabetes, tuberculosis, etc.

CONCLUSIONS

This longitudinal study revealed a slight tendency to increase the DALYs rates due to ACSCs. State measures to influence modifiable risk factors to reduce ACSCs-related DALYs were ineffective. To significantly reduce DALYs, a clearer and more systematic public policy in the field of public healthcare regarding ACSCs is needed, including a set of primary prevention measures, and organizational and economic strengthening of primary health care.

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ORIGINAL ARTICLE

ANALYSIS OF THE BURDEN OF CARDIOVASCULAR DISEASES IN UKRAINE IN 1990-2019

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ABSTRACT

The aim: To analyze the burden of cardiovascular diseases (CVD) and their modified risk factors in Ukraine to substantiate ways of prevention.

Materials and methods: The burden of CVD was estimated by DALYs (Disability-Adjusted Life Years). The statistical method was used to analyze the data obtained from the statistical database of the international epidemiological study «Global Burden of Disease», updated for 2019. The analysis was carried out in the dynamics for 1990-2019 in Ukraine in comparison with European and EU countries.

Results: Age-standardized DALYs per 100,000 population in Ukraine are 2.6 times higher than the average in European countries and 4 times higher than in the EU. Over the 1991-2019 the gap in DALYs increased due to a significant decrease in the burden of CVD in Europe, against the consistently high level in Ukraine. The burden of CVD in Ukraine can be reduced on 54.2% by normalizing blood pressure, on 42.1% by improving diet, on 37.3% by lowering low-density lipoprotein cholesterol, on 28.1% by lowering body mass index, and on 22.9% by quitting smoking.

Conclusions: The Ukrainian strategy of reducing the burden of CVD should be intersectoral, comprehensive, combine population and individual (for high-risk groups) approaches to the control of modified CVD risk factors with modern methods of secondary and tertiary prevention of CVD, which have proven their efficiency in European countries.

KEY WORDS: cardiovascular diseases, DALYs, risk factors, prevention, Ukraine

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INTRODUCTION

In the 21st century, cardiovascular disease (CVD) remains the dominant global public health problem [1,2]. In Europe, they are the leading cause of death and disability of the population [3,4]. In addition to human suffering, CVD has serious economic consequences [5].

Reducing premature mortality from non-epidemic diseases (including CVD) by 30% to 2030 is one of the tasks (3.4) of the Sustainable Development Goals adopted at the UN Summit in 2015 [6]. And for the countries of Western Europe, the achievement of this task, in accordance to the stable trend of decreasing mortality from CVD over the last decades in this region, looks quite real, then for the countries of Eastern Europe, which have the highest mortality rate from CVD in the world and less encouraging dynamic trends, in order to achieve this task, significant efforts in the field of control of CVD should be done with support of well-planned epidemiological studies [2-5].

Ukraine is one of the European and world leaders of mortality from CVD [2-4]. Premature mortality from CVD is one of the reasons for significantly lower life expectancy in Ukraine compared to Western European countries.

Improving control over CVD and preventing premature death from CVD is impossible without monitoring and evaluating the epidemiology of CVD in Ukraine and in comparison, with European countries.

An important component of monitoring of the population health, implemented at the international level for 30 years, is the evaluation of the burden of diseases according to such an indicator as DALYs, which include the Years of Life Lost (YLLs) and Years Lived with Disability (YLDs) [1, 7, 8]. Analysis of the DALYs from CVD and their risk factors allows us to consider the problem of the social significance of CVD and determine priority areas for their prevention from a new point of view, which defines the relevance of this study.

THE AIM

The purpose of the current study was to analyze the burden of cardiovascular diseases (CVD) and their modified risk factors in Ukraine to substantiate ways of prevention.

MATERIALS AND METHODS

A statistical method was used to analyze DALYs (Disability-Adjusted Life Years), YLLs (Years of Life Lost), YLDs (Years Lived with Disability) due to CVD in Ukraine, as well as the main risk factors of CVD. The information sources for the study were the materials of the statistical database of the international epidemiological study, which coordinated by the Institute of Health Metrics and Evaluation at the University of Washington, "Global Burden of Disease (GBD)" [8]. In this article the analysis of DALYs from CVD in Ukraine was carried out in the dynamics for 1990-2019 and in comparison with European and Europe Union (EU) countries. DALYs and its components (YLLs and YLDs) were analyzed both for the entire class of CVD and for individual diseases, such as: ischemic heart disease (IHD), strokes, cardiomyopathies and myocarditis, atrial fibrillation and flutter, rheumatic heart disease, hypertensive disease, endocarditis, non-rheumatic valvular heart disease.

The comparative characteristics of human resources and some diagnostic and interventional methods of treatment of CVD in Ukraine and European countries are based on the materials published by the European Society of Cardiology [4].

RESULTS

According to the results of the analysis of the materials of the database of the Global Burden of Diseases it is estimated that in Ukraine in 2019, CVD accounts for one third (38.3%) of all years of life lost due to disability and premature death and ranks first in the DALY structure among all diseases. In 2019, 8,305,261 years of healthy life were lost in Ukraine as a result of CVD, or 18,857.4 per 100,000 of the total population.

In the structure of burden of CVD, 67.2% years of healthy life are lost due to IHD, 22.4% - due to strokes, and 6% - due to cardiomyopathy (Table I).

The age-standardized DALYs for men is 2.1 times higher than the similar indicator for women. At the same time, the structure of DALYs is similar for men and women.

In the structure of DALYs for CVD, 95.9% of healthy life years of the population are lost due to premature mortality (YLLs), and 4.1% - due to disability (YLDs). In absolute terms, these losses in 2019 amounted to 7,964,599 and 340,663 years, respectively. A significant predominance of years lost due to premature death over years lived in disability is typical for almost all nosological forms of CVD, with the exception of atrial fibrillation and flutter and non-rheumatic heart disease, the proportion of years living with disability in the structure of the disease burden by these nosological forms were 54.2% and 39.1%, respectively.

The structure of years lost due to premature mortality (YLLs) is similar to the structure of DALYs: the first place with proportion 69.2% belongs to IHD, the second - to strokes (21.1%) and the third - to cardiomyopathies (6.2%). But in the structure of YLDs, half of healthy life years lost due to disability is caused by strokes (52.9%), and the fifth part (21.2%) is caused by IHD.

The ranking positions of the three main components in the structure of DALYs due to CVD in Ukraine correspond to those in the countries of Europe and EU, but the age-standardized DALYs per 100,000 population in Ukraine are significantly different from those in Europe. Per 100,000 people, the population of Ukraine loses 2.6 more healthy life years than European residents and 4.1 times more than in the residents in EU (Table II).

The situation with IHD is particularly unfavorable in Ukraine, which takes 3.3 times more years of healthy life from Ukrainians than the average in Europe and 5.8 times more than in the EU. Losses due to strokes are 2.1 and 3.3 times higher, due to cardiomyopathies and myocarditis by 2.7 and 6.6 times, rheumatic heart disease by 1.6 and 2.0 times, respectively.

Ukrainian indicators of DALYs for atrial fibrillation and flutter, as well as endocarditis, are close to the average European levels. But the DALYs due to hypertension and non-rheumatic valvular heart disease in Ukraine is significantly lower and is only 1/5 of the European rates.

A dynamic analysis of the Age-standardized DALYs per 100,000 population conducted over 1990–2019 revealed undulating high levels in Ukraine against the steady downward trend in DALYs for CVD in Europe and the European Union (Fig. 1). These dynamic trends of DALYs were determined by the dynamics of YLLs, as both in Ukraine and Europe, the years of life lost due to premature mortality make up the major share of the burden of CVD and led to a growing gap in DALYs indicators in Ukraine and Europe over 30 years of observation. The age-standardized rate of YLDs due to CVD in Ukraine less significantly exceeded the European rates and tends to decrease, but at a slower pace than in Europe and the EU.

The problem of premature mortality from CVD in Ukraine primarily concerns the male population. During 1990-2019, the gap in DALYs between men and women grew from 1.6 to 2.1 times due to multi-directional dynamic trends: over 30 years, a trend towards a decrease in the indicator in women and an increase in men was outlined (Fig. 2).

The main risk factors for the formation of DALYs due to CVD in men and women in Ukraine are a high level

Table I . CVD Disability-Adjusted Life Years (DALYs) lost by cause, males, females, both, Ukraine, 2019

Course (diseases)	Male		Female		Both	
	DALYs lost	% of total CVD DALYs lost	DALYs lost	% of total CVD DALYs lost	DALYs lost	% of total CVD DALYs lost
Cardiovascular diseases	4515370	100	3789891	100	8305261	100
Ischemic heart disease	3023564	67.0	2558574	67.5	5582137	67.2
Stroke	915741	20.3	941940	24.9	1857680	22.4
Cardiomyopathy and myocarditis	384858	8.5	116226	3.1	501085	6.0
Atrial fibrillation and flutter	46355	1.0	75236	2.0	121591	1.5
Aortic aneurysm	38265	0.8	12427	0.3	50692	0.6
Rheumatic heart disease	16063	0.4	18838	0.5	34901	0.4
Hypertensive heart disease	11916	0.3	10173	0.3	22089	0.3
Endocarditis	10438	0.2	3725	0.1	14164	0.2
Non-rheumatic valvular heart disease	5635	0.1	4661	0.1	10296	0.1
Other heart diseases	62535	1.4	48091	1.3	110626	1.3

Table II. Comparison of Age-standardized CVD DALYs rate in Ukraine, Europe, EU, 2019

Diseases	Age-standardized DALYs rate per 100,000			Comparison index (%)	
	Ukraine	Europe	EU	Ukraine / Europe(%)	Ukraine / EU(%)
Cardiovascular diseases	11316.7	4401.1	2758.8	257.1	410.2
Ischemic heart disease	7400.2	2237.9	1277.3	330.7	579.4
Stroke	2533.5	1230.5	754.3	205.9	335.9
Cardiomyopathy and myocarditis	864.5	314.2	130.8	275.2	661.1
Atrial fibrillation and flutter	155.9	132.0	134.5	118.1	115.9
Rheumatic heart disease	54.5	33.2	27.4	164.2	199.2
Hypertensive heart disease	31.9	160.3	152.1	19.9	21.0
Endocarditis	26.5	24.0	20.8	110.2	127.3
Non-rheumatic valvular heart disease	15.0	57.3	66.7	26.1	22.4

Table III. Percentage of CVD DALYs attributable to selected risk factors, by sex, 2019, Ukraine, (%)*

Risk factors	Male	Female	Both
Dietary risk factors	68.7	63.0	54.2
High systolic blood pressure	67.1	63.4	42.1
High low-density lipoprotein cholesterol	39.1	38.0	37.3
High body mass index	24.1	26.1	28.1
Smoking	32.7	5.7	22.9
High fasting plasma glucose	16.2	16.0	13.2
Alcohol use	9.5	11.2	4.2
Low physical activity	5.4	4.5	5.2

*The CVD burden attributable to each individual risk factor includes the individual contribution of each risk factor as well as its interaction with other risk factors. Hence, the sum of the CVD burden attributable to each risk factor exceeds 100%

of systolic pressure (causes 54.2% of DALYs due to CVD), an irrational diet (42.1%), a high level of low-density lipoprotein cholesterol (37.3%), a high body mass index (28.1%), smoking (22.9%) (Table III). Dietary risk factors include consumption of foods with a high sodium, trans fats, processed meat, insufficient consumption of whole grains, legumes, fruits, vegetables, nuts and seeds, seafood omega-3 fatty acids, polyunsaturated fatty acids.

The higher level of DALYs due to CVD in Ukraine, compared to European countries, can be associated not

Table IV. Comparison of human resources and some diagnostic and interventional methods for the treatment of CVD in Ukraine and in European Society of Cardiology member countries*

Indicator	Ukraine	Median (IQR)**	minimum	maximum
Interventional cardiologists per million people (2020)	4.5	12.1 (9.2–17.4)	1.9 (Uzbekistan)	25.2 (Bulgaria)
Diagnostic coronary angiograms per million people (2019)	1105	4084 (2563–5007)	394 (Kyrgyzstan)	6898 (Belgium)
Percutaneous coronary intervention per million people (2020)	533	1879 (1313–2550)	191 (Kyrgyzstan)	3767 (Latvia)
Ablation procedures per million people (2020)	64.3	372.3 (145.2–518.8)	9.0 (Egypt)	1112.3 (Germany)
Pacemaker implants per million people (2020)	142.4	652.2 (267.5–874.7)	17.8 (Uzbekistan)	1038.2 (Sweden)

*The table is based on the materials of the European Society of Cardiology, presented in [4].
**Median and IQR (interquartile range) in European Society of Cardiology member countries.

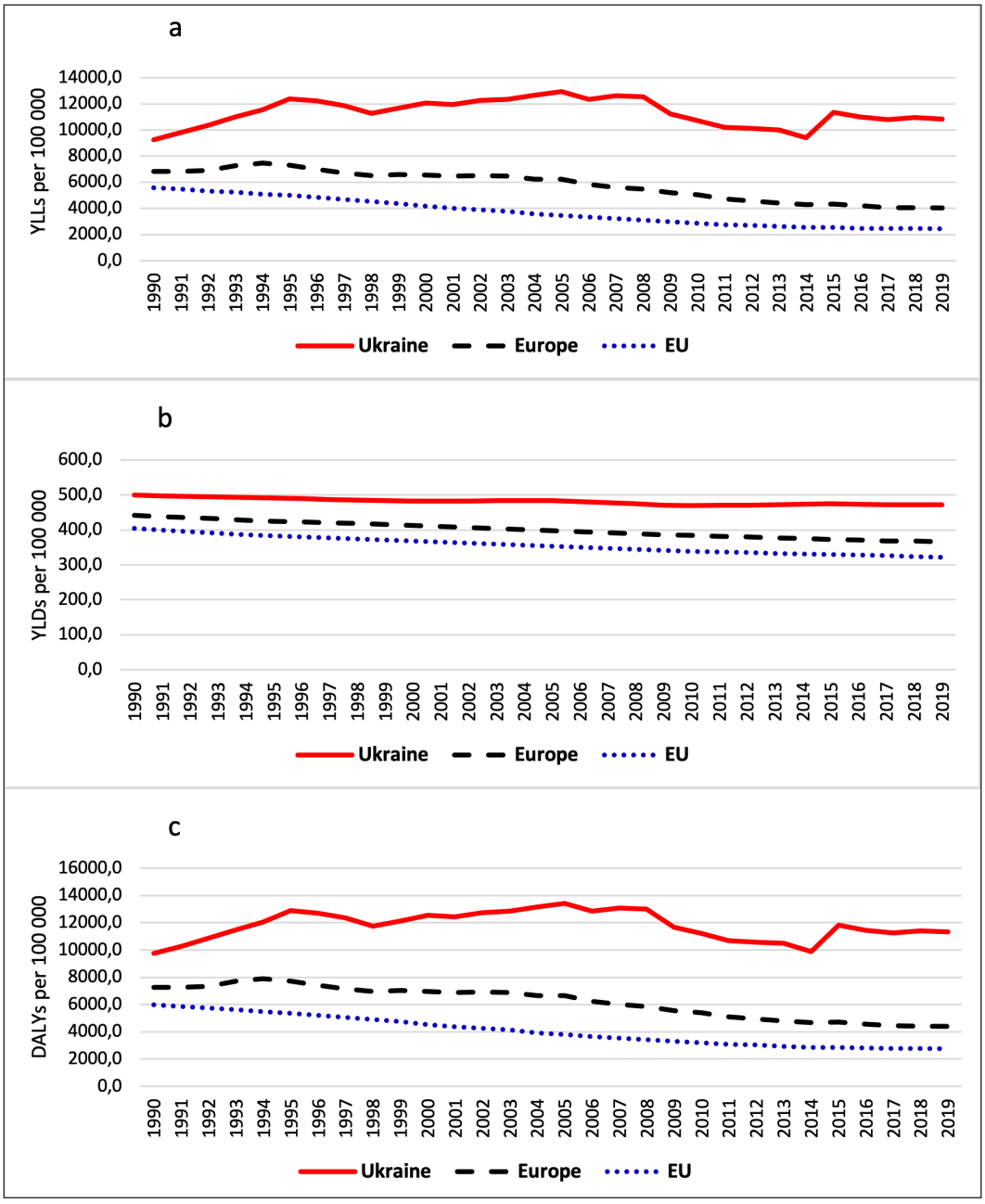

Fig. 1. Dynamics of the age-standardized YLLs (a), YLDs (b), DALYs (c) rates due CVD in Ukraine, Europe, EU, 1990-2019 (per 100,000)
YLLs = years of life lost, YLDs =years lived with disability, DALYs =disability-adjusted life years

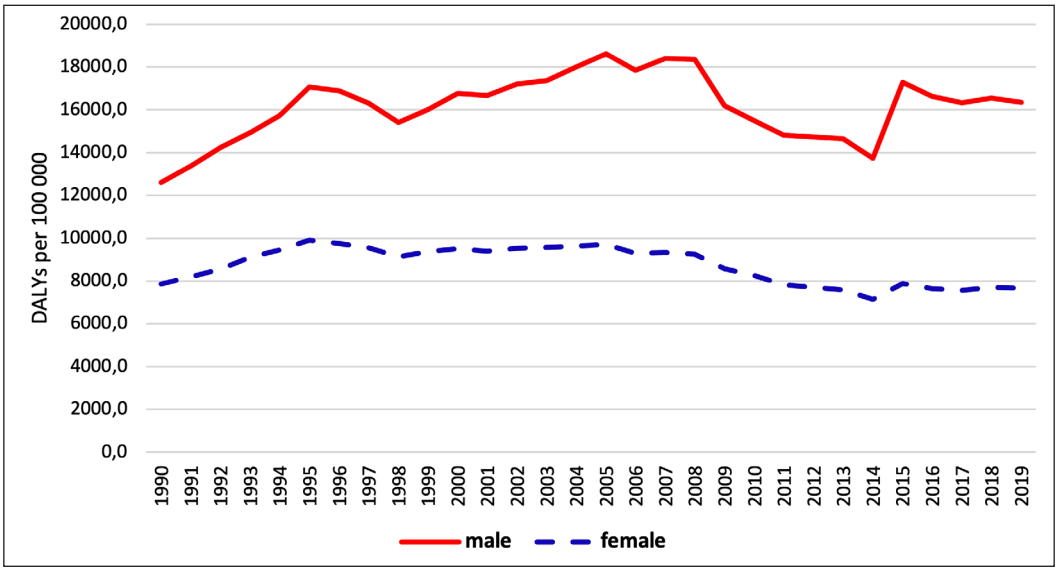

Fig. 2. Age-standardized CVD DALYs rates, male, female, Ukraine, 1990-2019 (per 100,000)

only with the significant prevalence of risk factors and insufficiency of primary prevention of CVD, but also less accessibility for the population of Ukraine to the modern (including invasive) methods of diagnosis and treatment of these diseases. For example, per 1 million population, on an average, European Society of Cardiology member countries have, 2.7 times more interventional cardiologists, 3.7 times more diagnostic coronary angiography, 3.5 times more percutaneous coronary interventions, 5.8 times more ablation procedures, 4.6 times more pacemaker implantations than in Ukraine (Table IV).

DISCUSSION

An appropriate evidence base should be used to set health priorities and shape disease prevention policies [9, 10]. The analysis of years of healthy life lost due to premature mortality and disability due to CVD is a methodological approach that allows monitoring and a comprehensive estimation of the burden of CVD at a modern scientific level. In the context of the development of the public health system in Ukraine, the use of the DALYs indicator and the quantitative assessment of its risk factors, instead of traditional indicators of mortality and disability, provides substantiated evidence for the development of an appropriate CVD prevention policy [9, 11].

According to the study results CVD is a leading cause of DALYs for the population of Ukraine. The most significant socio-medical losses due to CVD in Ukraine are caused by the loss of years of healthy life due to premature mortality from IHD and strokes. And these losses primarily concern the male population.

Ukraine has one of the highest rates of DALYs for CVD in Europe and lags far behind European countries in decline of it. The success of economically developed countries in Europe in reducing DALYs from CVD is primarily associated with a decrease in premature mortality from IHD, which is on 50% attributed to the control of modified risk factors and 40% - to improved diagnosis and treatment of IHD [12-15].

High DALYs due to CVD in Ukraine can be explained by the socio-psychological stress experienced by the population as a result of a protracted socio-economic crisis [11, 15], the extreme prevalence and insufficient control over the modified risk factors of CVD [10], among which, according to the results of our research, the most important are: high blood pressure, unhealthy diet, hypercholesterolemia, high body mass index and smoking.

Insufficient government spending on the health care system is a factor that causes problems with the accessibility of specialized and highly specialized medical care to the population and Ukraine's significant lag behind Western European countries in the introduction of high-tech interventional techniques for the effective treatment of CVD [11, 15].

The positive experience of Western Europe countries indicates the possibility of a significant reduction in the burden of CVD, both through the successful implementation of the population strategies for modifying the leading risk factors for CVD, and due to the timely detection and effective treatment of patients with CVD, including the use of invasive cardiac surgical technologies [12-14].

CONCLUSIONS

In Ukraine, the share of CVD is one third (38.3%) of all years of healthy life lost due to premature death and disability. They rank first place in the DALYs structure among all diseases. In 2019, 8,305,261 years of healthy life were lost due to CVD, or 18,857.4 years per 100,000 population.

Age-standardized DALYs per 100,000 population in Ukraine are 2.6 times higher than the average in European countries and 4 times higher than in the EU. During 1990-2019 the gap in DALYs rates increased due to a significant reduction in the burden of CVD in Europe, against the backdrop of a high level of rates in Ukraine.

The burden of CVD in Ukraine can be reduced on 54.2% by normalizing blood pressure, on 42.1% by improving diet, on 37.3% by lowering low-density lipoprotein cholesterol, on 28.1% by lowering body mass index, and on 22.9% by quitting smoking.

The Ukrainian strategy to reduce the burden of CVD should be intersectoral, comprehensive, combine population and individual (for high-risk groups) approaches to the control of modified CVD risk factors with modern methods of secondary and tertiary prevention of CVD, which have proven their efficiency in European countries.

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ORIGINAL ARTICLE

PHYSICAL HEALTH OF STUDENTS AND DIGITALIZATION OF HIGHER MEDICAL EDUCATION: RISK FACTORS

DOI: 10.36740/WLek202304109

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ABSTRACT

The aim: To study the dynamics of gadget use by higher education students of the Bogomolets National Medical University and to assess technological impact on the physical health of students.

Materials and methods: To accomplish the tasks set using theoretical and experimental methods of scientific research: systematic analysis, comparison and generalization of the bibliosemantic method, questionnaires, and interviews with students. Quantitative data collected during the survey of students studying in the «Dentistry», «Pediatrics», «Medicine», «Pharmacy, Industrial Pharmacy», «Physical Therapy, Occupational Therapy», and «Medical Psychology» specialties were processed using the MedCalc statistical software, and there was carried out comparative analysis afterwards.

Results: During the quarantine and martial law, medical university students were forced to study distantly or in a mixed format using various gadgets and computers. It is obvious that the physical condition of a person is affected by the duration of their use of various devices. In this paper, therefore, the risks and the researched dynamics of gadget use by higher education students of the Bogomolets National Medical University were identified. Thus, the technological impact on the physical health of students was also defined. Moreover, the data based on the results of height and weigh calculation of higher education students, which used to diagnose types of obesity by anthropometric indicators, were also collected.

Conclusions: According to the results of the research, it was established that the students of the Bogomolets National Medical University spent a significant part of their study time sitting in the classroom or at the computer (40 hours weekly average). We found that in the process of distance learning, prolonged sitting at a PC or other gadget (as well as general sedentary lifestyle) has affected the female higher education students majoring in 222 «Medicine» course their body mass index. The time spent using gadgets both in the educational and non-formal education (self-education) processes has increased significantly. We attribute this fact to the emergence of a significant number of online educational resources in the public domain, the growing number of webinars, trainings, and master classes conducted by both domestic and foreign experts online.

KEY WORDS: Higher medical education, physical health, gadget, students, distance learning

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INTRODUCTION

The process of digitalization is one of the defining trends in the development of modern society, and virtually all areas of our lives are transformed under its influence: education, economy, everyday life, and healthcare. The widespread use of technical innovations (gadgets) requires the study of various aspects related to this phenomenon: ethical, psychological, and health-preserving. The study of the relationship between time spent with gadgets and the state of physical and mental health of different age groups has become a subject of interest to scholars in various fields of knowledge. The large share of such research is focused on the impact of gadgets on the health of children and adolescents, and it is reflected in reasonable restrictions recommended at the state level by associations of national academies in different countries (e.g. the American Association of Pediatrics). A much smaller number of studies have examined the impact of gadgets on physical health (ophthalmic, musculoskeletal, obesity, etc.) of older age groups (more than 17 years). This happened due to the difficulty of isolating digitalization as an influence factor, the need for longitudinal studies, and the selection of a civilizational community outside of this influence as a control group to compare research results. The circumstances in which the national education system has been operating in recent years may provide grounds for such research and cautious assessments of such influence According to sociological research, most Ukrainians use screen gadgets (phones, computers, tablets, TVs) and the global Internet on a daily basis, with the vast majority of students and pupils. Therefore, this is quite obvious as the process of digitalization of society is closely linked to the educational process. With the

spread of the COVID-19 pandemic and the outbreak of hostilities in Ukraine, distance learning and, accordingly, the use of digital technologies have become even more important, and the time spent using any gadgets has increased significantly.

THE AIM

There were alalyzed the study of dynamics of gadget use by higher education students of the Bogomolets National Medical University and assessment of their impact on the physical health of students.

MATERIALS AND METHODS

The accomplishment of the tasks set using theoretical and experimental methods of scientific research was done: systematic analysis, comparison and generalization of the bibliosemantic method, questionnaires, and interviews with students. Quantitative data collected during the survey of students studying in the «Dentistry», «Pediatrics», «Medicine», «Pharmacy, Industrial Pharmacy», «Physical Therapy, Occupational Therapy» and «Medical Psychology» specialties were processed using the G*Power and MedStat software with the carried out comparative analysis of their results.

In order to diagnose physical health of students, the types of obesity (based on anthropometric indicators) were used the formula:

$$I = \frac{m}{h^2} \quad (1),$$

where *m* is a body weight in kilograms, and *h* is a height in meters (BMI is measured in kg/m^2).

A BMI of up to 18.5 is considered underweight. Normal BMI for men and women is measured between 18.5-24.9 kg/m^2. With an index of 25.0-29.9 kg/m^2, the presence of overweight is obviously stated, but this is not yet a diagnosis of obesity itself. In case of a first-degree obesity, the BMI is within the range of 30.0-34.9 kg/m^2; in case of second-degree obesity – it is 35.0-39.9 kg/m^2; and more than 40.0 kg/m2 means third-degree obesity [1-2].

In order to study the impact of the use of computer technology in blended (classroom and distance) learning under adaptive quarantine, we conducted a study at the Bogomolets National Medical University. In the fall of 2021-2022 academic year, 243 respondents of 3-5 courses took part in the survey, majoring in 221 «Dentistry» and «Pediatrics», 222 «Medicine», 226 «Pharmacy, Industrial Pharmacy», 227 «Physical Therapy, Occupational Therapy» and «Medical Psychology» disciplines. In the fall of the 2022-2023 academic year, we conducted a survey of mixed (classroom and distance) learning under martial law. The total of 434 higher education students were expressed. Those included 4 (2) respondents in the 073 «Management» specialty, 115 respondents in the 221 «Dentistry» specialty, 263 applicants in the 222 «Medicine» specialty, 18 future masters in the 226 «Pharmacy, Industrial Pharmacy» specialty, 1 in the 227 «Physical Therapy, Occupational Therapy» specialty, 29 in the 228 «Pediatrics» specialty, and 4 applicants in the «Public Health» specialty. Among them, there are 125 applicants of 4-6th courses in the 222 «Medicine» specialty. Last year, there were 101 female and 24 male respondents in the 222 «Medicine» specialty being surveyed who are currently studying the 4-6th academic year.

The questionnaires in 2021-2022 (retrospective group) and 2022-2023 (prospective group) were conducted according to the same methodology, and the calculations were performed within the G*Power software [3] according to Fisher's test in order to determine the power and sample size for comparing two independent binomial populations. According to the results of the calculations, it can be stated that the samples of 243 and 434 respondents (with an allocation ratio of 1.8) are sufficient to detect the possibility of excess weight at a power of 0.8 and at a significance level of 0.05, thus, it can be concluded to comparability of the studied groups.

To compare the samples of respondents in 2021-2022 and 2022-2023 was used the statistical package MedStat [4], and the calculations were made by the Chi-squared test. Two-sided extreme values were defined: Chi-square = 3.85, degrees freedom k = 5. There is a difference at significance level, p = 0,95 ($\chi^2 > \chi^2_{cr}$).

RESULTS

The development of modern society is influenced by the total digitalization of all spheres of life and is characterized by the widespread use of information technology. During the COVID-19 pandemic and subsequently martial law in Ukraine, the role of distance learning technologies has grown significantly and become crucial as they created the informational and educational environments of the university [5-7]. This has led to a significant increase in various gadgets used by students and teachers: laptops, tablets, smartphones, etc. Apparently, the organization of the educational process requires prolonged work with a gadget, and the process of teaching higher education students (users) acquires the characteristics of PC (personal computer) users with all its inherent features and health risk factors (sedentary and inactive lifestyle). Occupational pathologies of PC users have now reached such

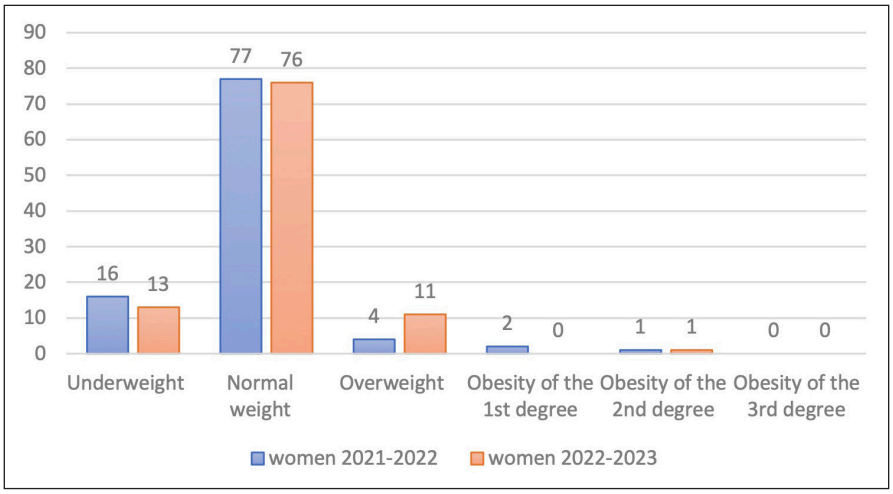

Fig. 1. Distribution of BMI of female higher education students in the specialty 222 «Medicine»

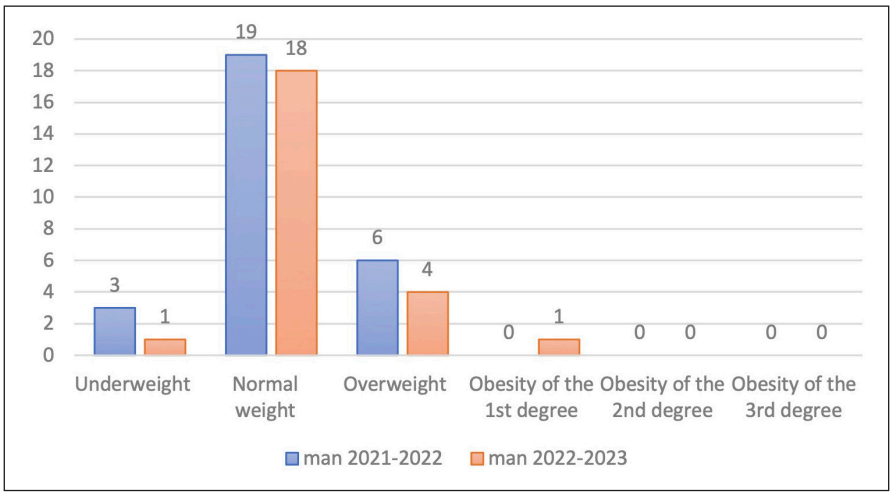

Fig. 2. Distribution of BMI of male applicants for higher education in the specialty 222 «Medicine»

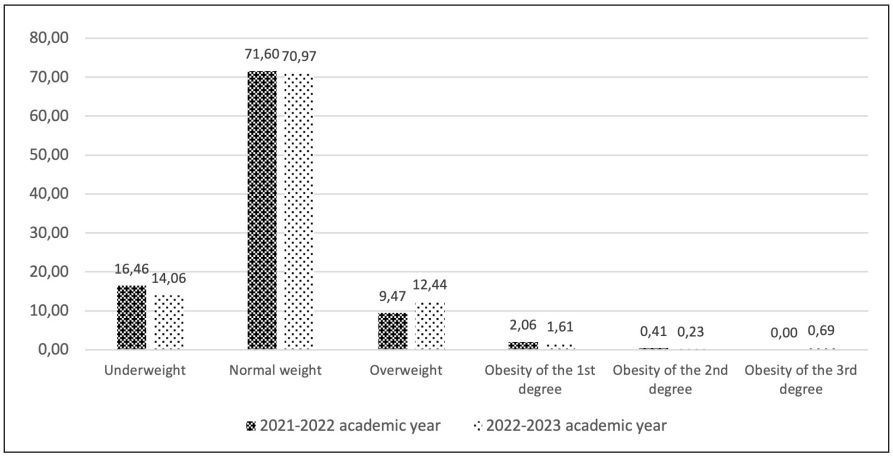

Fig. 3. Percentage distribution of BMI of higher education students in the 2022–2023 academic year

a scale that medical professionals have begun to use the term «repetitive strain injury» in order to define a complex set of symptoms caused by their long-term professional activities. Numerous studies by ergonomics, occupational safety, and biomechanics experts [8-13] show that one of the most threatening factors to the psychophysiological capabilities of PC users is static-dynamic stress on the spine caused by being in a static, uniform position against the background of a large number of stereotypical loads performed during coordinated movements of the hand muscles alone. The analysis of regulations and documents that establish safety, sanitary, and hygienic requirements for the equipment of workplaces of PC users shows that the defining regulatory document to date is the «State Sanitary Rules and Norms for Working with Visual Display Terminals of Electronic Computers» DSanPiN 3. 3.2.007-98, approved by the Resolution of the Chief State Sanitary Doctor of Ukraine No. 7 of 10.12.1998 [14], which clearly states the need for regulated rest

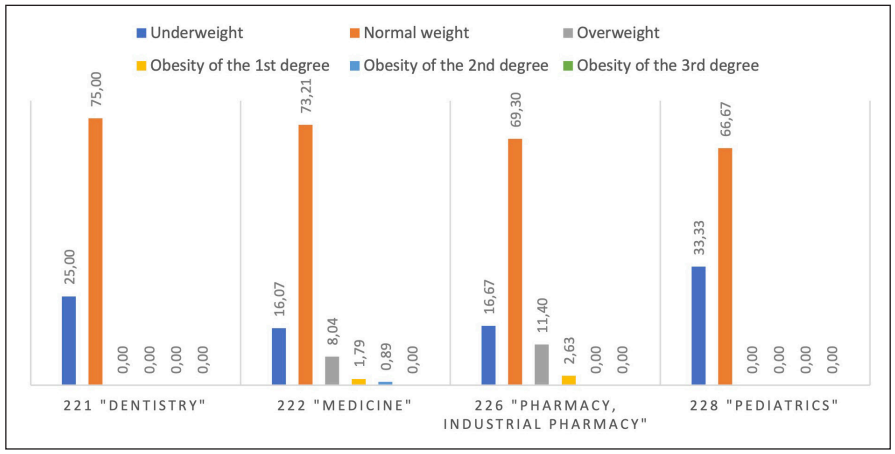

Fig. 4. Percentage distribution of BMI within specialties in the 2021–2022 academic year

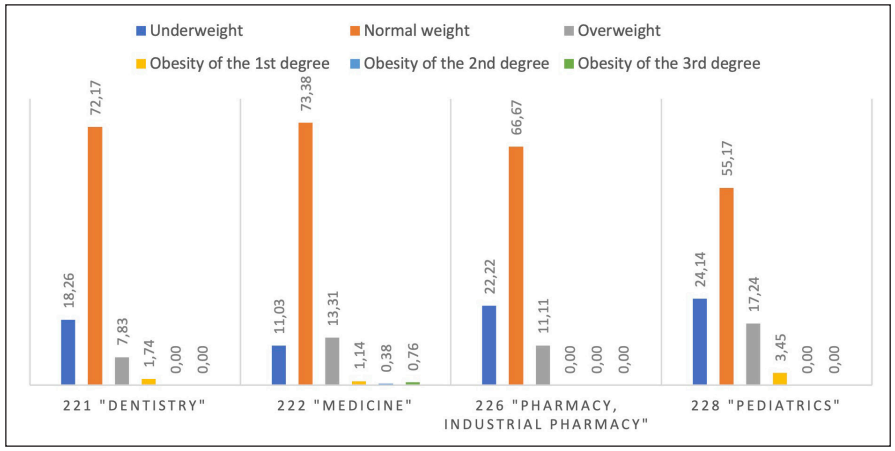

Fig. 5. Percentage distribution of BMI within specialties in the 2022–2023 academic year

breaks for PC users. However, both sources and our own experience show that, unfortunately, these breaks are either not used properly or are not available at all.

As a result of the study, we found that among female higher education students majoring in 222 «Medicine» discipline, the distribution of BMI has the following dynamics: the percentage of people with underweight decreased from 16% to 12.87%, the normal weight indicator also decreased from 77% to 75.25%, the overweight indicator has the opposite trend - the percentage of people with this indicator increased by almost 7% (from 4% to 10.89%), the rate of 1st degree obesity in 2022–2023 students also increased by 2%, and the rates of obesity of 2nd and 3rd degrees remain stable and amount to almost 1% and 0% respectively (Fig 1).

Moreover, in the dynamics of two years, the share of BMI of underweight persons decreased and amounted to 4.7%, the share of normal weight increased from 67.86% to 75%, the percentage of overweight decreased to 16.67%, and the rate of obesity of the 1st degree increased from 0 to 4.17% among male higher education students majoring in 222 "Medicine" discipline (Fig 2).

The overall percentage distribution of respondents by BMI is as follows (Fig 3): the rate of underweight decreased from 16.46% to 14.06%, the rate of normal weight decreased from 71.60% to 70.97%, the rate of overweight increased from 9.47% to 12.44%, the rate of obesity decreased from 2.06% to 1.61%, the rate of obesity of the 1st degree decreased from 0.41% to 0.23%, and the rate of obesity of the 3rd degree increased by 0.69%.

As for the last 2 academic years, the percentage distributions for the 221 «Dentistry», 222 «Medicine», 226 «Pharmacy, Industrial Pharmacy» and 228 «Pediatrics» specialties are shown in Figs 4 and 5.

As for the numerical data of 2021–2022 academic year, 40 respondents were underweight, 174 were normal, 23 were overweight, and 5 and 1 respondents were obese respectively, having no obese people of the 3rd degree. In the 2022-2023 academic year, 61 surveyed applicants were underweight, 308 applicants were of normal weight, 54 respondents were overweight, 7, 1, and 3 applicants were obese respectively.

During the survey of this academic year, almost half of the respondents indicated that they have posture disorders (44.9%), while 12% indicated the presence of spinal diseases. A significant proportion of respondents reported pain in the joints when using gadgets: 9.7% - in the elbow joints, 12% - in the wrist joints, 30.4% - in the knee joints. The applicants noted that they feel discomfort after long-term work at a computer or other gadgets in the cervical (50.2%), thoracic (25.1%) and lumbar (46.1%) departments.

Table I. Average time per day of PC use by higher education students for educational purposes

PC time per day	During the educational process		For the purpose of self-education	
	21–22	22–23	21–22	22–23
> 5 hours	32,5 %	34,1 % ↑	12 %	13,9 %↑
4-5 hours	24,3 %	23,7 %	7 %	10,4 %↑
3-4 hours	21,4 %	25,1 %↑	16,9 %	16,9 %
2-3 hours	14 %	12 %	25,6 %	30,5 %↑
1-2 hours	5,3 %	3,5 %	33,1 %	25,9 %
I do not use	2,5 %	1,6 %	5,4 %	2,5 %

Table II. Average time per day of PC use by higher education students for entertainment

PC time per day	For entertainment		Trend
	21–22	22–23	
> 4 hours	14,4 %	16,3 %	↑
3-4 hours	17,4 %	16,5 %	↓
2-3 hours	20,8 %	30,2 %	↑
< 2 hours	47,5 %	36,9 %	↓

Table III. Physical activity of students during prolonged using PC

Answer option	Physical exercises (mini sets of exercises) when working at the computer		Self-massage while working at the computer	
	21–22	22–23	21–22	22–23
Yes	26,7 %	25,8 %	27,6 %	31,3 %
No	41,6 %	44,5 %	50,6 %	45,6 %
At times	31,7 %	29,7 %	27,6 %	23 %

Table IV. Lifestyles of higher education students

Answer option	Your lifestyle	
	2021-2022	2022-2023
I lead an active lifestyle	27,2 %	22,4 % ↓
I follow the principles of a healthy lifestyle	50,6 %	48,8 % ↓
I lead a passive lifestyle	15,2 %	21 % ↑
I lead a lifestyle that is not conducive to maintaining my health	7%	7,8 % ↑

DISCUSSION

The obtained results prompted us to analyze the factors that determine them and find ways to reduce their negative impact on the health of young student. It is quite logical to assume the relationship between changes in the physical health of students and the time of using gadgets, which has significantly increased both in the process of formal and informal education (or self-education). (Tables I, II).

We associate the increase in time spent at the PC for the purpose of education and self-education with the appearance of a significant number of freely accessible online educational resources, the increase in the number of webinars, trainings, and master classes held online by local and foreign specialists.

As a part of our study, we tried to find out whether there was a redistribution of time spent at the PC. For this purpose, the duration of using gadgets for entertainment was investigated. It has been found that less than 6% (5.8% this year and 4.9% last year) of respondents do not use gadgets for entertainment despite the fact that according to students themselves, 59% of them use it «often» (54.3% during the last year) and 35.3% «very often» (40.7%).

According to the results of the questionnaire, the students note a decrease in physical activity by 8.4% during the present year compared to the last one despite the fact that the vast majority of classes are held in classrooms. A significant percentage of students (78–80%) feel that the length of time spent on a computer, phone, or other gadgets has increased over the past two years.

To reduce the feeling of discomfort, students try to control their working posture, systematically engage

in health gymnastics, take short breaks, massage or self-massage, strengthen muscles, etc. Therefore, we investigated the interval physical activity of students during long-term use of a PC (Table III) and their lifestyle (Table IV). In the course of the research, we also found that more than 25% of users are not familiar with the concept of «ergonomic posture» and neglect the correct one when using gadgets, although 35-40% of respondents are concerned about maintaining the posture. 23.4% of respondents constantly monitor their posture when using gadgets, and 17% do not think about what position they are in when using a PC, laptop, etc.

The state of their musculoskeletal system is positively assessed by 52.3% of applicants, satisfactorily by 39.2%, and unsatisfactorily by 8.5%.

The results of the questionnaire and their subsequent discussion in focus groups give reason to assume greater self-criticism of students in evaluating their lifestyle, noting a decrease in current physical activity compared to the last year despite the fact that the vast majority of classes are held in classrooms. In our opinion, this can be the evidence of a more responsible attitude to one's health and the basis for the development and implementation of measures aimed at preventing the negative impact on the physical health of students of the factors that necessarily accompany the processes of education digitalizing [5].

CONCLUSIONS

In the course of the study, we found that the level of both formal and non-formal education had been greatly increased. With the spread of COVID-19 pandemic and the start of hostilities in Ukraine, the distance learning has become a dominant education. In its turn, this has led to an increase in the length of time spent at a computer or other gadget, and as a result, led to a sedentary lifestyle and changes in physical health indicators. Thus, among Bogomolets National Medical University female higher education graduates of the 222 "Medicine", a redistribution of body mass index was stated. Namely, the rate of overweight increased by almost 7%, the share of respondents who noted a decrease in current motor activity compared to last year increased by 8.4%, and, finally, a significant share of higher education graduates neglects the correct posture when using gadgets and feels discomfort or pain in their joints, muscles, or spine during a prolonged using PC.

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ORIGINAL ARTICLE

PATIENTS' SAFETY: APPLICATION OF SIMULATION METHODS FOR THE TRAINING OF SPECIALISTS IN "ENT" SPECIALTY AT THE POSTGRADUATE LEVEL

DOI: 10.36740/WLek202304110

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ABSTRACT

The aim: The aim of the study was to analyze the results of the practical implementation of simulation training in educational practice at the postgraduate level at Bogomolets National Medical University, majoring in "otorhinolaryngology".

Materials and methods: The study of the opinion of intern doctors regarding the acquisition of practical skills on the clinical basis of the internship was conducted at the Department of Otorhinolaryngology (Bogomolets National Medical University). The survey was conducted according to a developed questionnaire with questions on the assessment of the acquisition of competencies and practical skills in the speciality "otorhinolaryngology" during the extramural part of the internship.

Results: The analysis of current thematic plans for the speciality "otorhinolaryngology" showed a significant number (45) of practical skills and operative interventions that an otorhinolaryngologist should master after completing the internship. The mandatory number of manipulations and medical procedures is about 3,500 during training. The results of the survey of intern doctors showed that the factors that influence the possibility of obtaining practical knowledge and skills at the clinical base of internship are: access to patients during the educational process, and the availability of sufficient amounts of medical assistance.

Conclusions: The use of simulation equipment and medical mannequins contributes to the continuous professional development of otorhinolaryngologists (acquiring modern practical skills, working out current protocols and standards of providing medical care to the population) and makes it possible to reduce the risk of defects in the provision of medical care, to prevent unintentional harm to patients at all levels of care.

KEY WORDS: postgraduate medical education, patient safety, otorhinolaryngology, simulation training

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INTRODUCTION

As a result of the reform of the medical industry in Ukraine, the work intensification of all medical workers is expected. Medical technologies are becoming more complex, and the role of informatization in the medical and diagnostic process is growing. This increases the risk of unintended harm to patients and adverse events (defects in the provision of medical care) [1].

WHO emphasizes that patient safety is a medical discipline, the emergence of which is a response to the growing complexity of the processes of providing medical services, which are accompanied by an increase in the scale of harm caused to patients in medical institutions (https://www.who.int/ru/news-room /fact-sheets/detail/patient-safety) [2-4].

The education and training of medical interns play an important role in shaping future medical professionals' attitudes toward safety. The main goal of the internship is for interns to acquire the competencies necessary to obtain the qualification of an otorhinolaryngologist, and to prepare for independent medical work in compliance with the principles of academic integrity, medical ethics and deontology, evidence-based medicine.

The reform of the health care system in Ukraine actualizes the need to train competitive domestic specialists, which can be ensured by the introduction of new educational technologies. The guaranty and earnest point of the effective professional activity of future doctors is a high level of their professional competence and includes substantive (knowledge) and procedural (skill) components, namely the level of mastery of practical skills [5].

Therefore, there are new requirements for the training program of intern doctors, more specifically, the use of modern technologies that are widely available and used in the training of doctors abroad, especially in countries with a high level of economic development [6,7].

Simulation training (from Latin *simulatio* — imitation, pretence) is a method of training based on the imitation of any physical process using an artificial (for example,

mechanical or computer) system. Teaching clinical skills using mannequins, simulators, and standardized patients is the "gold standard" of medical education in the developed world [8].

THE AIM

The aim of the study was to analyze the results of the practical implementation of simulation training in educational practice at the postgraduate level at Bogomolets National Medical University, majoring in "otorhinolaryngology".

MATERIALS AND METHODS

Programs for training specialists in the speciality "otorhinolaryngology" in Ukraine, the results of the practical implementation of simulation training in educational practice at the postgraduate level at the Bogomolets National Medical University were the research materials.

RESULTS

In Ukraine, postgraduate training of specialists in the specialty "otorhinolaryngology" lasts during 2-year specialization (internship), which all graduates of medical institutions of higher education must complete in order to obtain a clinical specialty [9]. The main goal of the internship is to increase the level of practical training of intern doctors in their professional readiness for independent medical work in their specialty [10].

In accordance with the order of the Ministry of Health of Ukraine dated June 22, 2021 No. 1254, "On approval of the Regulation on internship and secondary medical (pharmacological) specialization", registered in the Ministry of Justice of Ukraine on August 17, 2021 under No. 1081/36703 № 1254 Internship in Ukraine has two components - theoretical and practical. Theoretical training takes place based on institutions of higher medical education. The practical component of the internship is training at workplaces in healthcare institutions. From 2022, the ratio between the theoretical and practical parts of the internship has been changed – the theoretical part is three months per academic year, and the practical part is eight months per year. In the updated internship programs, emphasis is placed on mastering practical skills by the future doctor on a clinical internship base.

The analysis of current thematic plans for the specialty "otorhinolaryngology" showed a significant number (45) of practical skills and operative interventions that an otorhinolaryngologist should master after completing the internship. The mandatory number of manipulations and medical procedures is about 3,500 during training. For each competence, practical skills are defined in each of the ranges from A - independently, B - under the supervision of a supervisor, C - assistance D - teaches or supervises others.

Mastery level:

(A) – means that procedures qualified for independent execution;

(B) – could be performed only under supervision or as an assistant curator,

(C) – assistance,

(D) – performs, instructs, or supervises junior interns in demonstration and performance.

N.B.! Procedures qualified to be performed under supervision or assistance (B) may be performed independently at the time the speciality leader determines that the intern has sufficient competence to perform the manipulation independently.

Analysis of kinds and the number of invasive and non-invasive interventions that will help patients with acute and chronic diseases of the ENT organs (qualified for independent implementation), which should be mastered by an intern doctor after completing training in the speciality "otorhinolaryngology ", are presented in Table I.

Analysis of kinds and number of invasive and non-invasive interventions that will allow conservative and surgical care for patients with acute and chronic diseases of the ENT organs (under supervision or as an assistant curator), which should be mastered by an intern physician after completing training in the specialty "otorhinolaryngology", are presented in Table II.

Thus, the modern internship training program in the speciality "otorhinolaryngology" includes a significant amount of practical skills and operative interventions that an otorhinolaryngologist should master upon graduation. When working independently in health care facilities (treatment and prevention facilities) of various forms of ownership and subordination, the insufficient level of mastering these can lead to the risk of adverse events (defects in the provision of medical care) that are related to patient safety.

The study of the opinion of intern doctors regarding the acquisition of practical skills on the clinical basis of the internship was conducted at the Department of Otorhinolaryngology (Bogomolets National Medical University); 36 out of 39 intern doctors took part in the survey, which was 92.3%. The survey was conducted according to a developed questionnaire with questions on the assessment of the acquisition of competencies and practical skills in the speciality "otorhinolaryngology" during the extramural part of the internship.

The degree of mastery was determined by intern

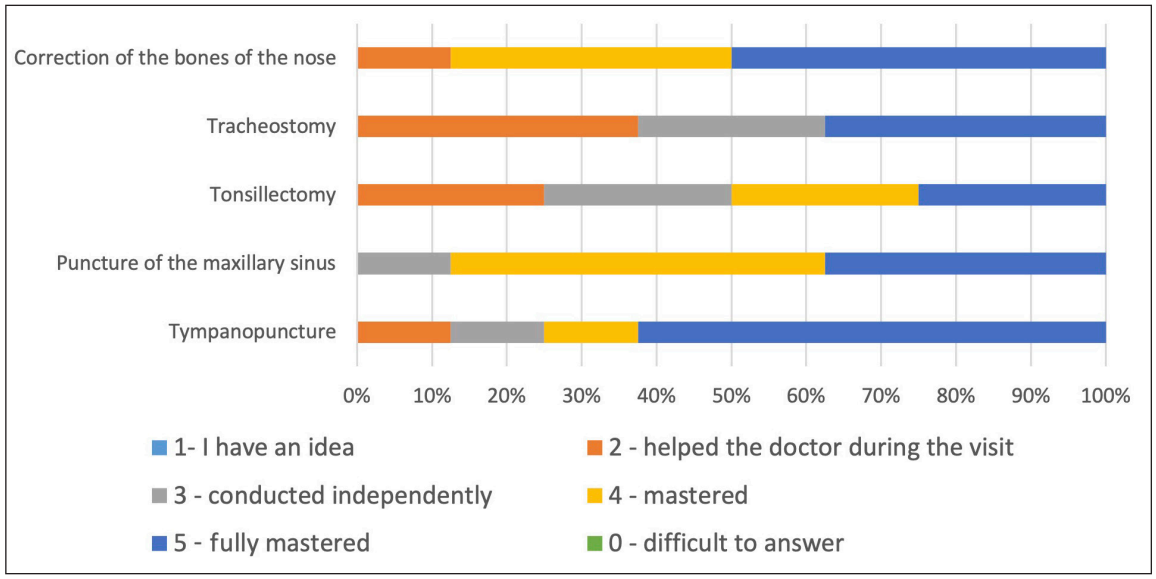

Fig. 1. Self-assessments by interns of acquiring competencies and practical skills

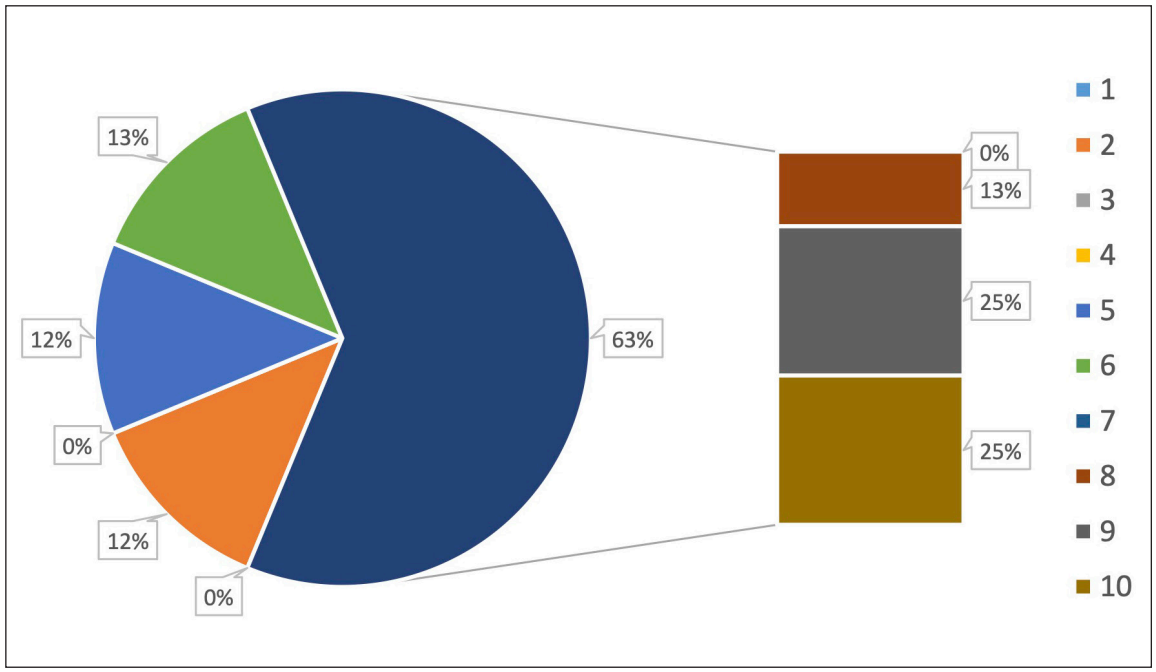

Fig. 2. Evaluation of simulation training methods (on phantoms)

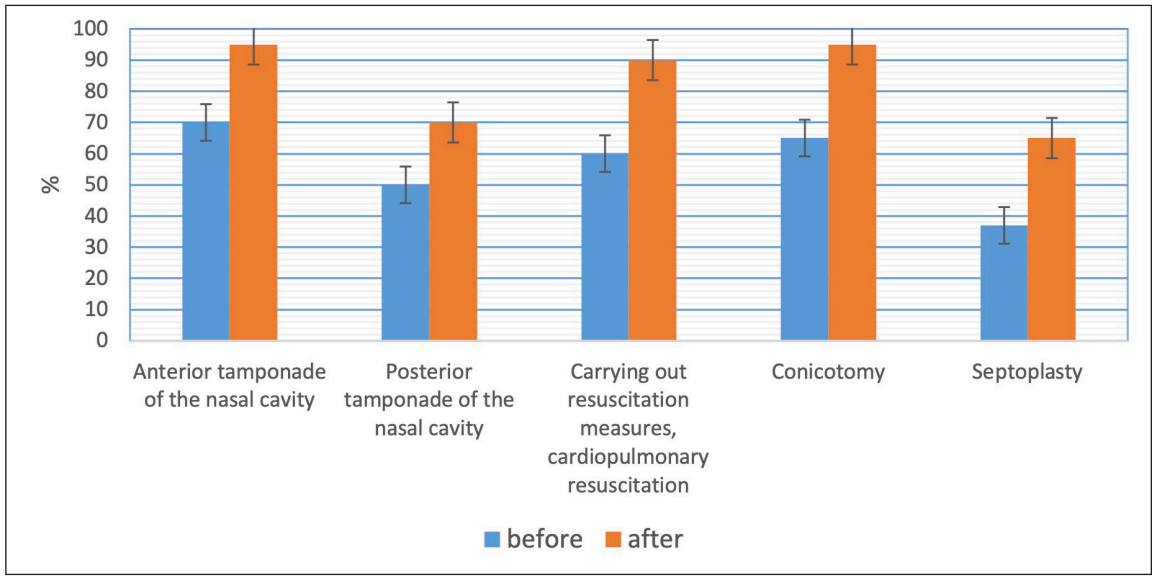

Fig. 3. Dynamics of self-assessment of the level of mastery of practical skills by doctors-interns in the speciality "otorhinolaryngology" during simulation training

Table I. Analysis of surgical interventions of doctors-interns in the speciality "otorhinolaryngology" (qualified for independent execution)

	LIST OF OPERATIONAL INTERVENTIONS	MASTERY LEVEL	MANDATORY QUANTITY
1.	Carrying out resuscitation measures, cardiopulmonary resuscitation	A	15
2.	Tracheostomy and tracheostomy care	A	30
3.	Cricothyroidectomy	A	30
4.	Front and back tamponade	A	20
5.	Myringotomy	A	15
6.	Removal of polyps from the ear canal	A	10
7.	Installation of a ventilation shunt	A	10
8.	Restoration of the integrity of the tympanic membrane at a linear perforation	A	10
9.	Nasal surgery	A	10
10.	Incision and drainage of an abscess of the nasal septum	A	20
	Total		170

Table II. Analysis of operational interventions of intern doctors in the speciality "otorhinolaryngology" (under supervision or as assistant curator)

	LIST OF OPERATIONAL INTERVENTIONS	MASTERY LEVEL	MANDATORY QUANTITY
1.	Treatment of external ear injuries	B	30
2.	Removal of exostoses	B	5
3.	Adenotomy	B	20
4.	Tonsillectomy and tonsillotomy	B	30
5.	Methods of stopping bleeding after tonsil surgery	B	30
6.	Dissection of paratonsillar and pharyngeal abscesses	B	30
7.	Dissection of an intratonsillar abscess	B	20
8.	Removal of foreign bodies	B	30
9.	Surgical closure of the tracheostomy	B	20
10.	Nasal polypectomy	B	15
11.	Septoplasty	B	20
12.	Hymorotomy (Caldwell-Luc surgery)	B	10
13.	Frontal sinus puncture	B	10
14.	Fractures of the nose	B	20
15.	Dissection of a hematoma of the nasal septum	B	10
16.	Assessment of airway patency in newborns and children	B	10
	Total		310

Table III. Distribution of questionnaire participants depending on experience by specialty

GROUPS	NUMBER OF RESPONDENTS
interns of the first and second year	39
doctors with experience of up to 3 years	12
doctors with more than three years of experience	10

doctors according to the scale: (where 0 - it is difficult to answer, 1 - I have an idea, 2 - helped the doctor in conducting, 3 - conducted independently, 4 - mastered, 5 - fully mastered)

The results of self-assessments by interns of acquiring competencies and practical skills in performing the most frequently performed operative interventions in the ENT hospital are presented in Fig. 1.

According to the results of self-assessment by interns (learned and completely mastered), the following operative interventions have the most considerable part (the range of assessments is more than 70%):

- " Tympanopuncture " (75%),
- "Puncture of the maxillary sinus" (88%),
- "Correction of the bones of the nose" (88%).

At the same time, according to the results of self-assessment by intern doctors (learned and completely mastered), the following surgical interventions have the smallest part (range of assessments 50% and less):

- " Tracheostomy " (38%),
- "Tonsillectomy" (50%).

In addition, the questionnaire included one question on evaluating simulation training methods (on phantoms) by definition on a scale: (where -1 is not effective at all, to -10 is very effective) and questions in an open format for the interns to express suggestions.

The results of the evaluations of intern doctors are presented in Fig. 2.

The conducted survey showed that the use of simulation training methods (on phantoms) is very effective, according to intern doctors - 76% of respondents confirmed this.

In addition, the results of the survey of intern doctors showed that the factors that affect the possibility of obtaining practical knowledge and skills at the clinical base of internship are: access to patients during the educational process and the availability of sufficient amounts of medical assistance.

Simulation trainings for interns in the speciality "otorhinolaryngology" to master some practical skills (invasive and non-invasive interventions) related to direct contact with patients were held at the Department of Otorhinolaryngology (Bogomolets National Medical University) in 2021-2023. In addition, doctors-specialists with various years of experience in the speciality "otorhinolaryngology" were involved in conducting these trainings on a voluntary basis. The study of the opinion of the training participants was carried out by means of a questionnaire before and after its implementation regarding the level of mastery of practical skills. The distribution of simulation training participants depending on their experience by specialty is presented in Table III.

The survey was conducted according to a developed questionnaire with questions to assess the importance of factors that influence the organization of the process of the correspondence part of the internship at the clinical training base.

The doctors assessed their level of knowledge before the training center session regarding the performance of all the listed manipulations as requiring improvement.

After the class was held in the simulation center with the practice of a certain list of practical skills, a repeated survey was conducted. The results of the dynamics of self-assessments of intern doctors are presented in Fig. 3.

The analysis of the dynamics of self-assessment of the level of mastery of practical skills showed that the respondents estimated their level of mastery after the training was probably higher compared to the results of the initial questionnaire. General medical experience does not affect the level of mastery of practical skills in conditions without their permanent practice and improvement.

DISCUSSION

Adverse events caused by unsafe care are among the top 10 causes of death and disability. Some researchers put unintentional harm to patients in third place among the causes of death worldwide. Reports of the Organization for Economic Cooperation and Development showed that up to 15% of the funds allocated to inpatient medical care are lost on treating consequences caused by hospital patient safety incidents [11].

In the United States alone, losses related to unintentional harm to primary and outpatient care patients exceed a trillion US dollars. But amidst these disheartening statistics, there is compelling evidence that 83% of patient safety incidents are preventable.

Unfortunately, Ukraine's healthcare reforms only exacerbate unintentional patient harm. The rapid growth of inpatient and postoperative mortality rates in recent years can testify to the patient safety problems in Ukraine. In the conditions of a patient safety incident, the second victim is the medical worker involved in this incident, whose state requires psychological and legal support.

The leading role in the prevention of medical personnel errors belongs to education. Institutions of higher medical education at the postgraduate level in Ukraine need changes and additions to curricula and programs considering patient safety issues and the development of necessary educational and methodological materials [12].

It is necessary to provide conditions under which patient safety training would contribute to forming positive behavior (safety culture) in future medical professionals. Professors and teaching staff of medical educational institutions and employees of clinical bases should not only know the educational material and be professionals but also possess simulation training methods for safe medical practice.

Implementing new learning technologies using simulation methods and medical mannequins contributes to interns' formation, mastery, evaluation, and maintenance of professional skills.

CONCLUSIONS

An otorhinolaryngologist upon completion of internship training must possess a significant amount of practical

skills, both invasive and non-invasive interventions related to patient safety. When working independently in health care institutions of various forms of ownership and subordination, an insufficient level of ownership may lead to the risk of adverse events related to patient safety.

The results of the survey of intern doctors showed that the factors that influence the possibility of obtaining practical knowledge and skills at the clinical base of internship are: access to patients during the educational process, and the availability of sufficient amounts of medical assistance.

The use of simulation equipment and medical mannequins contributes to the continuous professional development of otorhinolaryngologists (acquiring modern practical skills, working out current protocols and standards of providing medical care to the population) and makes it possible to reduce the risk of defects in the provision of medical care, to prevent unintentional harm to patients at all levels of care.

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ORIGINAL ARTICLE

PROFESSIONAL TRAINING OF MASTERS OF DENTISTRY WITHIN QUARANTINE RESTRICTIONS AND MARTIAL LAW: A COMPARATIVE ANALYSIS OF EDUCATIONAL PROCESS

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ABSTRACT

The aim: To present a comparative analysis of the educational technologies effectiveness that were used in the process of professional training of masters of dentistry during quarantine restrictions and martial law.

Materials and methods: To perform the set tasks, the following the empirical methods of scientific research were used: quantitative data were collected based on analyzing the results of students' educational achievements, as well as implementing special questionnaire that was sent to the students of the Faculty of Dentistry of NMU; qualitative data were collected with the help of several focus groups formed from students and teachers of the faculty. Analysis was undertaken using statistical methods (Pearson's test), and qualitative data were analyzed descriptively.

Results: This paper analyzes the effectiveness of educational technologies used during quarantine restrictions and martial law, the role of phantom classes in providing professional training of dentistry specialists, summarizes the results of a comprehensive analysis of scientific literature, teaching experience at the dental faculty and the results of sociological research (student surveys, discussion in focus groups).

Conclusions: The outbreak of the COVID-19 pandemic and the full-scale war unleashed by the russian federation in Ukraine forced to quickly find and implement mixed forms of teaching future masters of dentistry, which, in combination with digital technologies, enables implementing high-quality and effective training.

KEY WORDS: Professional training, masters of dentistry, blended learning, distance learning, simulation training, special competence

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INTRODUCTION

The modern actuals have shown that high-quality professional training of healthcare specialists is particularly vulnerable to the conditions in which Ukraine has been forced into in recent years – the COVID-19 pandemic and russian large-scale invasion afterwards. One of the best tools in facing these challenges can be blended learning technologies in combination with digital ones. The wide use of digital technologies in professional training is also important because the healthcare industry is undergoing significant transformations, one of the determinants of which is the use of digital technologies in everyday medical practice. Modern dentistry is one of the leading medical specialties as for the implementation of transformative innovations. Moreover, it widely involves leading scientists in the development and improvement of digital equipment and methods of its application in various dentistry areas and at various stages of medical interventions: in diagnosis, planning, treatment, prevention, processing of results, etc. It is obvious that the use of digital methods has become the paradigm of the dental industry in the 21st century. Undoubtedly, the use of digital technologies in the professional activities of dentists should be reflected in corresponding changes of training specialists. Such challenges and technological innovations require constructive, didactically justified transformations in the educational process of training specialists at the dental faculties of higher education medical institutions, e.g., revising the programs of educational disciplines, forms and methods of teaching, updating the material and technical base of departments, creating university clinics, etc.

THE AIM

The aim of the article is to conduct a comparative analysis of the educational technologies effectiveness that were used in the process of professional training of masters of dentistry during quarantine restrictions and martial law.

MATERIALS AND METHODS

To accomplish the tasks set were studied of blended learning that used experimental and theoretical methods has been conducted. First, quantitative data were collected based on analyzing the results of students' educational achievements, as well as implementing special questionnaire that was sent to the students of the Faculty of Dentistry of NMU. Second, qualitative data were collected with the help of several focus groups formed from students and teachers of the faculty. These groups discussed and analyzed the peculiarities of organizing the educational process in extreme conditions: strengths and weaknesses, opportunities and cautions regarding the use of various blended learning technologies. The survey was organized online via Gmail, the discussions in focus groups were conducted full-time and via MS Teams. Quantitative data were analyzed using statistical methods (Pearson's test), and qualitative data were analyzed descriptively.

RESULTS

With the beginning of the COVID-19 pandemic, higher education institutions around the world faced globalization challenges, the solution to which was found through the remote form of organizing the educational process under quarantine restrictions. The restoration of traditional (analogue) forms and methods of education was apparently an inevitable process that took place gradually, taking into account the epidemiological situation, in attempt to preserve valuable positive experience gained during 2020 and 2021. The large-scale russian invasion of the territory of Ukraine broke off all the plans rudely and cynically. The terrorist country destroyed the path to the exit of the education system from the pandemic state, along which the country was moving with international educational academic community.

By the beginning of 2022, virtually all the teachers of dental departments of Bogomolets National Medical University had clear ideas about the organization of the educational process in the conditions of blended learning, tested approaches to special support that proved to be effective during the active phase of COVID, formed skills in working with various distance learning platforms, prepared educational and methodological materials in electronic and paper forms. However, the challenges that had to be faced required new non-standard solutions and special efforts to deal with them. In the period from February 28, 2022 to March 13, 2022, in accordance with the Decree of the President of Ukraine "On the introduction of martial law in Ukraine" dated February 24, 2022 No. 64/2022 [1] and the Letter of the Ministry of Education and Culture of Ukraine "On the organization of the educational process" dated February 25, 2022 No. 1/3277-22 [2], holidays were introduced for all programs at all levels of education. Furthermore, the educational process in a blended format was implemented continuously, with the exception of relatively short periods of time. The validity of this order was later extended to October 21, 2022. The unstable circumstances in which it was necessary to carry out every day educational process at the university since the beginning of the full-scale invasion forced the personnel to change approaches very quickly. Stress resistance, adaptability, and creativity became the traits that helped teachers to qualitatively reorganize and conduct classes under various circumstances (air alert, lack of electricity, mobile telephony, internet connection, etc.), choosing appropriate forms and means while taking care, first of all, of the safety and health of students.

The development of a blended form of educational process (online and full-time studying) has acquired special significance, becoming an urgent requirement of the time and the only possible way of training qualified specialists in the field of health care in wartime conditions. Digital and blended learning technologies have become a powerful tool in confronting the challenges faced by the Ukrainian medical education system in recent years.

An important element was involving the students in decision-making processes, which fully corresponds to the principle of "student-centeredness" and helps to effectively take into account students' offers. In a short period of time, a flexible system of online and offline meetings was implemented, which helped to achieve a balance in the level of feedback received from students.

Next, a survey of dental faculty students using Google forms was conducted. Those were related to the assessment of the approaches, methods, and means of organizing the educational process (which were tested during quarantine restrictions and martial law) and the prospects for their development and improvement. The questionnaire was sent to 70 students of 3rd, 4th, and 5th grades, and 56 of them sent complete answers. According to the results of the survey, 78% of respondents consider it expedient to introduce separate selective disciplines aimed at forming the digital competence of the future dentists. It is important to distinguish the presence of skills covering five spheres of human activity being oriented towards information literacy, communication and cooperation, creation of digital content, security tools and strategies, creative use of digital tools for problem solving and creativity in the digital competence of a modern doctor [3]. Thus, three groups of skills that differed in the level of their application in professional activity were

identified. These are basic skills of a general nature, namely those required for effective daily work and communication (searching and evaluating information, organizing digital security activities, working with Google survey forms, Excel and PowerPoint skills, working with Google Meet platforms and Zoom, etc.); professionally oriented skills of a general nature (work in medical information systems, DICOM, e-Health system); and special skills determined by the specifics of the specialists' professional activity, their specializations, and positions occupied. It was necessary to investigate the students' opinions on these groups of skills with the help of a questionnaire and to understand what skills are primarily to be further shaped and developed. More than 70% of respondents consider it necessary to have special professional digital skills that will enable them to use digital technologies for diagnosis and treatment planning in their own dental practice. In the comments, many students added that the use of digital technologies in dentistry can ensure "high accuracy of data acquisition" (56% of them) and "convenience for both the patient and the doctor" (51%). The vast majority of respondents (91%) noted that they have sufficient awareness in the field of general skills.

According to medical students' opinion, among the latest technologies, the most effective one is working in a phantom class, which is a kind of simulation center for applying practical skills. Hence, 86% of respondents consider it appropriate to use phantom classes to practice medical manipulations. Therefore, 75% believe that the skills learned while working in phantom classrooms will become fundamental in their future professional activities. The vast majority of interviewees considered the following main advantages of working in simulation classes: "absence of risk for the patient" (90%), "an unlimited number of attempts to practice medical manipulations" (95%).

A number of offers related to the form of study at the Faculty of Dentistry were also made: traditional (auditorium training), remote (online), and blended. Next, 92% of respondents preferred a blended form of study while answering the following question: "Which form is the most effective for the professional training of a future doctor?" In their opinion, the main advantages of a blended form of education are "flexibility of the educational process", "accessibility", and "increased motivation to study". This result is fully consistent with the assessment of the "American Society for Training and Development", which identified blended learning as one of the top ten trends in education [4] and predicted 80-90% of its use among all educational courses in the near future.

According to teachers, the main advantage of blended learning is the possibility of combining interchangeable tools and methods of learning, which ensures the flexibility and efficiency of the latter.

Naturally, the format of training and the method of organizing feedback have an impact on educational achievements (the acquisition of clinical skills primarily) and the psychological state of dentistry students. With distance learning only, the students demonstrated a decrease in success level, growing sense of insecurity, and deterioration in communication skills. The severity of the problem was partially decreased when focus groups shifting from distance learning to auditorium and blended one.

During the period of martial law, the intensity of the use of digital laboratories and simulation centers increased, and the classes were held in group rotation mode on the basis of the Dental Medical Center of Bogomolets NMU. The technical tools used in dental digital laboratories can vary from standard, easy to purchase and use ones to quite complex systems of patient simulators or virtual reality devices and holographic images of three-dimensional objects. The laboratory of computer modeling and digital technologies of the Dental Medical Center of Bogomolets NMU has the following equipment: a laboratory 3D scanner, a CAD/CAM milling machine, a 3D printer, etc. Additionally, the dental center is equipped with three phantom classrooms, each having 12 dental phantom heads with models of jaws, necessary dental equipment, and a multimedia system for conducting theoretical classes.

The structure of a typical class involving a digital laboratory, a dental phantom class, a multimedia system, and students' personal computers will be shown below with the use of an example. The developed method of conducting "Indirect placement of braces with the involvement of digital technologies" class involves implementing an activity change algorithm, mixing online and classroom training, content of the LIKAR_NMU corporate network, and independent and group training. Students master the basic theoretical knowledge on their own in the mode of the flipped class according to the recommended plan and information resources, and the practical component is exercised directly in the digital laboratory and phantom classroom. There are four stages in the structure of the 6-hour lesson on the specified topic, which is held for 4th grade students of the Faculty of Dentistry:

1. A short discussion
2. Work in a digital laboratory.
3. Work in a phantom classroom.
4. The final stage solves two tasks: objective assessment of the knowledge and skills acquired by students (test control is often used); generalization of acquired knowledge and skills, analysis of typical mistakes (conducted as a discussion).

Due to the objective circumstances of learning under martial law, it was sometimes necessary to change the above order of the lesson stages implementation, to reduce the time

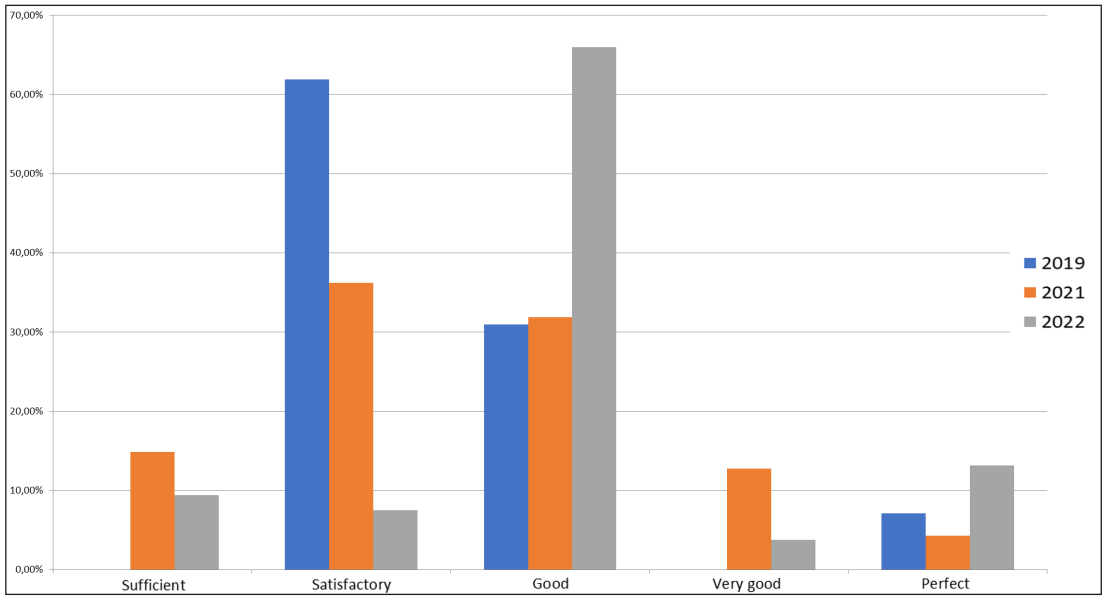

Fig. 1. Distribution in the studied groups after the pedagogical experiment

Table I. The results of data processing after the implementation of pedagogical experiment

№	Groups	χ^2_{exp}	χ^2_{cr} (α = 0,05)
1.	2019 (full-time studying) / 2021 (blended studying, quarantine restrictions)	14,993	9,488
2.	2019 (full-time studying) / 2022 (blended studying, full-scale war)	33,999	9,488
3.	2021 (blended studying, quarantine restrictions) / 2022 (blended studying, full-scale war)	21,397	9,488

of working in a phantom classroom or digital laboratory, to shift the discussion to independent work with individual (or small group) counseling. The students' opinions regarding these forced (due to air alertsraids, power outages, etc.) transformations were also interesting for the study. Only 10% of respondents believe that the order of actions does not matter, while the vast majority (86.6%) would prefer the abovementioned logical sequence. Moreover, many students also noted the positive role of working in digital laboratory and phantom classroom, mentioning their importance for shaping a practical component of professional competence and confidence in one's own actions. The respondents positively accessed the quality of theoretical material offered for independent study, with the vast majority of students considering it as "good" or "excellent", with 96.6% of the material rated in one of these two categories. Only 1.6% of students indicated that the content of the materials was poorly structured and not logically presented. The fact that the method of indirect braces positioning with the involvement of laboratory scanners and specialized software has become widely used among practicing orthodontists was important for the students as well. This method demonstrates precise positioning accuracy, due to which the process of orthodontic treatment becomes more advanced, comfortable, and faster for patients.

The analysis of the educational achievements of medical students at the department of orthodontics and propaedeutics of orthopedic dentistry was conducted. Three homogeneous samples of students were formed, whose education was realized differently: classroom form of education (2019) – group I, blended form of education with a predominance of distance learning during the period of quarantine restrictions (2021) – group II, blended form of education in the period of full-scale invasion (2022) – group III. To compare the results, the total points of current success, points of assessing practical skills, points for passing the test, and points for creative theoretical works (professional cases) were taken. It is worth mentioning that a pairwise comparison of the entrance control results of student groups proved the statistical homogeneity of the samples at the beginning of studying the "Orthodontics" academic discipline.

In order to test the null and alternative hypotheses after the pedagogical experiment, the χ^2 criterion was used since: the samples are random; the samples are independent, and their members are also independent from each other; the measurement scale is a 5-category designation scale. A comparison of the educational achievements results (Figure 1) gives reasons for rejecting the null hypothesis H_0 and indicates the presence of statistically significant differences in the studied student groups (Table I) at the level of significance $\alpha = 0.05$ and $\nu = 4$.

Upon completion of studying the discipline, 14.9% of the sample group II and 9.4% of the sample group III had a sufficient level. A satisfactory level was demonstrated by 36.2% of group II and 7.5% of group III. 31.9% of the students of group II and 66.0% of group III had the total points corresponding to the "Good" level. 12.8% of the students of group II and 3.8% of group III received the rating "Very good"; respectively, 4.3% of group II and 13.2% of group III had "Excellent" mark. The difference in the percentage ratio within the groups is explained by the increase in the number of students with a higher level of educational achievements.

DISCUSSION

The conducted analysis of students' success gave reasons for making an assumption that a didactically justified, balanced, and adapted to the requirements of the time combination of forms and methods of blended learning, classes in the digital laboratory and in the simulation, center is able to ensure the proper theoretical and practical preparation of dentistry students for mastering the professional basics of their future profession.

The share of classroom activities and face-to-face communication have increased in the conditions of martial law. This contributed to restoring the sense of confidence in one's own abilities, integration into the educational community, demand and security and, presumably, was partly reflected in the academic achievements of students. Indeed, the researchers argue that the sense of confidence is central to personal development and continuous learning. This, firstly, leads to an improved ability to perform tasks; secondly, the confidence is a product of relationship and trust of the people associated with a person or professional; and, thirdly, the right level of challenge is important for confidence [5].

Comparing the peculiarities of education during the period of quarantine restrictions and martial law, the majority of respondents and the analysis of statistical data indicate an improvement in the students' educational achievements. The reasons for this fact are not entirely clear at the moment. Apparently, one of them implies that learning acquires features of inclusiveness in such conditions, and the synergy between theoretical online learning and practical acquisition of clinical skills is significantly enhanced. Other researches obtained similar results, for example, educational model developed in Singapore during the active phase of the pandemic, which combines traditional (analogue) and digital educational technologies [6], achievements of our colleagues [7-11] and other authors [12].

A special feature of wartime education war is that the proportion of students who work in practical medicine, primarily on a volunteer basis in a military hospital, increases significantly. A great number of injured people require the intervention of specialists in maxillofacial surgery, orthodontics, gnathology, etc. This provides many specific professional cases that students try to formulate independently and bring to the classroom for joint discussion and consideration. At the same time, it stimulates emotional involvement in the learning process and the growth of motivation, which is the basis of increased students' confidence.

During the period of martial law, the technologies of blended learning acquired development and transformational changes, both in terms of methods of combining traditional and distance methods and in the use of digital potential of higher education along with traditional forms and means of education.

All this enables achieving the results that are comparable (or even better in some cases) than the ones before 2020. This improvement inspires optimism, but the long-term impact of extreme conditions on the education of dental students, especially on such aspects as the practical component of professional competence, communication skills, etc., requires time-deferred studies.

CONCLUSIONS

The outbreak of the COVID-19 pandemic and the full-scale war unleashed by the russian federation in Ukraine forced to quickly find and implement mixed forms of teaching future masters of dentistry, which, in combination with digital technologies, enables implementing high-quality and effective training.

The wide implementation of online and mixed forms of education has a significant impact on the psychological state of students and requires research and development of adaptive methods that correspond to new psychological and pedagogical conditions of implementing the educational process.

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ORIGINAL ARTICLE

PSYCHOEMOTIONAL PROBLEMS OF PARTICIPANTS IN THE EDUCATIONAL PROCESS UNDER MARTIAL LAW: FROM EMERGENCE TO OVERCOMING

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ABSTRACT

The aim: To study the peculiarities of psycho-emotional problems and needs of the subjects of the educational process and to determine the priority areas of their psychological and pedagogical support in the conditions of martial law.

Materials and methods: To update the aspects of the problem, we used the methods of analysis of normative and scientific sources, system analysis and generalizations, the results of our own empirical studies, materials of the questionnaire, to study the specifics of psycho-emotional problems and needs of the subjects of the educational process.

Results: The problem of socio-psychological protection and support of all participants in the educational process in the conditions of martial law, especially children, is extremely important. Challenge for schools in Kyiv is the organization of the educational process for children who are abroad but continue to obtain general secondary education according to Ukrainian educational standards and programs. This ensures the realization of their constitutional right to education and demonstrates certain support for our citizens who do not yet have the opportunity to return to Ukraine.

Conclusions: Considering the massive nature of traumatization of the population during military operations, there is a need to involve social institutions in the maintenance of public health, for which assistance to the population is not the main function, but which they can perform in these extraordinary circumstances. This can form the basis for establishing psychological and pedagogical support for war-traumatized children and adults.

KEY WORDS: public health, consequences of war, psycho-emotional states, psycho-education, social-emotional skills

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INTRODUCTION

In the conditions of war, the importance of the interaction of social institutions in ensuring public health is increasing. The American Public Health Association (APHA) issued a Political statement «The Role of Public Health Practitioners, Academics, and Advocates concerning Armed Conflict and War», which states that doctors and educators can play an important role in preventing war, as well as in mitigating its consequences [1]. The education system has one of the leading roles in supporting public health. Teachers, students, their parents and relatives, educational psychologists, and social pedagogues, experiencing traumatic effects as a result of military actions, at the same time are a significant social resource for their minimization and overcoming.

The Office of the United Nations High Commissioner for Human Rights recorded that during the year of the large-scale armed attack by the Russian Federation, which began on February 24, 2022, Ukraine lost 21,580 civilians, including 8,101 dead and 13,479 wounded. Among the killed were 3,584 men, 2,127 women, 256 boys, and 201 girls, as well as 31 children and 1,902 adults, whose gender is still unknown. Among the injured were 3,536 men, 2,421 women, 398 boys, and 293 girls, as well as 271 children [2]. The psychological well-being of adults and children is also affected by the death or maiming of their relatives and friends who resisted Russian aggression in the armed forces.

According to studies conducted in various countries, military actions cause psychological consequences, including mental health problems, provoking post-traumatic stress disorder (PTSD) (15-42%), depression (16-68%), anxiety (60 -72%), and other disorders [3]. It was found that the psychological problems of parents can affect children, primarily this concerns parents with post-traumatic stress disorder [1, 4].

It has been established that psycho-emotional problems are also experienced by those children who left the places of active hostilities to other cities or countries. The anxiety for relatives and friends who have remained is deepened by the difficulties of adaptation to a new sociocultural and linguistic environment and the uncertainty of the future [5]. One of the first Ukrainian studies, conducted shortly after the beginning of the Russian aggression, in March 2022, showed manifestations of psychological problems among internally displaced persons. It was found that two-thirds of the respondents (67.1%) experienced fear, almost half experienced panic (47.0%), and slightly less than a third experienced shock (30.9%) [6].

A survey of teachers, students, and parents, which was conducted in Ukraine a month after the beginning of large-scale Russian aggression, revealed problems in interpersonal interaction (family conflicts, difficulties in communicating with friends and establishing contact); difficulties in emotional regulation, constant or prolonged experiences of fear, anxiety, despair, sadness, guilt, mood swings, inhibition, drowsiness, headache, tachycardia, appetite disorders [7].

Power outages due to Russia's periodic missile attacks on the infrastructure of Ukrainian cities also affect the mood and well-being of children. It is not only about everyday problems or the impossibility of studying (even remotely, due to the lack of an Internet connection). Every blackout is a reminder that a missile strike is about to happen again and there is a real danger of dying far from the front line, in any corner of the country. Kokun's study [8], conducted during the seventh week after the beginning (from October 10, 2022) of massive missile attacks and drone attacks on the energy infrastructure of Ukraine, showed that 70% of respondents had a worsening of their well-being. The negative psychological consequences of power outages were manifested in sleep disturbances, depressive tendencies, increased levels of irritability, and aggressiveness.

As a result of a sociological survey of 2,000 respondents at the end of January 2023, it was found that traumatic mental states in Ukrainian children of middle and high school age manifest as irritability, apathy, indifference to learning, and former hobbies, and problems with memorization and concentration. Outbursts of anger and aggression are a relatively common problem. High school students (16-17 years old) show signs of anxiety, such as fear of the future, sleep problems, and terror. The youngest children reflect traumatic events in games and creativity. According to the mothers, children were significantly traumatized in the following situations: parting with family and friends (28%), moving to another region of the country (25%), shelling and bombing (24%), staying in a cold room for a long time (17%). Among those surveyed, 11% moved abroad, 8% were under occupation, 6% witnessed the death of relatives or loved ones, 5% lost their homes, and 5% experienced hunger and lack of water [9].

Based on the analysis of scientific literature, Ukrainian researchers Zlyvkov et al. distinguish two main approaches to psychological assistance for children who are traumatized by the war: «the first is trauma-oriented and emphasizes the need to overcome (treat) the traumatic experience so that children get rid of their traumatic memories as soon as possible and continue to live their natural childhood life; the second is preventive, instead of focusing on experience, interventions are aimed at solving current problems of children so that they can adapt to a maximally productive life in a safe place» [10].

Examples of a trauma-oriented approach are trauma-focused cognitive-behavioral therapy (TF-CBT) and the eye movement desensitization and reprocessing method (EMDR) [11].

The preventive approach is based on proactive interventions aimed at preventing injury or minimizing the consequences of injury when it cannot be avoided. It is natural for the education system, as it is based on the process of spreading knowledge, skills, and values. Wolmer et al. prove that «a teacher-mediated, protocol-based intervention focused on resilience enhancement is an effective method to grant students coping skills to help them face daily stressors and transfer the knowledge to cope with severe life events, process them, and recover swiftly to regain normal routine» [12].

An example of the implementation of this approach is the Stress Inoculation Training (SIT), developed by Meichenbaum [13, 14]. SIT has repeatedly proven its effectiveness. SIT consists of several phases: educational, aimed at understanding the nature of stress and the predictability and control of its consequences; phases of the formation of skills to reduce anxiety and affective behavior in stressful situations; and coping phases under conditions of simulated stressogenic influences. Wolmer et al. [12] within SIT offer an instructional protocol consisting of fourteen 45-minute didactic modules and provides 20 hours of training for school counselors and 4 hours for teachers. As noted by Werner [15], school-based interventions implemented by teachers or trained local professionals have proven to be a viable and inexpensive alternative to individual or group therapy.

THE AIM

To study the peculiarities of psycho-emotional problems and needs of the subjects of the educational

process and to determine the priority areas of their psychological and pedagogical support in the conditions of martial law.

MATERIALS AND METHODS

Information collection method: an online survey. Questionnaires were opened using Internet links that were placed on the main page of the KNP website «Educational Agency of the City of Kyiv» (https://monitoring.in.ua). As part of this survey, questionnaires were developed for four groups of respondents: 1) students of grades 8-11 of general secondary education institutions (GSEs) in Kyiv; 2) parents of students of grades 1-11 of GSEs of Kyiv; 3) teachers of GSEs of Kyiv; 3) directors of the Kyiv City Public Health Service. 61,023 respondents took part in the survey, among them: 10,370 students of grades 8–11, 44,651 parents of students, 5,625 teachers, and 377 directors of community-owned preschools. Survey period: November 4, 2022 - November 15, 2022. The research was conducted by the Analytical Center «Education Analyst» of the Borys Grinchenko Kyiv University in partnership with the KNP «Educational Agency of the City of Kyiv».

RESULTS

The problem of socio-psychological protection and support of all participants in the educational process in the conditions of martial law, especially children, is extremely important. The relevant issue could not pass by the attention of educators and psychologists, as the prolonged stay of children in a state of severe stress, caused by the loss of a sense of security and confidence in the future, can lead to serious consequences.

To the question «What help do you need today?» teachers and students revealed a significant demand for emotional support, psychologist's advice, and other forms of social-emotional support. As shown in Figure 1, 26.2% of students noted the need for adult support; 11.4% need support from teachers; 23.6% need the advice of psychologists, and 38.8% lose motivation to study and need appropriate advice. As for teachers, 34.6% of them also need emotional support, 10.1% need advice from psychologists, 13.7% need psychological support from the administration of the educational institution, and 33.1% of teachers need to share experiences with colleagues, 8.5% – methodical assistance of the administration of the educational institution. The latter is quite relevant for teachers because 74.8% noted a significant overload at work, which also affects emotional and mental health. This is also correlated with parents' assessments of targeted socio-psychological assistance to children. 19.9% of parents believe that their children need emotional support, and 17.2% seek to receive appropriate advice from specialists on maintaining children's mental health.

The primary task of the educational community of Kyiv today is to provide emergency aid and psychological support to children, which will allow them to cope with the stress of the war, as well as prevent the emergence of more complex problems. An additional challenge for schools in Kyiv is the organization of the educational process for children who are abroad but continue to obtain general secondary education according to Ukrainian educational standards and programs. This ensures the realization of their constitutional right to education and demonstrates certain support for our citizens (parents, children) who do not yet have the opportunity to return to Ukraine.

Most of the interviewed respondents who are students of Kyiv schools live with their families in Germany (32.9%), Poland (17.4%), the Czech Republic (5.1%), Great Britain (4.9%), and in other countries. According to the results of their survey, it was established that 46.7% of them are not yet studying in local schools, and 26.6% are already fully educated in the school of the host country, 15.5% are studying only a foreign language. 25.7% of respondents reported opening Ukrainian-language classes abroad in local schools, which allows them to gently adapt to a foreign-language educational environment, reduce stress, preserve the language, national culture, etc., as well as integration classes where there is no assessment and children learn the language of the host country.

The education of children who simultaneously acquire general secondary education abroad and in Kyiv schools has its advantages and disadvantages. On the one hand, these children socialize and adapt more quickly to another intercultural environment, learn the language of the host country, communicate with other peers, and study in an educational environment that differs from the domestic one. And on the other hand, they experience significant mental stress. New language environment, educational overload (from the morning studying at a local school, and then studying in an online format at a Ukrainian school, or independently with parents). Therefore, studying under two programs takes away all their free time, overloads the psyche, slows down physical development, etc. The above cannot be ignored by the teacher when conducting online lessons with such children.

The group of students also changed due to new ones who moved to Kyiv from temporarily occupied territories or from those where active hostilities are taking place. Only 1% of schools do not have a single

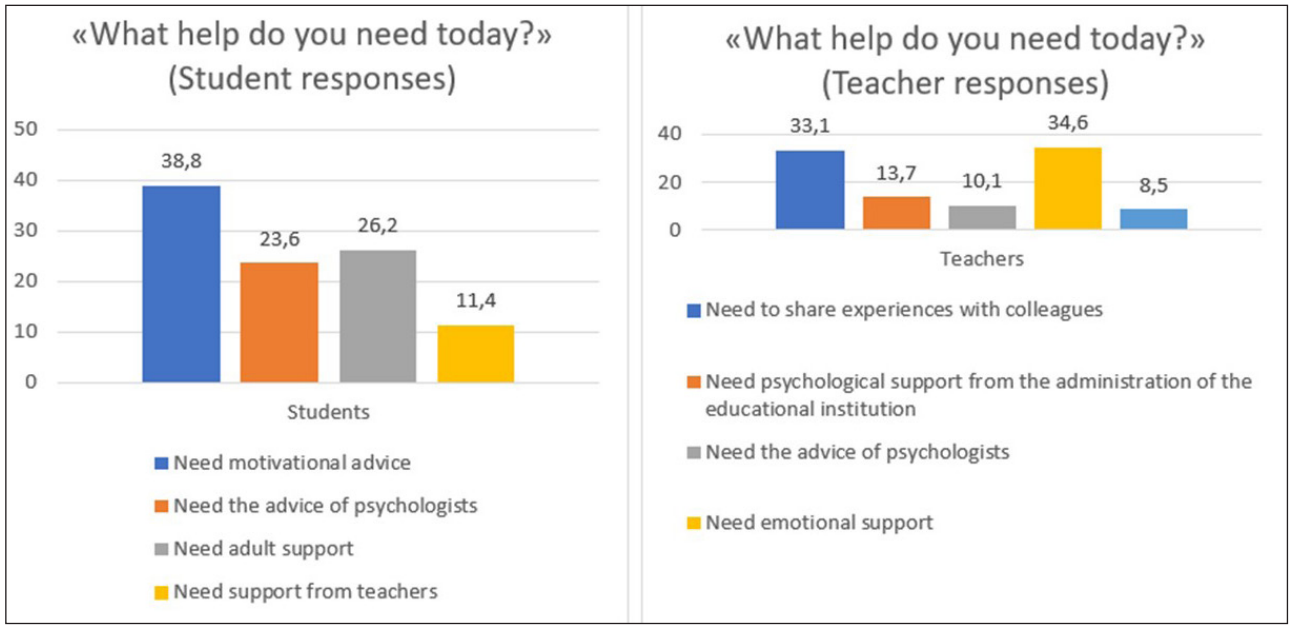

Fig.1. Distribution of students' and teachers' answers to questions «What help do you need today?»

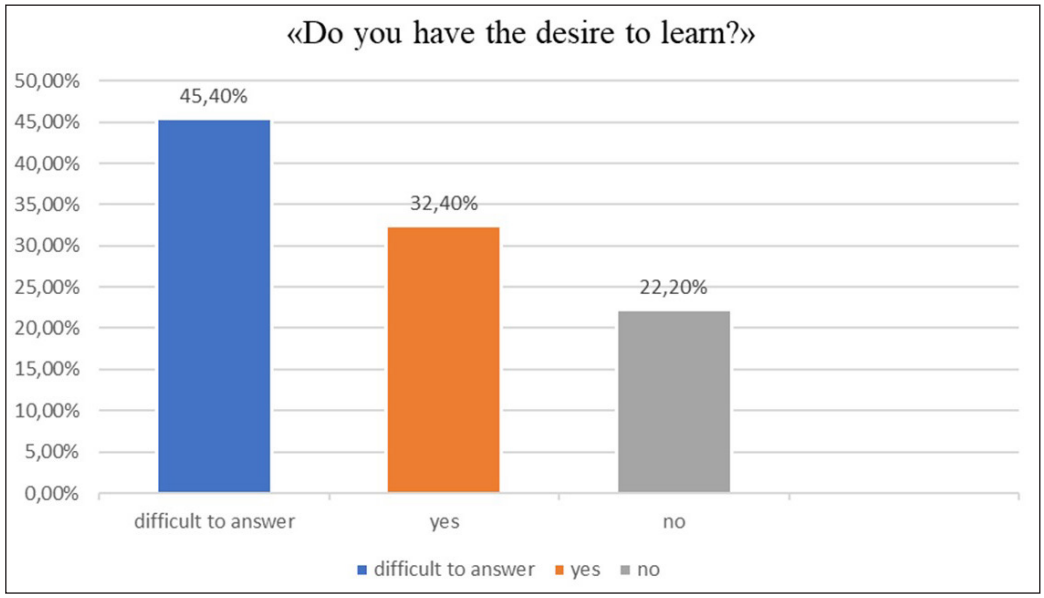

Fig. 2. Distribution of students' answers to questions «Do you have the desire to learn?»

such student. The rest of the schools have: from 31 to 50 students - 22.7%; from 11 to 20 - 22%; from 1 to 5 – 17.4%; from 51 to 300 – 11.2%; from 6 to 10 - 9.5% of schools. These children have varied experiences of the impact of war, from the most tragic to the need to move to a safe place. Everyone has their psychological trauma.

Analysis of students' motivation for learning in difficult conditions of martial law, increased anxiety, uncertainty, and tension of the situation also affected its character. Thus, to the question «Do you have the desire to learn?» the majority of students (45.4%) found it difficult to answer, and 22.2% expressed their reluctance to study in such conditions. Only 32.4% of respondents confirmed their desire to study. In our opinion, not only external factors but also internal factors affect the decrease in students' motivation to study. Because the education of an individual at school coincides with the period of development of his/her social emotions, the need to communicate with peers, etc. However, in the conditions of distance learning, these social and psychological needs of students are not always fully met.

Heads of general secondary education institutions, realizing the importance of this problem, strive to constantly organize such work in schools. Thus, 92.9% of directors noted that in the institutions headed by them, measures were organized to provide psychological assistance to participants in the educational process. However, according to students' estimates, the school does not hold such events (27.8%), most children were not interested in such events (55.7%), and only 4.3% were participants in such events.

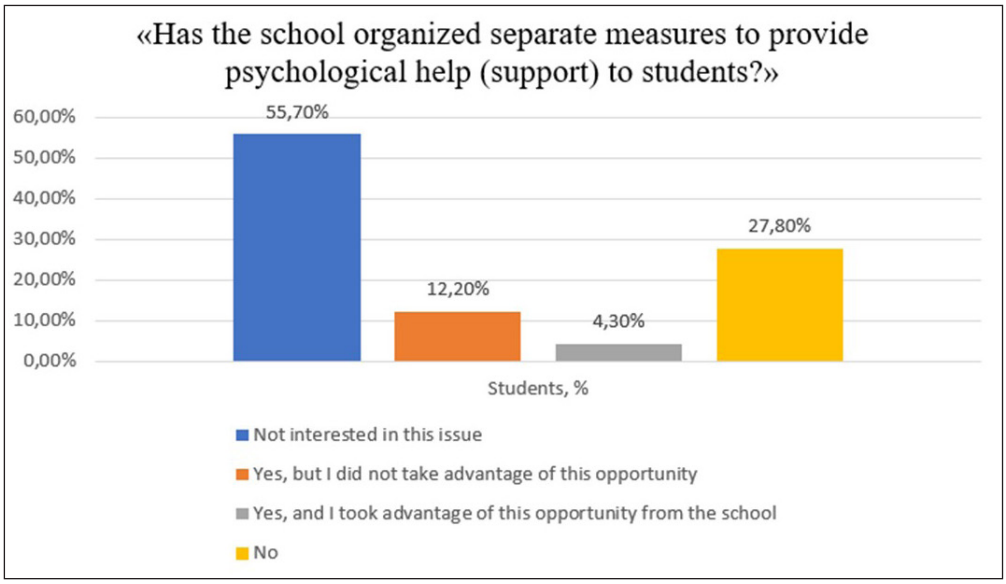

Fig. 3. Data on the organization of measures to provide psychological support.

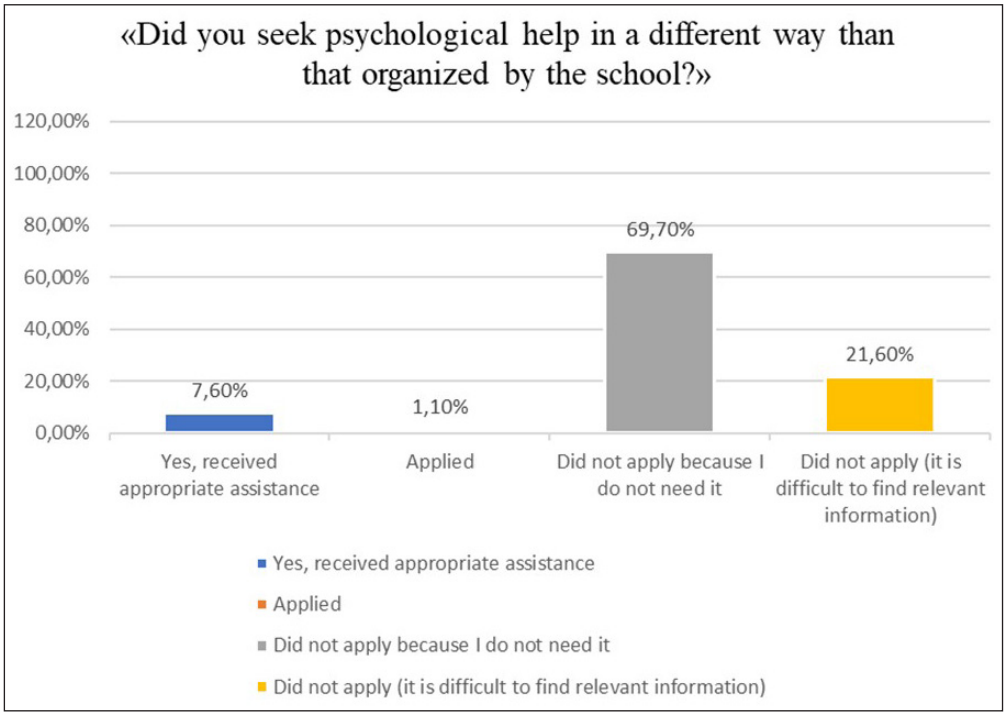

Fig. 4. Distribution of teachers' answers to questions «Did you seek psychological help in a different way than that organized by the school?»

The analysis of teachers' answers showed that the school had organized psychological support for teachers, but they did not take advantage of this opportunity (50.0%), and a little more than 30.0%, on the contrary, were participants in psychological consultations and training. 69.7% of teachers indicated that they also do not need psychological support that can be provided outside the school. Only 7.6% of teachers needed such help and received it in another way. Work on providing psychological support to all subjects of the educational process cannot be formal. After all, the heads of educational institutions determined in the questionnaires a sufficiently high indicator (92.9%) regarding their organization of measures to provide psychological assistance to the participants of the educational process. At the same time, teachers and students were not always informed about such events, so they did not participate in such events, although they need psychological support. It is also urgent to identify specific psychological problems of participants in the educational process, establish their nature and provide targeted assistance.

To the question «Does the school organize measures to provide psychological assistance (support) to participants in the educational process?» 93% of respondents-directors answered optimistically «yes» and 7% - «no».

As for the teacher respondents, their answers to the question «Did the school organize separate measures to provide psychological help (support) to teachers?» were distributed as follows: 31% answered «yes, I used it»; 47% - «yes, but I didn't use it»; 22% - «no».

Accordingly, student respondents answered the question «Has the school organized separate measures to provide psychological help (support) to students?». 55.7% of students answered that they were «not interested in this issue»; 12.2% - «yes, but I did not take advantage of this opportunity»; 4.3% - «yes, and I took advantage of this opportunity from the school»; 27.8% - «no».

It should be noted that the answers of different groups of respondents to the mentioned question differed significantly. In particular, the answer «no» was given by only 7% of respondents-directors, but this answer was given by 22% of respondents-teachers and 27.8% of respondents-students. Therefore, it can be concluded that representatives of the school administration are somewhat embellishing the situation. Perhaps the interested parties were not sufficiently informed about the possibility of involvement in measures to provide psychological assistance (support). In any case, the provision of psychological assistance (support) to the participants of the educational process in the conditions of martial law is an important and necessary component of the activities of general secondary education institutions and requires special attention. The students themselves feel stressed and, as a result, quickly get tired. But teachers, like other participants in the educational process, can use psychological help outside the general secondary education institution, therefore, during the research, the teacher respondents gave answers to the question «Did you seek psychological help in a different way than that organized by the school?». The answers to this question were distributed as follows: 69.7% - «did not apply because I do not need it»; 21.6% - «did not apply (it is difficult to find relevant information)»; 7.6% - «yes, received appropriate assistance; 1.1% - «applied».

The results of the survey demonstrated the importance of timely assistance and psychological support to all subjects of the educational process, which should become mandatory elements of the educational process and should not be of a formal nature.

DISCUSSION

War with its inherent dangers and the proximity of hostilities has a significant impact on the mental and psychological health of both children and adults. Conditions that pose a danger to life and health are a source of constant stress for all participants in the educational process. Therefore, timely psychological help and social-emotional support can minimize the harmful effects of stress on the human psyche.

Important in this context is the monitoring of the psycho-emotional state of teaching staff and students, the main tools of which are observation and conversation, and the use of valid and reliable methods approved by the professional community. It is urgent that school psychologists work in cooperation with parents. At the same time, they retain the right to choose a specialist - a psychologist and the place of receiving the appropriate help. The task of the general secondary education institution is to convince parents of the importance of timely referral to a specialist to prevent possible psychological problems in children. At the same time, the relevant institution should not remove itself from the socio-emotional support of students, children remain in the attention zone, and changes in their psycho-emotional state are monitored [10].

In our opinion, it is also worth paying attention to the potential of extracurricular education as a factor of psychological relief, and the introduction of new forms of it regarding the collective and individual participation of children.

In turn, we recommend:

• to carry out constant communication with all participants of the educational process regarding the organization of the educational process in the conditions of martial law, using its various forms;

• to continue the practice of conducting "psychological support minutes" for employees of general secondary education institutions and "psychological minutes" for students to strengthen the mental health and improve the psychological culture of all participants in the educational process;

- to diversify the forms of extracurricular education as a factor in the psychological relief of students, taking into account the peculiarities of the organization of the educational process in a mixed format. It is appropriate to involve students in various forms of creative, project, and volunteer activities, as well as the organization of thematic exhibitions, humanitarian actions, etc.;
- to determine one of the important directions of the work of the psychological service of educational institutions - educational activity, which should be aimed at increasing the competence of participants in the educational process (in particular, teaching staff) in the context of providing psychological first aid and mastering modern technologies of such aid, teaching methods of psycho-emotional stabilization concerning methods of psycho-hygiene, psychological support for children in a crisis period, support and recovery of their psychological health, providing knowledge to create a psychologically safe environment in an educational institution. To implement this direction of work through the teaching of educational material according to the programs of

optional courses, electives, and psychological and socio-pedagogical circles.

CONCLUSIONS

Considering the massive nature of traumatization of the population during military operations, there is a need to involve social institutions in the maintenance of public health, for which assistance to the population is not the main function, but which they can perform in these extraordinary circumstances. The education system covers a significant number of students and their families, it employs qualified teachers with a psychological and pedagogical education, and interaction has already been established between these groups. This can form the basis for establishing psychological and pedagogical support for war-traumatized children and adults.

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ORIGINAL ARTICLE

INDIVIDUAL FACTORS OF MEDICAL PHD STUDENTS' ENGLISH COMMUNICATIVE COMPETENCE

DOI: 10.36740/WLek202304113

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ABSTRACT

The aim: The paper is aimed to find correlations between English language communicative academic and medical competence components (theoretical, practical, and individual by certain methods), to improve design of the course "Academic English for PhDs in Medicine", its methods and strategy.

Materials and methods: The study sample includes postgraduate groups studying for PhD in Healthcare, aged 21-59 years, in Bukovinian State Medical University (39 respondents), Zaporizhzhia State Medical University (32 respondents), Kharkiv Medical Academy of Postgraduate Education (33 respondents), and Bogomolets National Medical University (318 respondents). The study was held in 2019-2023. We assessed theoretical and practical components using our tests, individual component – psychological methods. The values of three components were transformed into general English communicative academic and medical competence level. The data were treated with SPSS Statistica 18.0, using Spearman correlation significance.

Results: We found positive correlation between English communicative competence and communicative tolerance, general communicative skills level, and high or medium communicative control level. Also, positive correlation characterizes interaction as a conflict-resolving strategy and communicative competence. Highly manifested intolerance in communication, predominance of negative mindsets, intolerance to stress negatively affect the level of English communicative academic and professional competence of PhD students.

Conclusions: Analysis of the English speaking competence, and its components, showed positive correlation between interaction as a conflict-resolving strategy and English communicative competence of respondents.

Regarding the results, the curriculum of the "Academic English for Medical PhDs" should be modified, including interactive methods, case studies, problem solving, and other methods for individual component training.

KEY WORDS: Communicative competence, medical PhDs, academic English, individual psychological characteristics

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INTRODUCTION

The course "Academic English for future PhDs in Medicine" teaches general, academic and medical English, and aims to shape English language communicative academic and medical competence of attendees. The course is taught during the first medical PhD year, as prepares audience for further interaction in academic and professional English-speaking environment. In 2018 a new concept of medical PhD training was accepted by the Ministry of Education, which necessitated introduction of course "Academic English for future PhDs in Medicine" into the PhDs curriculum. The authors have assessed levels of competence and competence components, and found correlations between components, to correct the course and improve methods of English language communicative academic and medical competence training.

Numerous authors define the communicative competence in different ways, which is proven in the review by V. Bagarić and J. Djigunović [1]. This is why English teachers emphasize training competence as a whole, and its separate components, like S. Savignon [2]. C. Howard states that difficulties of language course should be overcome regarding the attendees' perception of the course [3], which, according to J. Lourdunathan could be reached in interaction, using strategy training methods [4]. The knowledge how to organize such interaction, according to R.Chen, is based on individual peculiarities of the attendees, their communicative competence and communicative mindset, which may define communicative skills of them[5].

THE AIM

The paper is aimed to find correlations between English language communicative academic and medical competence components (theoretical, practical, and individual by certain methods), to improve design of

the course "Academic English for PhDs in Medicine", its methods and strategy.

MATERIALS AND METHODS

The study sample includes postgraduate groups studying for PhD in Healthcare, aged 21-59 years, in Bukovinian State Medical University (39 respondents), Zaporizhyzhia State Medical University (32 respondents), Kharkiv Medical Academy of Postgraduate Education (33 respondents), and Bogomolets National Medical University (318 respondents). The study was held in 2019-2023.

We assessed theoretical (knowledge which enables communication in English academic and medical environment), practical (skills of direct communication), and individual English communicative competence level (individual psychological traits which define productive theoretical and practical levels), to define general English communicative competence level, according to the author model by L. Lymar and K. Storozhuk [6]. A four-point grading scale was used, where 5 points mean high level, 4 points - good, 3 points - average, and point "2" - bad level of value. We assessed theoretical and practical components using our tests, individual component – psychological methods "Communicative and Organization Skills" (to diagnose general communication characteristics), M. Snider's "Communicative Control" (to diagnose academic and medical compliance and adaptation skills), V. Boiko "Communicative Tolerance" and V. Boiko "Communicative Mindset (to diagnose communicative strategies), and K. Tomas "Conflict Behavior" (to diagnose productive interaction skills). The values of three components were transformed into general English communicative academic and medical competence level. The data were treated with SPSS Statistica 18.0, using Spearman correlation significance.

RESULTS

The authors defined several correlations which justify development of individual psychological characteristics of medical PhD students within the "Academic English"

Table I. Correlations of communicative skills, theoretical component, practical component, and general level of English communicative competence (Spearman test)

		Theoretical component (knowledge)	Practical component (communication)	General level of com. competence
Communicative skills	Significance	0.001	0.001	0.001
	Correlation	0.556	0.645	0.797

Table II. Practical component of communicative competence and communicative skills values

Communicative skills level	Practical component level							
	High (44)		Good (173)		Satisfactory (190)		Bad (43)	
	Resp.	%, in subgroup	Resp.	%, in subgroup	Resp.	%, in subgroup	Resp.	%, in subgroup
High	26	59.1	13	7.5	1	0.5	0	0
Good	16	36.4	119	68.8	41	21.6	7	16.3
Satisfactory	2	4.5	41	23.7	133	70	24	55.8
Bad	0	0	0	0	15	7.9	12	27.9

Table III. Correlation of interaction, theoretical component, practical component, and general level of English communicative competence(Spearman test)

		Theoretical component (knowledge)	Practical component (communication)	General level of com.competence
Interaction	Significance	0.001	0.001	0.001
	Correlation	0.351	0.378	0.489

Table IV. Correlations of communicative control, theoretical component, practical component, and general level of English communicative competence (Spearman test)

		Theoretical component (knowledge)	Practical component (communication)	General level of com. competence
Communicative control	Significance	0.001	0.001	0.001
	Correlation	0.515	0.584	0.731

Table V. Correlations of "Communicative tolerance diagnostic by V. Boiko" and English communicative competence level components (by Spearman test)

		Theoretical component (knowledge)	Practical component (communication)	General level of com. competence
One's self-perception as a standard for others	Significance	0.001	0.001	0.001
	Correlation	- 0.313	-0.391	-0.473
Poor perception of others' individuality	Significance	0.001	0.001	0.001
	Correlation	- 0.460	- 0.587	- 0.691
Inability to hide unpleasant feelings	Significance	0.001	0.001	0.001
	Correlation	- 0.334	- 0.348	- 0.462
Intolerance to discomfort by the others	Significance	0.001	0.001	0.001
	Correlation	- 0.324	- 0.418	- 0.514

Table VI. Practical communicative competence level and communicative tolerance level values

Communicative tolerance level	Practical communicative competence component level							
	High (44)		Good (173)		Satisfactory (190)		Bad (43)	
	Resp.	%, in group	Resp.	%, in group	Resp.	%, in group	Resp	%m in group
High	37	84.1	70	40.5	14	7.4	3	7
Good	7	15.9	101	58.4	151	79.5	27	62.8
Low	0	0	2	1.1	25	13.1	13	30.2

Table VII. Correlation of general communicative tolerance level by V. Boiko, theoretical component, practical component, and general level of English communicative competence(Spearman test)

		Theoretical component (knowledge)	Practical component (communication)	General level of com. competence
Communicative tolerance	Significance	0.001	0.001	0.001
	Correlation	- 0.521	- 0.647	- 0.775

Table VIII. Correlations of negative communicative mindset by V. Boiko, theoretical component, practical component, and general level of English communicative competence(Spearman test)

		Theoretical component (knowledge)	Practical component (communication)	General level of com. competence
Hidden violence to others	Significance	0.001	0.001	0.001
	Correlation	- 0.376	- 0.429	- 0.529
Open violence to others	Significance	0.001	0.001	0.001
	Correlation	- 0.251	- 0.320	- 0.408
General communicative mindset	Significance	0.001	0.001	0.001
	Correlation	- 0.456	- 0.522	- 0.659

course. Analysis found positive moderate correlation of English communicative competence components, and communicative skills by "Communicative and Organization Skills" method (see table I). Respondents with high English communicative competence level have high communicative skills level, and vice versa. This proves that respondents with high communicative skills better acquire knowledge and skills of communicative interaction, and show them in academic and professional medical English interaction. Consequently, high communicative skills level predisposes for effective English language communication, so the course "Academic English for medical PhDs" should comprise interactive cases, aimed at communicative skills practice.

As table II proves, respondents with high level of practical competence show mostly high communicative skills (59.1%) and good communicative skills (36.4%). Respondents with good practical communicative

competence have predominantly good (68.8%) and satisfactory (23.7%), which proves necessity of training communicative skills, which may improve general communicative competence level. Consequently, those with bad communicative competence have primitive communicative skills level (satisfactory 55.8%, bad – 27.9%). We explain this by relation between communicative skills, ability to learn, and manifesting oneself in interaction, so, communicative skills need emphasis in postgraduate curriculum.

Also, analysis defined positive weak and moderate correlation of the English communicative competence and interaction by K. Tomas conflict behavior assessment (see table III). Respondents who choose interaction in conflicts have high communicative competence levels (high or good levels). This may show that interaction communicative style positively affects both English communicative competence, and its manifestations under academic or professional medical interaction, i.e., evidence about person's communicative effectiveness.

Positive moderate correlation of communicative control and general level of English communicative competence (see table IV) proves significance of self-monitoring and self-correction for respondents. The PhD students with high communicative control level showed higher communicative competence, so, high communicative control level stipulates for the high communicative competence of PhD students, and it should be emphasized in the course.

The analysis of "Communicative tolerance" by V. Boiko showed negative correlations, which proves positive communicative tolerant tendency due to peculiarities of the method. Negative medium and weak correlation of one's self-perception as a standard and English communicative competence level was found. This means, one's high opinion of himself is unfavorable for the respondent's high communicative competence, due to arrogant attitude which destroys productive academic and professional medical interaction (see table V).

The analysis also defined negative medium correlation of inability to perceive others and English communicative competence level, as respondents with prejudiced attitude to others generally show lower English communicative competence levels. Overall, high level of unprejudiced attitude positively affects general communicative competence of the respondent.

We found negative medium correlation of inability to hide one's negative feelings and English communicative competence level. High emotional control provides for high English communicative competence, and this quality should be trained during the course. Negative medium correlation of low tolerance to discomfort caused by other people and English communicative competence level proves that not only self-control. Respondents with high tolerance level also show high or good levels of English communicative competence, so tolerance as a trait of character needs emphasis during interaction at academic English classes.

As for general analysis of the communicative tolerance diagnostics by V. Boiko and communicative competence levels, negative strong and medium correlation of communicative tolerance and levels of communicative tolerance has been established (see table VII). The respondents with high communicative intolerance, show poor English communicative competence, and vice versa, which Table VI shows. In the group of respondents with high practical communicative competence level, 84.1 % showed high tolerance, and in good communicative competence subgroup the tolerance ranged from high (40.5%), to good (58.4%). This proves emphasis of the communicative tolerance, which provides higher communicative competence, as the speakers perceive the others without prejudice, with their drawbacks, aiming to set contact.

Analysis of negative communicative mindset and general English communicative competence level showed negative medium and weak correlation of hidden violence and English communicative competence levels (see table VIII).

The respondents with high level of hidden violence generally demonstrated low level of English communicative competence. Negative weak correlation was also detected between open violence and level of communicative academic and medical professional competence.

Negative moderate correlation was also revealed between general level of communicative negative mindsets and the English communicative competence level. Respondents with high negative communicative mindsets level showed the low level of English communicative competence, but those with high and good levels of communicative competence showed negative communicative mindset at low level. Suppose, low expression of negative communicative mindsets will provide better communication in academic and medical environment, which directly reflects in learning, and level of communicative competence.

DISCUSSION

Our study aimed to investigate the relationship between English communicative competence and other communicative factors in 422 medical PhD students. Our analysis revealed a positive correlation between high English communicative competence and communicative tolerance, general communicative skills level, and high or medium communicative control level. This correlates

with the general theory of successful teaching English and communicative competence training [2]. These findings suggest that a high level of English communicative competence plays a critical role in effective English language communication and should be emphasized during the postgraduate studies of medical PhDs.

Additionally, our research found that a positive correlation characterizes interaction as a conflict-resolving strategy and communicative competence, highlighting the importance of teamwork and small groups during the education of medical PhDs. On the other hand, high levels of intolerance in communication, negative mindsets, and intolerance to stress can negatively impact the English communicative academic and professional competence of medical PhD students, which was earlier suggested by J. Lourdunathan and S. Menon [4]. Such communication strategies are known to be destructive and can hinder successful academic and medical communication, which was proven in the authors' previous studies [6].

Based on these findings, we recommend that the curriculum of "Academic English for medical PhDs" integrate components that train communicative tolerance, skills, interaction, high communicative control, and positive communicative mindsets. The course should aim to minimize negative communicative mindsets and increase mind flexibility of medical PhDs via interactive training strategies, common goals between tutors and PhDs, case studies, and continuous interaction in the academic environment, as R.H. Chen recommends [5]. Additionally, author's training exercises and reflexive drills can be utilized to achieve these goals.

In conclusion, the results of our study emphasize the importance of English language skills, communicative tolerance, and positive communicative mindsets for medical PhD students. These findings provide crucial insights into designing effective curricula for academic and medical communication and can be utilized by educational institutions to develop training programs that enhance the communicative competence of medical PhDs.

CONCLUSIONS

New English Curriculum of training PhDs in Medicine necessitated introduction of course "Academic English for Medical PhDs" in 2017, which emphasized not only theoretical knowledge and practical skills, but a wider range of individual skills for the English communicative competence development.

English speaking competence comprises three components: theoretical (regarded as knowledge), practical (regarded as communicative skills), and individual one, which defines effective application of previous two.

Analysis of the English speaking competence, and its components, showed positive correlation between interaction as a conflict-resolving strategy and English communicative competence of respondents.

Highly manifested intolerance in communication, predominance of negative mindsets, intolerance to stress negatively affect the level of English communicative academic and professional competence of PhD students, and these characteristics should be corrected during the PhD study.

Regarding the results, the curriculum of the "Academic English for Medical PhDs" should be modified, including interactive methods, case studies, problem solving, and other methods for individual component training.

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ORIGINAL ARTICLE

EFFECTIVENESS OF USING THE BED FUND AND HUMAN RESOURCES FOR PROVIDING MEDICAL CARE TO CHILDREN WITH RESPIRATORY DISEASES

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ABSTRACT

The aim: Retrospectively evaluate the effectiveness of the use of beds and human resources for the treatment of children with respiratory diseases in hospitals in the period 2008-2021.

Materials and methods: We calculated indicators that characterize the efficiency of the use of bed and personnel resources: the density of beds per 10,000, the rate of hospitalized children per 10,000 (RH per 10,000), the bed occupancy rate per year (BOR), average length of stay (ALOS), full-time positions (FTP) per 100,000, number of beds per 1 FTP of doctors.

Results: During 2008-2021, there was a significant decrease in the density of all types of beds. The percentage of hospitalized children for inpatient treatment decreased, BOR decreased, and ALOS decreased. The density of full-time positions of allergists increased by +23.78%, pediatricians by +4.86%, pulmonologists decreased by -13.15%. In 2021, there were 10.31 beds for 1 FTP of an allergist, 12.8 beds for 1 FTP of a pulmonologist, and 5.83 beds for 1 FTP of a pediatrician. According to the correlation matrix, it was established that the more beds there are for 1 full-time position of a pediatrician and 1 full-time position of an allergist, the longer the ALOS and the bed occupancy rate are.

Conclusions: When planning staffing of health care institutions, it is necessary to mind the level of urbanization of the region, and ensure status of the general practitioner as a leading medical specialist responsible for medical care during the first meeting with the patient and his subsequent follow-up.

KEY WORDS: respiratory diseases, density of beds, rate of hospitalized children, bed occupancy rate, ALOS, FTP pediatricians

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INTRODUCTION

The main goal of improving children's health is to ensure general coverage of medical services at a high level of safety and quality. Accessible, equitable and effective pediatric care is critical to achieving optimal child health. Investments in pediatric services can lead to improved child health outcomes [1,2]. Equitable distribution of medical care in the healthcare system is provided by hospitals as the main providers of medical services. Hospitals are the most important, and, at the same time, the most expensive part of the healthcare system. Accordingly, hospitals account for 80% of healthcare costs [3]. In healthcare system management, the issue of optimal utilization of beds and human resources under constrained financial resources becomes a pertinent concern.

To analyze the effectiveness of the use of bed resources, various indicators are used, including the annual bed occupancy rate and the average length of stay in bed [4,5]. By 2018, there was a worldwide downward trend in the number of beds due to increased bed occupancy and shorter hospital stays [6]. Reducing beds saves money, but hospital overcrowding negatively affects access to emergency and routine care, quality and safety, and patient and staff satisfaction [7]. It is important to achieve the optimal number of beds, and the quality of medical care.

In Ukraine, there has been a consistent trend towards a reduction in the overall quantity of beds available in pediatric hospitals, spanning the period between 1991 and 2021 [8]. However, the COVID-19 pandemic in the world has changed attitude to the number of beds in hospitals. The pandemic has highlighted a fundamental need for sufficient hospital beds, coupled with equipment and medical staff, to meet the unexpected increase in demand for hospitalization and intensive care [9]. At the same time, due to introduction of complex anti-epidemic measures in the world during the pandemic, the number of hospitalized children decreased and, accordingly, there was no need to increase the

number of pediatric beds. Respiratory diseases remain the main reason for hospitalization of children [10].

In Ukraine, inpatient medical care is provided to children with respiratory diseases in hospital departments on beds for the treatment of bronchial asthma, obstructive bronchitis (AB), on pulmonology beds (PB) and on pediatric somatic beds (PSB) for the treatment of all respiratory diseases, depending on regional distribution. This assistance is provided by children's allergists, children's pulmonologists and pediatricians who work in full-time positions (FTP) in hospital departments.

To enhance the overall accessibility of medical services for children, it is imperative to conduct a retrospective evaluation of the utilization of human resources and bed allocation towards providing medical care to pediatric patients with respiratory disorders. Such an analysis will aid in formulating evidence-based management strategies at the state level.

THE AIM

Retrospectively evaluate the effectiveness of the bed allocation and human resources utilization for the treatment of children with respiratory diseases (RDs) in hospitals in the period 2008-2021.

MATERIALS AND METHODS

In order to calculate availability of beds for the respiratory diseases treatment (RDs) in children and the density of full-time positions of doctors, we used the data from report standard 47 «Report on the network and activity of medical institutions» of the Center for Public Health of the Ministry of Health of Ukraine during 2008-2021 [11]. Data on the population of the State Statistics Service of Ukraine were used to calculate indicators per 10,000 children (0-17 years) [12].

We calculated indicators that characterize the utilization efficiency of allocation bed and personnel resources: the density of beds per 10,000 (density of beds per 10,000), the rate of hospitalized children per 10,000 (RH per 10,000), the bed occupancy rate per year (BOR, %), average length of stay (ALOS), full-time positions (FTP) per 100,000, number of beds per 1 full-time position of doctors. The effectiveness of the bed fund utilization, as well as staffing potential of hospital departments with different beds (AB, PB, PSB) were retrospectively analyzed.

Correlation and regression analysis of data was performed using the statistical analysis package MedCalc v.19.4.1 (MedCalc Software Inc, Broekstraat, Belgium, 1993–2020).

RESULTS

In 2021, the density of beds per 10,000 child population was 0.66 AB, 0.96 PB, 15.9 PSB. During 2008-2021, there was a significant decrease in the density of all types of beds (R^2_{AB} =0,86, R^2_{PB} =0,59, R^2_{PSB} =0,87, p<0.05) (Fig. 1). The trend of availability of beds for RDs treatment in children in Ukraine has a linear character (p<0.05). From 2008 to 2021, the provision of beds decreased by 25.0% in AB, 17.8% in PB and 36.7% in PSB compared to 2008.

In 2021, the rate of hospitalizations per 10,000 child population was 13.82 for AB, 21.27 for PB, and 419.53 for PSB. The dynamics of this indicator from 2008 to 2021 had a parabolic curve for the indicator of hospitalized AB and PB (R^2_{AB} =0, 72, R^2_{PB} =0,66, p<0,05) and a linear straight line for the indicator of hospitalized PSB (R^2_{PSB} =0,86, p<0,05) (Fig. 2). During the COVID-19 pandemic, there was a significant decrease in the rate of hospitalizations for inpatient treatment (by -42% on AB, -30% on PB, -23% on PSB, respectively).

In 2021, the annual bed occupancy rate was 49.4% for AB, 47.5% for PB, 56.15% for PSB. From 2008 to 2021, the indicated coefficient decreased by -41.5% for AB, by -48.54% for PB, by -34.01% for PSB. The bed occupancy rate especially decreased during the COVID 19 pandemic (Fig. 3). Before the pandemic in 2019, this ratio was 82.84% for AB, 88.15% for PB, 77.39% for PSB. The dynamics of the employment rate in the period from 2008 to 2019 had a significant downward trend (R^2_{AB} =0,66, R^2). The pandemic increased the downward trend of this ratio for all types of beds.

In 2021, the average length of stay on AB was 8.18 days, on PB 7.68 days, on PSB 7.56 days. In 2021, the average length of stay in all beds (AB, PB, PSB) decreased compared to 2008: by -32.5% (AB), by -32.24% (PB), by -29.66% (PSB). The dynamics of the average length of stay in bed from 2008 to 2021 has a linear downward trend (R^2_{AB}=0,96, R^2_{PB}=0,81, R^2_{PSB}=0,96, p<0,05) (Fig. 4)

In 2021, the FTP density of allergists was 0.64, FTP pulmonologists - 0.75, FTP pediatricians - 27.25 per 100,000 children. From 2008 to 2021, the FTP density of allergists increased by +23.78%, FTP pediatricians by +4.86%, and the FTP density of pulmonologists decreased by -13.15%. From 2008 to 2021, Ukraine observed a significant decrease in the FTP density of pulmonologists (R^2_{PB} =0,81, p<0,05), and a significant increase in the FTP density of allergists per 100,000 children (R^2_{AB}=0,93, p<0,05) (Fig. 5). The trend is linear. The FTP density of pediatricians remains stable with a tendency to increase (R^2_{PSB} = 0,20, p>0,05).

In 2021, there were 10.31 AB for 1 FTP of an allergist in an inpatient department in Ukraine, 12.8 PB for 1 FTP of a pulmonologist, and 5.83 PSB for 1 FTP of a pediatrician. From 2008 to 2021, the number of beds per

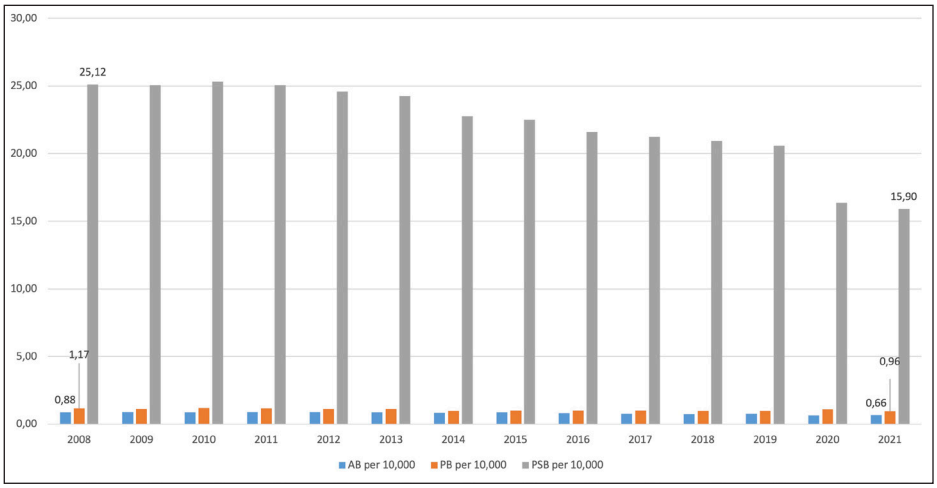

Fig. 1. Dynamics of bed density in Ukraine per 10,000 child population, 2008-2021

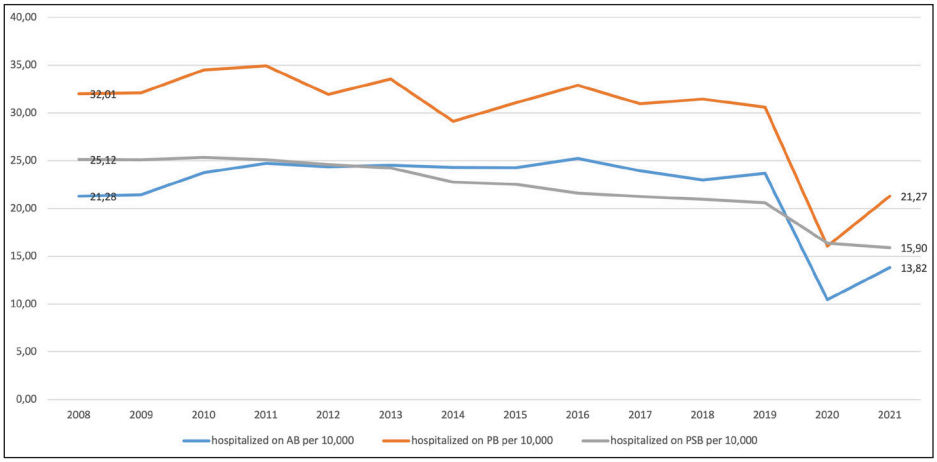

Fig. 2. Dynamics of the rate of hospitalizations per 10,000 children in Ukraine, 2008-2021

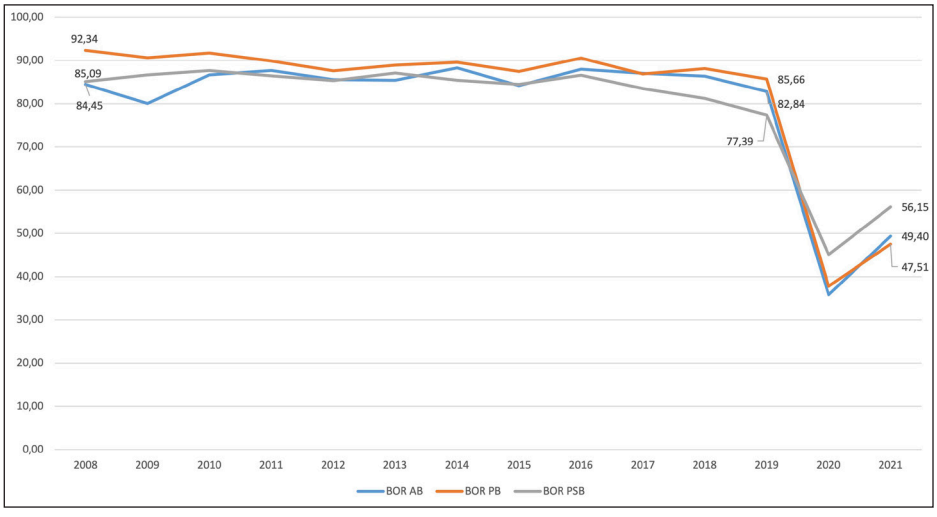

Fig. 3. The bed occupancy rate per year in different beds in Ukraine, 2008-2021, %

1 FTP of an allergist – 39,47% and pediatrician decreased significantly (R^2_{AB}=0,93, R^2_{PSB} = 0,83, p<0,05) (Fig. 6).

From 2008 to 2021, the number of beds for 1 FTP of an allergist decreased significantly by -39.47%, for 1 full-time position of a pediatrician - by -39.69%(-5,35%) (p<0.05).

To find out the relationship between the indicators of the use of bed resources (average length of stay on the bed, the bed occupancy rate per year) and the availability of personnel resources (the number of beds per 1 full-time position and the density of doctors per 100,000 children), a correlation analysis was conducted (Table I).

The bed occupancy rate per year has a positive correlation with the number of beds per 1 FTP of pediatrician and 1 FTP of allergist (p<0.05%). That is, the greater the number of PSBs and ABs per 1 doctor's FTP, the higher the bed occupancy rate per year of PSBs and

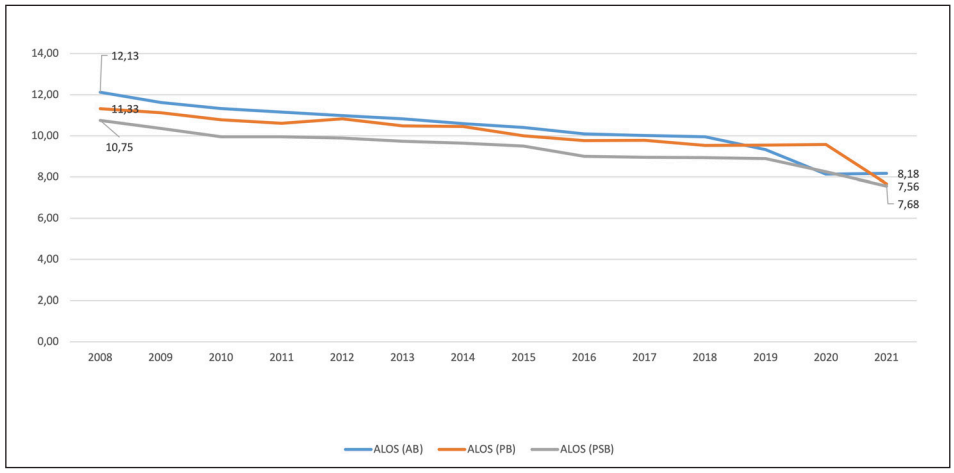

Fig. 4. Dynamics of the average length of stay in different beds in Ukraine in 2008-2021.

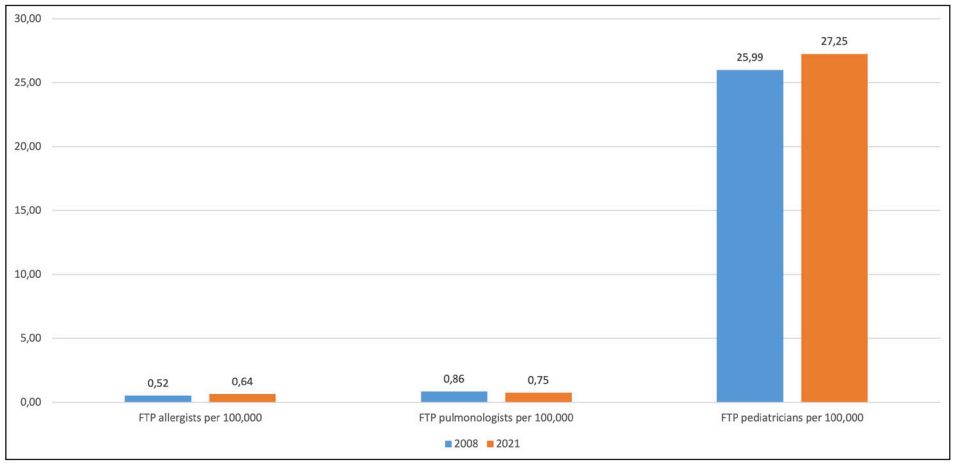

Fig. 5. The density of FTP of doctors in 2008 and 2021 in Ukraine per 100,000, in 2008-2021

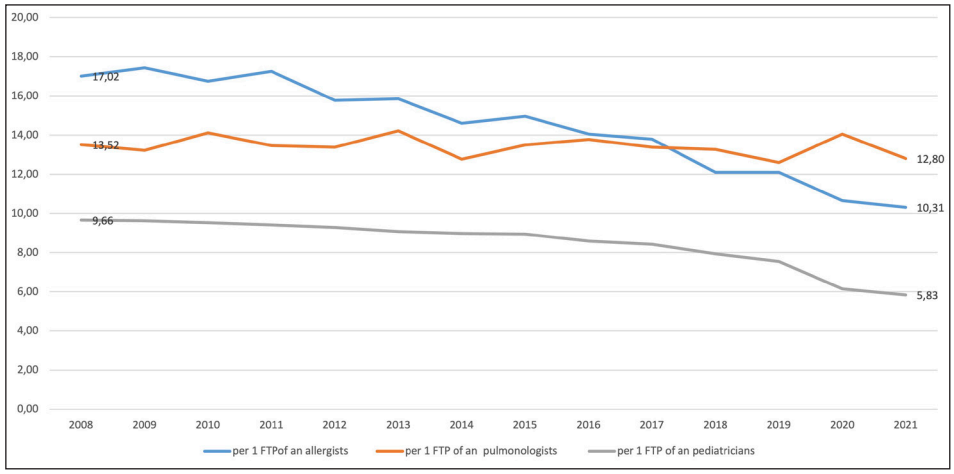

Fig. 6. Dynamics of the number of beds per 1 FTP hospital doctor in Ukrainian hospitals, 2008-2021

ABs per year is. The average length of hospital stay has a positive relationship with the FTP density of pediatricians and pulmonologists. The greater the number and density of the specified doctors in the department, the longer the average length of stay on the bed. At the same time, a negative relationship was found between the average length of stay and the FTP density of allergists. According to the correlation matrix, it was established that the greater the number of beds per 1 FTP of pediatricians and 1 FTP of allergists, the longer the average length of stay in the hospital is.

So, the number of beds per 1 FTP of doctors and the density of FTP affects the bed occupancy rate and the average length of bed stay. However, certain features are characteristic of different types of beds.

DISCUSSION

Between 2008 and 2021, there was a decline in the density of beds available for the treatment of RDs (Rare Diseases) in children in Ukraine, with a reduction of 25.0% in the availability of acute beds (AB), 17.8% in

Table I. Pearson's correlation coefficient between indicators of the use of bed resources and provision of personnel resources

Indicator	Average length of stay in bed, days	Bed occupancy rate per year, %
Density of FTP of pediatricians per 100000	-0,27	-0,43
Density of FTP of pulmonologists per 100000	0,74 *	0,28
Density of FTP of allergists per 100000	-0,9 *	-0,548
Number of PSB for 1 FTP of pediatrician	0,95 *	0,91*
Number of PB for 1 FTP of pulmonologist	0,34	0,001
Number of AB for 1 FTP of allergist	0,96 *	0,66*

*-reliable correlation, $p<0.05$

the availability of pediatric beds (PB), and 36.7% in the availability of pediatric specialized beds (PSB). This trend is consistent with the overall pattern observed in European Union countries [13]. During this period, there was an increase in the FTP density of pediatricians and allergists per 100,000 children in Ukraine. Also, during this period, there was a decrease in the number of children hospitalized in hospitals, which also corresponds to trends in other countries of the world [14]. The trend towards a decrease in the number of hospitalized children was especially intensified during the COVID-19 pandemic [15]. The decrease in hospitalized children was due to the introduction of anti-epidemic measures [16].

An indicator of the efficiency of bed utilization is the bed occupancy rate per year. In 2021, this ratio was 49.4% for AB, 47.51% for PB and 56.15% for PSB. From 2008 to 2021, the specified ratio decreased. A significant decrease in the employment rate occurred during the COVID 19 pandemic. In Ukraine the employment rate depends on the number of beds per 1 FTP of an allergist and pediatrician. The greater the number of beds per 1 FTP of doctors, the greater the bed occupancy rate per year.

According to international standards, the optimal value of the occupancy rate should be 84%-85% [17]. It is recommended to have 15%-16% of beds per year reserved, in case of emergency hospitalization [17]. Bed occupancy greater than 85% creates a shortage of acute care beds, and increases the number of hospital-acquired infections [18]. Bed occupancy under 80% indicates ineffective management of beds, inappropriate use of financial resources for bed maintenance, lack of adequate workload for medical staff. For effective use of bed resources in Ukraine, it is necessary to plan beds taking into account the occupancy rate at the level of 85%.

Average hospital length of stay, as well as bed occupancy rates, indicate the effectiveness of healthcare provision [5]. A reduction in average length of stay has been associated with a reduction in the risk of opportunistic infections and treatment adverse events, as well as improved treatment outcomes and reduced mortality [4]. Shortening the length of stay in the hospital reduces financial costs of maintaining beds [4]. However, Tiessen J et al. indicate existence of certain international differences in length of hospital stay, based on professional and cultural norms, payment systems [19].

Between 2008 and 2021, the average length of bed stay decreased in Ukraine. The average length of stay at PSB and PB has a positive relationship with the number of beds per 1 doctor's FTP. The greater the number of beds per 1 doctor's FTP, the longer the average length of stay on the bed is. It is likely that with a larger number of beds per 1 doctor's FTP, the burden on the doctor increases, which leads to a decrease in the efficiency and quality of providing medical care.

In 2021, there were 10.31 beds for 1 FTP of an allergist in Ukraine, 12.80 beds for 1 FTP of pulmonologist, and 5.83 beds for 1 FTP of pediatrician. The authors state, the recommended rate is from 6 to 8 beds per 1 FTP of pediatrician, depending on the number of beds in the department [18]. That is, it can be assumed that the ratio of the number of beds and FTP is optimal in Ukraine. However, the number of beds per 1 FTP of an allergist and a pulmonologist needs to be optimized. For high-quality medical care, it is necessary to mind the optimal number of beds per 1 doctor's FTP when planning doctors' FTP.

Therefore, in Ukraine, there is a decrease in the density of beds per 10,000 of the child population against the background of a decrease in the rate of children hospitalized for inpatient treatment, a decrease in the employment rate and the average length of stay in bed, a decrease in the load per 1 doctor's FTP in hospital departments and an increase in the density of full-time doctor positions. The fact that the beds for treating children are not being fully utilized highlights the importance of implementing measures to enhance resource management in hospitals.

CONCLUSION

When making managerial decisions about optimizing bed resources in healthcare institutions that care of children with respiratory illnesses, it is important to consider indicators of resource utilization effectiveness, as well as indicators of staffing.

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ORIGINAL ARTICLE

CHARACTERISTICS OF THE VOLUME AND OUTCOMES OF MEDICAL CARE FOR PATIENTS WITH SKIN CANCER IN UKRAINE IN 2010-2020

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ABSTRACT

The aim: To investigate the dynamics of the volumes and outcomes of medical care for patients with skin cancer in Ukraine during 2010-2020.

Materials and methods: Official statistical data from the reports of the Center for Medical Statistics of the Center for public health of the Ministry of Health of Ukraine and the National Cancer Registry for 2010–2020. Statistical and bibliosemantic methods were used in the work.

Results: A decrease in the capacity to provide medical care to patients with skin cancer was identified, as evidenced by a decrease in the number of oncological dispensaries, oncological and examination rooms in outpatient clinics, oncological and radiological beds, with a relatively unchanged level of staffing. An analysis of the main indicators of the organization and activities of medical care for patients with cancer skin revealed problems with early detection of tumors, in particular during preventive examinations, and incomplete coverage of patients with stages I-II of the disease with special treatment.

The positive dynamics of melanoma treatment outcome indicators were revealed (increase in accumulation index, 5-year patient survival rate, decrease in lethality and mortality).

Conclusions: the organization of medical care for patients with skin tumors, especially non-melanoma ones, needs further improvement in the context of preventive interventions, ensuring the coverage of patients with special treatment.

KEY WORDS: skin cancer, organization of medical care, availability of doctors, hospital beds, timeliness of detection, completeness of treatment coverage

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INTRODUCTION

The problem of skin cancer remains relevant both in Ukraine and throughout the world. Among numerous skin diseases, neoplasms, which are classified as malignant and benign, occupy a prominent place. According to the World Cancer Research Fund [1] on the prevalence of cancer in the world in 2020, skin melanoma ranked 17th (13th in men and 15th in women). The age-standardized melanoma incidence rate was 3.4 cases per 100,000 population; the mortality rate was 0.6 cases per 100,000 population (for other, so-called "non-melanoma", skin neoplasms – 11.0 and 0.6, respectively).

In the structure of primary cancer morbidity in Ukraine, non-melanoma malignancies of the skin rank third (9.9%) in men and second (12.9%) in women [2].

THE AIM

To investigate the dynamics of the volumes and outcomes of medical care for patients with skin cancer in Ukraine during 2010-2020.

MATERIALS AND METHODS

In the course of the work, it was used official statistical data from the reports of the Center for Medical Statistics of the Center for public health of the Ministry of Health of Ukraine "Incidence rates of malignant neoplasms and activities of the oncology service in Ukraine", the National Cancer Registry (Bulletin "Cancer in Ukraine", Vol. 23) for 2010–2020. Statistical and bibliosemantic methods were used in the work.

RESULTS

An analysis of the organization of medical care is impossible without a preliminary assessment of the capacity to provide it. Currently, Ukraine has a network of institutions providing qualified specialized medical care to patients with skin cancer, which is mainly represented by oncological dispensaries. In 2020, there were 27 of them (in 2010, there were 41), meaning that their number decreased by 34.1% in 10 years. None of them has a specialized department for the treatment of skin cancer patients. Most of these patients are treated on

Table I. Dynamics of provision of the population of Ukraine with oncologists and oncological surgeons in Ukraine in 2010, 2020

Indicator	2010	2020
Oncologists (Abs)	843	714
Oncologists (per 10,000)	0.18	0.17
Surgical Oncologist (Abs)	777	676
Surgical Oncologist (per 10,000)	0.17	0.16

Table II. Dynamics of the bed capacity of the Oncology Service in Ukraine in 2010, 2020

Indicator	2010	2020
Oncology beds for adults (Abs)	9557	7680
Oncology beds for adults (per 10,000)	2.09	1.85
Radiology beds (Abs)	2674	1995
Radiology beds (per 10,000)	0.58	0.48

Table III. Dynamics of indicators of oncology and radiology bed usage in Ukraine in 2010, 2020

Indicator	Oncology beds		Radiological beds	
	2010	2020	2010	2020
Average annual occupation of the bed	342.5	253.9	378.4	308.9
Average length of stay in a hospital	12.5	6.8	21.9	21.1
Bed turnover	27.4	37.2	17.2	14.7

an outpatient basis, as in most cases they do not require long-term hospitalization.

Medical care is also provided by specialists in oncology and examination rooms of outpatient facilities. Over the past 10 years, the number of oncology rooms has decreased by 34.9%, and the number of examination rooms has almost tripled.

Medical care for patients with skin cancer is provided by oncologists and surgical oncologists, the availability of which is shown in Table I.

Over the past decade, the supply of oncologists and surgical oncologists has decreased by 5.5%, but there are significant regional differences. In particular, the number of oncologists per 10,000 inhabitants ranges from 0.06 in the Dnipropetrovsk region to 0.31 in the Chernivtsi region, and the number of surgical oncologists per 10,000 inhabitants ranges from 0.05 in the Zakarpattia to 0.28 in Ternopil region.

It should be noted that the group of "oncologists" in the list of medical specialties in Ukraine includes surgical oncologists, gynecologic oncologists, oncologists-otolaryngologists, but there is no specialty of oncologists-dermatologists despite the high prevalence of skin cancer.

The parallel decrease in the supply of dermato-venerologists over the past 10 years by 37.8% to 0.46 per 10,000 population in 2020 may be justified and is associated with a decrease in morbidity, primarily venereal diseases. However, such a decrease is an unfavorable factor, since it is to these specialists, as a rule, that the family doctor refers patients with skin diseases. The frequency of detection of malignant skin tumors among patients who have consulted a dermatologist is 2% [3].

It is the oncological alertness of the dermato-venerologist and the quality of the initial professional examination of the patients that subsequently have a significant impact on the timeliness of diagnosis and the effectiveness of treatment of patients with skin cancer by the oncologist.

In the last five years, the professional qualification of doctors providing medical care to patients with skin cancer has improved. Thus, the proportion of doctors with a higher category has increased: among oncologists - up to 55% and among oncological surgeons - up to 75%, which may in part be due to the aging of medical personnel in the health system as a whole. Data on the bed capacity of the oncology service and the availability of oncology and radiology beds for medical care, including for patients with skin cancer, are presented in Table II.

The overall decrease in the number of beds in the country was also reflected in the number of oncology beds, which decreased by 19.6% over 10 years, and the availability of beds - by 11.4%. The provision of the population with oncology beds is characterized by certain regional features: it was the highest in the Chernihiv and Poltava regions (2.9 and 2.8 beds per 10,000 population, respectively); the lowest - in the Ivano-Frankivsk and the Rivne regions (1.3 and 1.4 beds per 10,000 inhabitants, respectively).

It is known that radiation therapy is one of the most common methods of cancer treatment. Therefore, consideration should be given to the availability of this type of treatment for the population. Over the past decade, not only the absolute number of beds has decreased (by 25.3%), but also the provision with them (by 17.2%).

At the same time, it should be noted that the demand for appropriate treatment is significant. This is evidenced by the overload of radiology beds, and hence their deficiency. The average annual occupation of radiology beds in 2020 in Zhytomyr, Chernihiv regions and the city of Kyiv was 553.7; 433.1 and 501.8, respectively. The availability of radiology beds for the population also has some regional differences - from 1.0 per 10,000 people in the Sumy region to 0.3 in Odesa region.

The dynamic of availability of beds for the treatment of cancer patients per 1,000 patients turned out to be

Table IV. The main indicators of the state of oncological care for patients with malignant neoplasms of the skin in Ukraine in 2010, 2020

Indicator	Skin melanoma		Other skin neoplasms		All neoplasms	
	2010	2020	2010	2020	2010	2020
Morphologically confirmed diagnosis (per 100 new patients)	98.5	98.3	97.6	97.1	81.4	83.5
Percentage of patients detected during preventive examinations (%)	42.8	43.6	64.9	54.9	27.8	21.1
The specific weight of patients detected in the stages among patients with a newly established diagnosis (%):						
I - II	68.6	79.3	91.1	90.8	51.0	46.6
III	17.1	5.0	1.0	1.6	19.1	17.7
IV	4.3	5.1	0.1	0.3	14.9	19.9
the stage is not established	9.9	10.6	7.7	7.3	15.1	15.8
Specific weight of patients who received special treatment to the number of patients registered in the reporting year (%)	89.8	90.2	87.4	85.3	66.8	67.9

Table V. Some indicators of treatment outcomes for patients with melanoma and other skin tumors in Ukraine in 2010, 2020

Indicator	Skin melanoma		Others neoplasm skin		All neoplasms	
	2010	2020	2010	2020	2010	2020
Accumulation index (prevalence ratio to primary morbidity)	8.5	13.6	0.3	0.2	6.8	11.1
The specific weight of patients who were under dispensary supervision for 5 years or more among all such patients (%)	60.9	68.8	59.9	63.7	58.8	64.3
Mortality rate up to a year (per 100 newly registered in the previous year)	13.9	7.3	0.7	0.7	30.0	24.2
Mortality rate (per 100 patients)	0.3	0.2	5.5	3.0	8.7	5.3
Mortality (per 100,000 people)	2.4	2.1	1,2	1,2	178.5	138.4

positive: in 2020, it was 91.0 (from 130.7 in the Chernivtsi region to 53.1 in Kyiv region) and increased by 10.7% over the previous 10 years.

The analysis of the dynamics of indicators of oncology and radiology bed usage (Table III) shows its diversity. Thus, the average number of days occupied by oncology beds decreased by 25.8%, which is not so much due to the lack of specialized patients as to the reorganization of inpatient care during the Covid-19 pandemic. The average length of stay of a patient on an oncology bed was almost halved, which accelerated the bed turnover to 37.2 patients (an increase of 35.7%) and improved the opportunities for oncology patients to receive inpatient care.

The situation with the use of radiology beds is different: although the average number of days of their employment has decreased by 18.4%, it continues to be too high in some areas, as was mentioned above. At the same time, treatment duration remains stable, as radiotherapy requires adherence to a clinical protocol, and bed turnover decreased by 14.5%.

A number of indicators of the state of oncological care (relating to diagnosis and treatment) were analyzed for patients with skin cancer in comparison with all patients with malignancies (Table IV). Based on all the indicators above, it is evident that the situation with the diagnosis and treatment of patients with skin cancer is better in comparison with all neoplasm locations: a greater specific weight of skin neoplasms is morphologically confirmed, revealed during professional examinations, including at stage I-II, and, with the rest, a greater percentage of patients (about 85-90%) will receive special treatment immediately after diagnosis. However, 10-15% of untreated patients demonstrate the inability of medical facilities to provide specialized medical care [4].

Comparing the situation according to the above indicators between the diagnosis and treatment of melanoma and other skin neoplasms is better in favor of the latter, although the ten-year dynamics of these indicators is positive for melanoma. Thus, the share of melanoma cases diagnosed at stage I-II increased by 15.6%. At the same time, the specific weight of patients with other skin neoplasms, as a whole, detected during professional examinations decreased by 15.4%. The latest developments in diagnostic imaging techniques have been an advancement in the management of patients, especially those with melanoma, as they allow the detection of distant metastases in asymptomatic melanoma.

Attention is drawn to the unfavorable situation in some regions of Ukraine according to certain indicators. For example, in the Chernivtsi region, only 5% of melanomas are detected during medical examinations, in the Volyn region, only 2%, but 89% are in stage I-II. The situation is similar in the Kherson region with regard to non-melanoma skin tumors (the indicators are 8.6% and 92.5%, respectively). The level of neglect of malignancies of the so-called "visual localization" (which includes skin tumors) is evidenced not only by their late detection in stages III-IV, but also by the specific weight of cases of diseases whose stage remained undetermined, especially in relation to melanoma: in the Kharkiv region such were 40%, in Chernivtsi - 35%, in Rivne - 29%. The conducted studies showed [2] that the annual mortality of patients in this group is close to the annual mortality of patients with malignancies of neglected stages.

An important characteristic of the organization of medical care is its effectiveness, which largely depends on the quality of treatment. Performance indicators can be considered the index of accumulation (the ratio of the prevalence to incidence); the specific weight of patients who were under dispensary supervision for 5 years or more among all such patients; lethality rate up to one year (per 100 newly registered in the previous year); total lethality (per 100 patients and mortality (per 100,000 population) [5], the values of which demonstrate positive dynamics in relation to all neoplasms (Table V).

According to the index of accumulation, the increase of which indirectly indicates an improvement in the level of medical care for the population, there is a positive trend in relation to melanoma (by 60%). The proportion of patients with melanoma and other skin neoplasms who were under dispensary observation for 5 years or more also increased.

Such patients are usually considered cured because their mortality rate is close to that of the general population [2]. Mortality from melanoma is gradually reaching a stable level, which is associated with the emergence of new effective methods of treatment.

Annual lethality of melanoma patients decreased by almost half, total lethality by a third, mortality by 12.5% (compared to all cancer patients by 19.3%, 39.3%, and 22.4%, respectively). In patients with other skin neoplasms, a positive trend was observed only in terms of mortality, but its decrease was the most noticeable - by 45.5%. Annual lethality of melanoma patients decreased by almost half, total lethality by a third, and mortality by 12.5% (compared to all cancer patients by 19.3%, 39.3%, and 22.4%, respectively).

Thus, the problem of improving the organization of medical care for patients with skin cancer remains relevant [6] and requires an increase in the level of early detection, as well as the creation of a comprehensive program for the diagnosis, treatment and prevention of this group of malignant neoplasms and the development of educational programs for the country's population. Patients with skin tumors are cared for by doctors of several specialties, and close cooperation between family doctors, dermatologists, and oncologists will be important to ensure early diagnosis, adequate treatment, comprehensive support, and competent monitoring of patients [7].

DISCUSSION

An analysis of the state of medical care for patients with skin cancer in Ukraine has shown certain negative trends, and, consequently, the imperfection of the existing system for diagnosing and treating skin cancer. However, the main goal of optimal treatment is not only to reduce mortality, which, in particular, was used to evaluate the effectiveness of treatment, but also to ensure a better quality of life and long-term treatment of relapses and side effects [8]. According to the survey, patients found that they are worried about the occurrence of recurrence and a cosmetic defect. Patients also consider communication with the attending physician to be an important point, they seek to receive detailed information about their disease and actively participate in decision-making on diagnostics and treatment [9].

The provision of medical care to patients with skin cancer is a complex step-by-step process that involves several specialists, often without communication among themselves regarding an individual patient. There is also an obvious need for continuous treatment, the positive results of which are improved adherence to medical regimens, reduced likelihood of hospitalization and financial costs [10].

Thanks to the introduction of the latest technologies in the treatment of skin cancer, the survival rate of patients is increasing. But until now, the weak link in medical care for patients with skin cancer is its early diagnosis. Timely detection of suspicious skin changes using imaging techniques can help in the early diagnosis of skin cancer, increasing the likelihood of a favorable treatment outcome [11]. A progressive step forward could be the use of telemedicine, especially for patients who have barriers to traditional in-person doctor visits (who live outside major cities or have limited functionality) [12].

It should be noted that the state of medical care for patients with skin cancer is not well understood. The vast majority of publications both in Ukraine and abroad are devoted to the specifics of the diagnosis

and treatment of skin cancer. The conducted research should become the basis for the improvement this area of medical care. In order to fully characterize the state of medical care for patients with skin cancer, it is necessary to assess the factors affecting its organization by interviewing doctors involved in providing care to patients with skin cancer (oncologists, surgical oncologists, dermatologists, family doctors).

In order to fully characterize the state of medical care for patients with skin cancer, it is necessary to assess the factors affecting its organization by interviewing doctors involved in helping patients with skin cancer (oncologists, surgical oncologists, dermatologists, family doctors).

The opinion of patients regarding their satisfaction with the care received is also important. A separate study needs to be done on the prevention of skin cancer.

CONCLUSIONS

The possibilities of providing medical care to patients with skin cancer have decreased: the number of oncological dispensaries, oncological and examination rooms in outpatient facilities, oncological and radiological beds has decreased, while the level of staffing has remained relatively unchanged.

The analysis of the main indicators of oncological care for patients with malignant skin neoplasms revealed problems with the early detection of tumors, in particular during preventive examinations, and incomplete coverage of patients with the I-II stage of the disease with special treatment.

The positive dynamics of melanoma outcome indicators have been established (increase in accumulation index, five-year patient survival, decrease in lethality and mortality). The organization of medical care for patients with skin tumors, especially non-melanoma ones, needs further improvement.

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ORIGINAL ARTICLE

ORGANIZATION OF OPHTHALMOLOGICAL CARE IN UKRAINE

DOI: 10.36740/WLek202304116

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ABSTRACT

The aim: To consider the organization of ophthalmological care in Ukraine for cataract and glaucoma and find out whether it is appropriate to implement advanced good practices of reference countries for Ukraine.

Materials and methods: The method of desk review was used, supported by secondary analysis of data, in particular legislative acts. The research included conducting expert interviews with ophthalmologist of the public and private sectors, heads of public healthcare institutions, and management of the National Health Service of Ukraine. We also used materials on good practices from partners within the project ID 22120107 supported by Visegrád Fund.

Results: Since the burden of ophthalmological pathologies is increasing and processes of reforming the health care system are taking place, changes in the organization and financing of ophthalmological services are taking place. Within the framework of the partner project, "Access to healthcare services in the context of financing mechanisms. The case of ophthalmology" identified good practices in the organization of ophthalmological care in the context of improving access to services and improving quality. The results of interviews with key stakeholders led to the fact that the respondents generally support all the good practices proposed by the partner countries and indicate their arguments why the proposed practices are (not)appropriate to implement in Ukraine.

Conclusions: The organization and financing of healthcare in Ukraine still require the study and implementation of good practices so that patients can have access to quality services and treatment.

KEY WORDS: organization of ophthalmological care, financing, ophthalmology, good practices, DRG

Wiad Lek. 2023;76(4):805-810

INTRODUCTION

For a long time in Ukraine, ophthalmological care was provided as only specialized medical care. Ophthalmological care, like all specialized medical care, was provided at all three levels. Medical care was provided by ophthalmologisti in outpatient, specialized and highly specialized levels, such as the Institute of Eye Diseases and Tissue Therapy named after V.P. Filatov National Academy of Sciences of Ukraine.

Until April 1, 2020, the financing of the treatment of ophthalmological cases in the public sector was carried out according to the fixed budget method, which was calculated considering extensive indicators of the activity of providers (full-time positions of medical personnel, number of beds etc.).

The reform of the healthcare system in Ukraine began with the adoption of relevant legislation, in particular, the Law of Ukraine "On State Financial Guarantees of Medical Services for the Population" dated October 9, 2017, No. 2168-VIII [1]. The reformation of healthcare system in Ukraine started with the changes in primary care in 2018. The part of the functions of ophthalmic care were transferred to the primary level to the family doctor. Within these changes, the National Health Service of Ukraine (NHSU) became a customer and healthcare service provider. The change in financing consisted in the transition to a capitation rate.

The financing reform was extended to secondary outpatient and inpatient care in 2020. Packages and specific tariffs of medical services were developed and implemented within the Programme of Medical Guarantees. In the same year, surgical treatment of patients with ophthalmological cases was included in the package of medical services "Surgeries for adults and children in hospital" [2-3]. In 2022, ophthalmological cases are included in the package "Surgeries for adults and children as a one-day hospitalization" [4].

Moreover, the lack of funding in recent years led to the fact that ophthalmological care was separated into a separate commercial component and many ophthalmological services provided by private suppliers. Also, in recent years, the burden of ophthalmological pathology has been increasing, and some diseases are becoming "younger" and affect the younger working population, for example, glaucoma and cataract. Cataract and glaucoma are one of the most common oph-

thalmic diseases, therefore they need special attention of the state, because they bear the greatest burden of ophthalmic diseases [5]. These processes are also prompting changes in the financing of ophthalmological care in the country.

This publication is based on research on best practices from reference countries on how to balance access to ophthalmological services and finance a healthcare system from state budget, in order to provide recommendations to stakeholders that can be used to address ophthalmological care challenges.

THE AIM

The purpose of the study is to review the organization of ophthalmic care in Ukraine, to outline the main gaps in the organization and financing of medical services for cataract and glaucoma. Also, the objectives of this study are to find out whether the identified good practices in the organization of ophthalmological care in Poland, Hungary, Slovakia and the Czech Republic contribute to improving access to medical care and improving the quality of medical care in the treatment of cataract and glaucoma in Ukraine.

MATERIALS AND METHODS

Based on a comprehensive desk review supported by secondary data analysis, we synthesize available information for further data collection in the country. Further work consisted of interviews with local stakeholders to address information gaps, gather ideas and determine the perception of the proposed good practices by representatives of different healthcare sectors. In the future, a briefing with key stakeholders is planned to share preliminary conclusions and recommendations regarding the implementation of good practices in the organization of ophthalmological care in Ukraine.

The source base of the analysis is decrees and materials of the Cabinet of Ministers of Ukraine, the National Health Service of Ukraine (NHSU), and the main legislative framework of the Ministry of Health of Ukraine (MoH). The following search terms were used: "healthcare reform in Ukraine", "organization of the healthcare system in Ukraine", "National Health Service of Ukraine", "program of medical guarantees", "ophthalmology in Ukraine" and "financial mechanisms of the healthcare system in Ukraine". It was analysed packages of the Programme of Medical Guarantees of 2020 [2], 2021 [3], 2022 [4] as follows: «Surgery for adults and children in hospital», «Outpatient secondary (specialized) and tertiary (highly specialized) medical care for adults and children, including medical rehabilitation and dental care», «Surgeries for adults and children as a one-day hospitalization».

To determine the good practices of the reference countries, the materials developed by the partners from the scientific project "Access to healthcare services in the context of financing mechanisms. The case of ophthalmology", which is financed by the Visegrad Fund. The methodology for determining good practices is approved within the scope of the specified project.

In order to discuss the possibility of implementing good practices, we conducted 6 expert interviews with specialists in ophthalmology, in particular, ophthalmologist-surgeons from the public and private sectors, heads of public and communal health care institutions, the department of ophthalmology, as well as the head and management of the National Health Service of Ukraine. All expert interviews were conducted in accordance with all conditions of qualitative research methods, including interview recording, transcription, protection of the respondent's rights during the interview and was approved by Scientific Research Ethics Committee of National University of Kyiv-Mohyla Academy, Decree No. 3 dated July 7, 2022. All respondents gave informed consent for the use of their feedback for scientific purposes and publications.

RESULTS

The disease burden of glaucoma and cataract increases every year in Ukraine. From the management point of view, it is important to understand the clear mechanisms of the organization of ophthalmological surgical care. This needs special attention because cataract ranks first in Ukraine in terms of prevalence among ophthalmological diseases and remains not only one of the topical ophthalmological problems, but also an important medical and social problem. As of 2017, cataract prevalence rate is 448,474 patients among the entire population aged 0-100 years (1045.3 per 100 thousand population), the incidence rate is 109,217 (257.5 per 100 thousand population). In the age group of 18-100 years and older, the prevalence of cataracts is 429,931 (1,235.5 per 100,000 population), the incidence is 109,062 (313.4 per 100,000 population) [5].

About 220,000 peope with glaucoma are registered in Ukraine, and about 20,000 new cases are detected annually. In 2017, at the age group of 18-100 years and older, the prevalence of glaucoma is 213,223 (612.7 per 100,000 population), the incidence is 17,934 (51.5 per 100,000 population) [5].

Statistical information on the prevalence and incidence of diseases, in particular cataract and glaucoma, is not collected since 2018, as the Order of the Ministry

Table I. DRG for cataract and glaucoma and the corresponding correction coefficients

Year	DRG code	DRG	Weight coefficient of DRG	Package	Tariff*
2021	C15	Surgical treatment of glaucoma and complex surgeries for the treatment of cataracts	0.593	Surgery for adults and children in hospital	4563.64 UAH / 148 EUR
2022	C15	Surgical treatment of glaucoma and complex surgeries for the treatment of cataracts	0.593	Surgery for adults and children in hospital	7506.00 UAH / 196 EUR
	C15-01	Surgical treatment of glaucoma and complex surgeries for the treatment of cataracts up to 24 hours	0.534	Surgery for adults and children within one-day hospitalization	7506.00 UAH / 196 EUR

*Note: In 2021, the share of the applied rate for the treated case for the period from April 1, 2022, to the end of December 2022 ranged from 5% to 15%. In 2022, it is planned that by the end of the financial year, the additional payment at the tariff (global rate) under the DRG will increase to 35% [7-9].

of Health of Ukraine №801802 dated November 10, 2018, abolishes a reporting form № 12 "Report on the number of diseases registered in patients".

An average of 65,883 cataract surgeries per year were performed in public and communal healthcare facilities (15.6 per 10,000 of adult population), of which 93.2% were cataract surgery with implantation of an artificial lens [5]. In the period 2010-2018, in the public and communal sector, cataract surgeries were provided mainly at an inpatient care level, the share of surgical interventions in outpatient conditions was only 7% (4,731 operations or 1.1 cataract surgeries per 10,000 adult population).

In the private sector, the situation is the opposite. In 2010, 70.4% of cataract surgeries were performed at an outpatient care level and up to 29.6% at an inpatient care level. The situation changed in 2020, 92.9% of all cataract surgeries were performed on an outpatient basis and 7.1% in hospital [5]. As the private sector is paid usually by fee-for-service, it focuses on surgical treatment only in the outpatient care level and 1-day hospitalization.

In the period 2010-2017, surgical treatment of glaucoma in public and communal health care institutions was carried out mainly in inpatient settings, with an average of 5,470 surgeries per year (1.31 per 100,000 population). According to the National Health Service of Ukraine, in 2021, 5,648 patients with glaucoma underwent surgical treatment, 74.2% of whom were 65 years old or older. As part of the Programme of Medical Guarantees, 1,595 "one-day" surgeries were performed in 2022 [6].

In private clinics, surgical treatment is provided to patients with glaucoma on an outpatient basis (6,184 surgical operations or 1.5 per 100,000 population in 2017) [5].

The principle of payment for specialized care, in particular ophthalmology, through the National Health Service of Ukraine is carried out using the DRG tool with prioritization of one-day surgery or provision of services in an outpatient care level.

So, currently, the emphasis in cataract and glaucoma treatment is shifted to outpatient care. In 2022, a separate package "Surgery for adults and children within one-day hospitalization" is included in the Programme of Medical Guarantees, and the new DRG group C15-01 "Operations on the lens up to 24 hours" (weight coefficient is 0.458) is included in the list of diagnostic and related groups (Table I) [7-9].

Cataract and glaucoma care is provided as both inpatient and outpatient care, including one-day hospitalization, within the Programme of Medical Guarantees of the National Health Service of Ukraine. The calculated packages are far from the real financial costs and leave a large percentage of the financial burden for patients in medical treatment and obtained lenses of higher quality. We considered in detail the packages and tariffs 2020-2022 within the Programme of Medical Guarantees in our previous publication "Financing mechanisms of ophthalmological care in Ukraine: current state and main problems" (2022) [10].

Within the framework of the partnership project, "Access to healthcare services in the context of financing mechanisms. The case of ophthalmology", the results showed that each country has different practices in the organization of ophthalmological care. This allowed us to identify the main differences and identify good practices in organization of ophthalmological services. Good practice in this partnership project refers to actions taken by healthcare systems to ensure that care is provided at a level that meets healthcare system needs or to improve the quality of care. More details on good practices in the reference countries can be found in the final report of the project "Access to healthcare services in the context of financing mechanisms. The case of ophthalmology".

The results of our research showed that it is currently important for Ukraine to implement the following good practices:

1. Co-payment for different type of lenses, especially those with individual indicators, and determining the approximate price of lenses used to treat cataract and glaucoma. Not all government programmes can currently cover all cataract and glaucoma treatment costs of lenses, so there should be co-payments for certain types of lenses. Due to the high specificity, a very small percentage of toric and aniridia lenses are used, so that state programmes cover mainly average used lenses.
2. Involvement of the local state budget. Some treatment for cataract and glaucoma patients are already covered by local public programmes. For example, in the city of Kyiv, there is a programme "Health of Kyivans", which fully covers all consumables: lenses, knives, and medicines for surgery.
3. Introduction of financial limit mechanisms for cataract and glaucoma treatment. It is currently impossible to cover all treatment from the state budget, and there will be limits for patients. Currently, the state cannot cover all lenses within the Programme of Medical Guarantees. Also, the head of the National Health Service of Ukraine added that the plans for 2023-2024 are to include a review of pricing and allocation of individual services or medical products for which the patient will have to pay separately. The government is preparing a detailed list of to be paid services, which will be included in a separate Cabinet of Ministries Decree. It will be clearly understood what the state pays for and what patients should pay from out-of-pocket or as co-payment.
4. Expansion of the National List of Medicines (both original medicines and generics) and inclusion in the "Affordable Medicines" reimbursement programme all the medicines used in the treatment of glaucoma. Medicines for glaucoma treatment are expensive, not all patients can pay for them, so many patients stop treatment or try to find cheaper medicines, what can lead to blindness and disability, which then may become a burden on the state.

The results of interviews with key stakeholders among doctors, ophthalmic surgeons, managers of health care facilities and the National Health Service of Ukraine led to the fact that the respondents generally support all the good practices identified by the partner countries. Since the DRG system and the corresponding financing mechanisms are currently being implemented in Ukraine, clinicians do not yet see how good practices related to DRG can be implemented in Ukrainian healthcare system, but they see the possibility of applying them at further stages of the system's development. Although, managers have a more present vision of how good practices can be applied and whether they are good for the system.

DISCUSSION

According to the results of the research, the stated goals were achieved. This research can be considered exploratory, since scientific publications in ophthalmology focus on the clinical side of the problem, and there are almost no publications covering the management and organization of ophthalmological care [5].

The structure of the ophthalmological service remains widely branched, moreover, in connection with the different subordination of health care institutions, both state and communal, there is no clear definition of the number of ophthalmological departments and polyclinic offices in the country. The country has an extensive network of private ophthalmology clinics, the data of most of which are not included in the statistical reporting for Ukraine as a whole. Accurate data apply only to public and communal ophthalmological institutions that provide specialized and highly specialized medical care. Therefore, challenges may arise when planning certain ophthalmological care in public healthcare facilities.

Research into the issues of finding solutions for the optimal organization and financing of ophthalmological care are becoming more and more relevant. In this context, studies based on the exchange of experience between reference countries are important.

This can be done through the exchange of experience between reference countries that have already gone through all the ways of establishing the organization of high-quality ophthalmological care and where the financing systems by the DRG is developed. Poland, Hungary, Czech Republic, Slovakia, and Ukraine face the same problems, but due to the lack of exchange of experience and good practices, some organizational issues are solved for a long time. The experience of sharing good practices is valuable and important, especially for Ukraine, because the transformational processes in the health care system and changes in financing mechanisms implemented over the past three years in the public sector require the study and implementation of advanced practices.

Thus, this research has shown that funding approaches in different countries may differ, but they are all aimed at improving the availability and quality of services. Since good practices in the provision of ophthalmological care were identified, and some of them found support among clinical practitioners from Ukraine, it makes sense to consider in more detail the possibilities of implementing such good practices in Ukraine in the future.

CONCLUSIONS

The results of the study showed that Ukraine has a high level of ophthalmic medical care that meets all modern

standards. However, the availability and financial protection of patients with ophthalmic pathology, in particular with cataract and glaucoma, is a big challenge. Therefore, the issue of improving the organization and financing of ophthalmological services in Ukraine requires special attention.

The results of interviews with key stakeholders among doctors, ophthalmic surgeons, managers of health care facilities and the National Health Service led to the fact that the respondents generally support all the good practices identified by the partner countries. Since the DRG system and the corresponding financing mechanisms are currently being implemented in Ukraine, clinicians do not yet see how these good practices can be implemented in our health care system, but they see the possibility of applying them at further stages of the system's development. Although, managers have a more present vision of how good practices can be applied and whether they are good for the system.

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ORIGINAL ARTICLE

EFFECT OF URBANIZATION ON DENSITY OF THE GENERAL PRACTITIONERS, AVERAGE LIFE EXPECTANCY AND MORTALITY FROM THE DISEASES OF CIRCULATORY SYSTEM

DOI: 10.36740/WLek202304117

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ABSTRACT

The aim: Comparative analysis of average life expectancy, mortality from diseases of the circulatory system, gross regional product, and density of general practitioners in regions with different levels of urbanization.

Materials and methods: We compared the following characteristics of groups classified by level of urbanization: average density of general practitioners per 10,000, average life expectancy and mortality from diseases of the circulatory system per 1,000, average gross regional product per 1 person.

Results: The groups did not differ in average life expectancy. The highest rate of mortality from diseases of the circulatory system- in the group with average level of urbanization, the lowest- in the group with low level of urbanization ($p<0.05$). The highest value of gross regional product per person is in the group with high level of urbanization, and the lowest is in the group with low level ($p<0.05$). The lowest density of primary care doctors per 10,000 is in the group with high level of urbanization, and the highest is in the group with low level of urbanization ($p<0.05$).

Conclusions: When planning staffing of health care institutions, it is necessary to take into account the level of urbanization of the region and ensure status of the general practitioner as a leading medical specialist responsible for medical care during the first meeting with the patient and his subsequent follow-up.

KEY WORDS: urbanization, density of general practitioners, life expectancy, mortality from diseases of the circulatory system, gross regional product

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INTRODUCTION

Urbanization processes in the world cause significant changes in living standards, social behavior and population health [1]. Urbanization can create new dangers for human health (injuries, non-communicable diseases, unhealthy diet and lack of physical activity, harmful alcohol consumption), as well as risks of infectious diseases outbreaks [2].

Urbanization, is often cited as a key factor in the development of the diseases of circulatory system, an increase in body mass index (BMI), obesity, prevalence of type 2 diabetes, hyperlipidemia, and hypertension [3-5]. Urbanization leads to a change in the general requests for medical care, including medical appointments. However, its effect on the chronic diseases development decreases with advances in healthcare system and increase in its financing [6-9].

The urbanization and economic level of the region affect medical care provided to the population [7]. As we know, living in cities in high- and middle-income countries ensures for people affordable and high-quality medical care [2]. In contrast, poor people living in areas of highly urbanized cities have limited access to healthcare.

Urbanization provides certain features of the medical care organization in cities and villages. Traditionally, the main resources of health care system are concentrated in cities. Higher prevalence of the physicians treating people is observed in more urbanized and populated areas [10, 11]. In rural areas, lack of physicians is observed, which causes dependence on providers of primary medical care. In addition, cities are characterized by an extensive network of healthcare facilities, due to the medical service demands of highly populated urbanized regions.

As of 2020 year, 4,190,416 people lived in Ukraine, of which 69.5% were urban residents [12]. In 2020, general practitioners (GPs) provided primary medical care in in 808 primary health care centers. The availability of medical care for the population is primarily ensured by a sufficient number of GPs [13-15].

Of great urgency are the studies of the urbanization effect on availability of primary medical care by GPs, assessment of the availability effect on the average life expectancy and mortality from cardiovascular diseases, as the leading health indicators of the population.

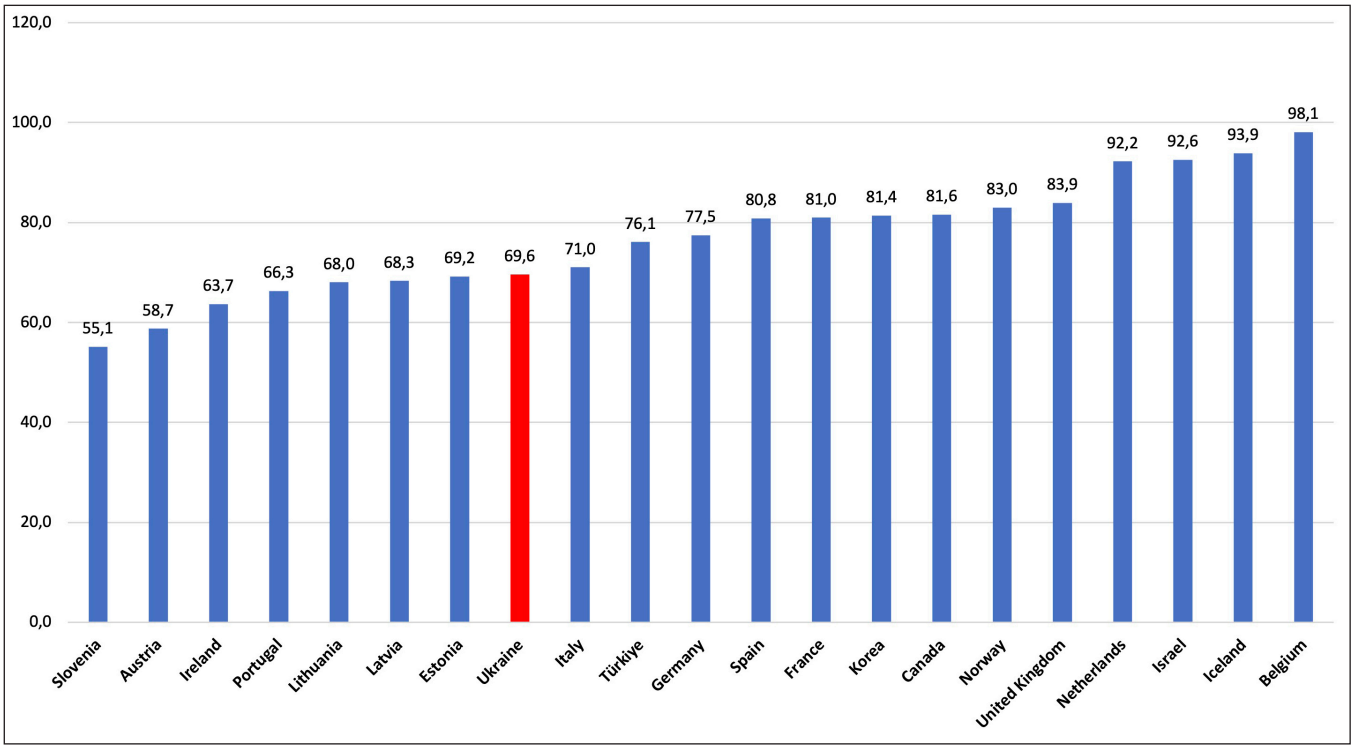

Fig. 1. The level of urbanization in the countries of the world (% of total population)

THE AIM

The aim of the study was to compare the average life expectancy, the mortality rate from the diseases of circulatory system, gross regional product per 1 person, the density of GPs in regions with different levels of urbanization.

MATERIALS AND METHODS

According to the share of the urban population in the 2020 population structure, the regions of Ukraine are divided into 3 groups, according to the urbanization level [12]. The first group, which belongs to a low level of urbanization, included up to 50% of the city population, the second group, which belongs to the average urbanization level - from 50 to 70%, the third group, which belongs to high urbanization level - more than 70%.

For each group, the density of GPs per 10,000 people was calculated according to the data of Standard 17 «Report on medical personnel» of the Public Health Center of the Ministry of Health of Ukraine for 2020 [13]. In addition, for each group, the average life expectancy, and the average value of the 2020 mortality rate due to circulatory diseases per 1,000 people were calculated, according to the State Statistics Service of Ukraine [12]. To calculate the 2020 average gross regional product (Per capita gross regional product) in groups, information from the website of the Ministry of Finance of Ukraine [14] was used.

The density of GPs in the world and share of the urban population was obtained from the website of the Organization for Economic Co-operation and Development (OECD) (https://stats.oecd.org) for the year 2020 [16].

The Kruskal-Wallis test was used to compare groups by mean value and standard deviation (± SD). A posteriori comparisons were made according to Dunn's test. Pearson coefficient was used for correlation matrix between the level of urbanization and density of GPs per 10,000 people in OECD countries, between the density of GPs per 10,000 people and average life expectancy in Ukraine.

Statistical data treatment was by the statistical analysis package MedCalc v.19.4.1 (MedCalc Software Inc, Broekstraat, Belgium, 1993–2020).

RESULTS

In 2020, the share of urban population in Ukraine was 69.6% of the total population, varying between regions from 36.8% to 100%. In the group of OECD countries, the 2020 value was 81.0% (from 55.1% to 98.1%), and ranged from 55.1 to 98.1% (Figure 1).

In Ukraine, the level of urbanization corresponds to that in Lithuania, Latvia, Estonia, Italy, exceeding that in Slovenia, Austria, Ireland and Portugal.

In 2020, the density of GPs in Ukraine was 3.57 per 10,000 people (Figure 2). This is one of the lowest values, compared to OECD countries.

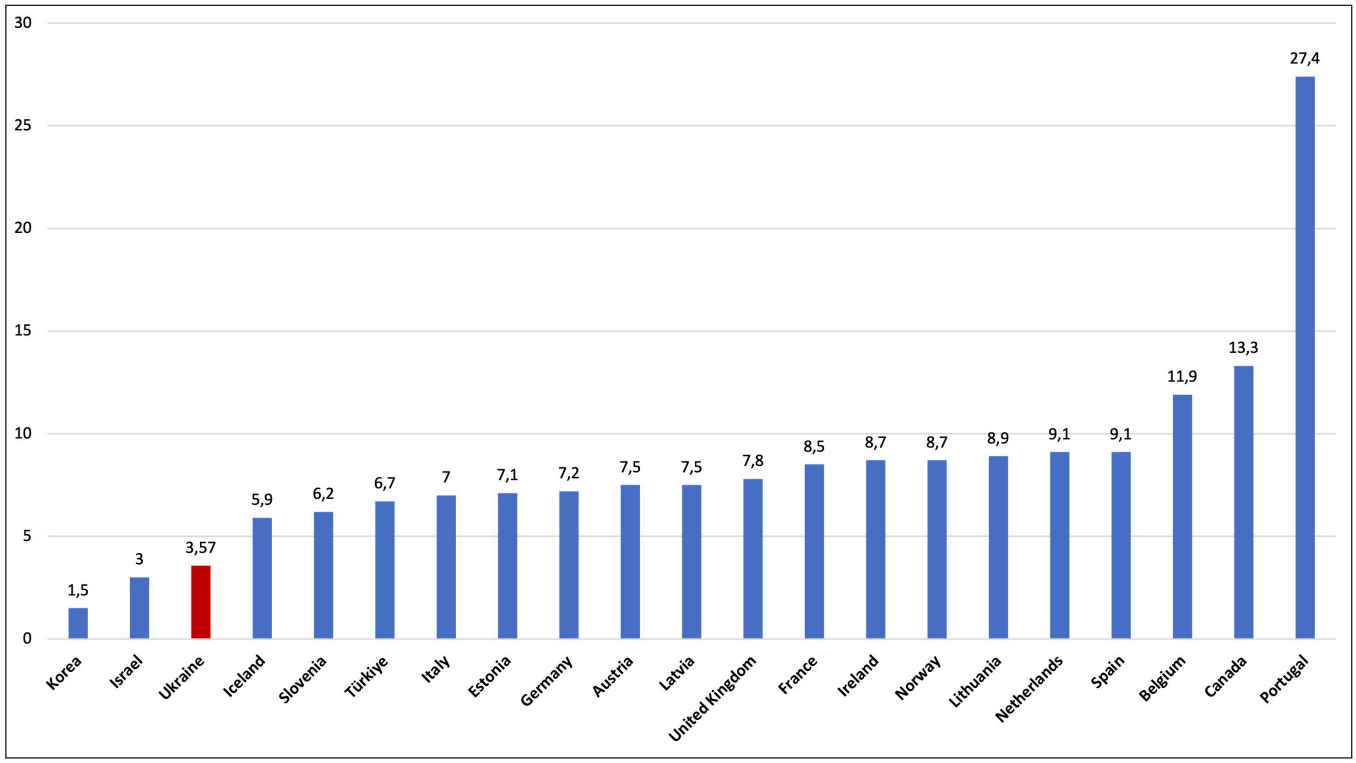

Fig. 2. The density of general practitioners per 10,000 people, in the countries of the world, 2020

Table I. Density of GPs per 10,000 people, average life expectancy, mortality rate due to diseases of the circulatory system per 1,000 people, gross regional product per 1 person in regions from different urbanization groups

Value	Gr.1 (n=5)	Gr.2 (n=14)	Gr.3 (n=6)	p
Average life expectancy	72,1±1,2	71±0,9	71,4±1,5	0,217
Gross regional product per 1 person ($)	2021±264	3158±734*	4289±3991*	0,017
Mortality rate from circulatory system diseases per 1000 people	14,1±0.8	16,8±1,6*	16±2,5	0,023
GPs density per 10,000 people	4,71±0.52	3,90±0.84	2,73±14,5*	0,024

* - significant difference $p<0.05$

The correlation matrix between the density of GPs per 10,000 people, and the level of urbanization of countries indicates absence of a reliable correlation ($r=-0.11$, $p>0.05$). However, in Ukraine, correlation matrix between the density of GPs per 10,000 people, and the level of the region urbanization indicates a reliable negative relation ($r=-0.67$, $p<0.05$). The higher the level of urbanization of the region, the lower density of GPs per 10,000 people is.

To study the effect of the urbanization level on density of GPs, average life expectancy, mortality from diseases of the circulatory system, gross regional product per 1 person ($), we divided regions of Ukraine into three groups by urbanization level.

The first group, with a low level of urbanization (up to 50% of the urban population), includes Zakarpattia (36.8%), Chernivtsi (42.9%), Ivano-Frankivsk (44.0%), Ternopil (45.3%), and Rivne (47.1%) regions. The second group, with an average level of urbanization (50%-70% of the urban population), includes Vinnytsia (51.4%), Volynska (51.8%), Cherkasy (56.6%), Khmelnytsky (57.1%), Zhytomyr (59.1%), Lviv (60.6%), Kherson (61.2%), Kyiv (61.6%), Poltava (62.0%), Kirovohrad (63.2%), Chernihiv (65.0%), Odesa (66.7%), Mykolaiv (68.4%), and Sumy (69.1%) regions. The third group, with a high level of urbanization (more than 70% of the urban population), includes Zaporizhzhya (77.2%), Kharkiv (80.9%), Dnipropetrovsk (83.9%), Luhansk (87.0%), Donetsk (90.8%) oblasts, and the city of Kyiv (100.0%).

For each group, we assessed density of GPs per 10,000 people, gross regional product (GRP), average life expectancy, and mortality rate due to diseases of the circulatory system per 1,000 people (Table **I**).

The analysis of Table I values shows no significant difference in average life expectancy between different levels of urbanization. In group 1, with a low level of urbanization, average life expectancy slightly exceeds that one in groups 2 and 3 ($p>0.05$).

According to the mortality from diseases of the circulatory system per 1,000 people, groups 1 and 2 differ significantly ($p<0.05$). The highest mortality rate was in group 2, with an average level of urbanization (16.8±1.6 per 1,000 people), while in group 1, with a low level of urbanization, it was the lowest (14.1±0.8 per 1,000 people).

We established that three groups differ significantly in terms of gross regional product per person ($p<0.05$). The highest gross regional product value is in the group with high level of urbanization (4289±3991 $), and the smallest is in the group with low urbanization level (2021±264 $) ($p<0.05$).

The lowest density of GPs per 10,000 people is observed in the group with high level of urbanization, 2.73±14.5 per 10,000 people, and the highest - in the group with low level of urbanization ($p<0.05$).

The correlation matrix indicates a reliable relation between the density of GPs per 10,000 people and average life expectancy ($r = 0.826$, $p<0.05$). We established that the greater the density of GPs in the region, the higher the average life expectancy is. There was no reliable correlation with other indicators ($p>0.05$).

However, there also was no reliable correlation between the density of GPs per 10,000 people, and average life expectancy in OECD countries ($r=0.09$, $p>0.05$).

DISCUSSION

Ukraine has an average level of urbanization in terms of the share of the urban population. In Ukraine, the level of urbanization is higher than in Slovenia, Austria, Ireland and Portugal. In terms of the level of urbanization, Ukraine is close to Lithuania, Latvia, Estonia and Italy.

In Ukraine, the density of GPs is significantly lower than that in OECD countries, except for the Republic of Korea and Israel. In Ukraine, the density of GPs has a reliable negative relation with the level of urbanization. The higher the level of urbanization, the lower the density of GPs in Ukraine is. In OECD countries, such dependence is not observed. In addition, it was found that in regions with high level of urbanization in Ukraine, the density of GPs is significantly lower than in regions with a low level of urbanization.

The obtained data contradict the OECD data, regarding the inverse dependence of the density of GPs and level of urbanization [16]. On the contrary, in the OECD countries, the greatest concentration of GPs is in the cities, where there is a demand for medical services, and where the GP necessarily performs functions of the doctor of «first meeting», or «primary link» in healthcare system [17-23]. According to the decision of the Alma-Ata Declaration of the World Health Organization, GPs have the status of a leading medical specialty, «representatives of which are responsible for providing medical assistance during the first contact with the patient and follow-up of patients, as well as for issues of health promotion and disease prevention» [15]. In OECD countries, the availability of medical services at GPs in rural areas is a significant problem [22, 23]. According to OECD data, in many countries there is a particularly high concentration of doctors in national capital regions, in particular, in Austria, the Czech Republic, Greece, Hungary, Portugal, Slovakia, and Germany [23, 24].

Probably, in Ukraine, lower density of GPs in regions with high level of urbanization is due to two reasons. The first reason is that not only GPs, but also specialist doctors in Ukraine perform functions of the «first meeting» doctor in health care. A patient can choose both a GP and a specialist doctor for the «first meeting». Ukraine has the smallest share of primary care doctors (13.45%) compared to OECD countries (Portugal (53.26%), Canada (47.8%), the Netherlands (46.41%), France (43.86%), Belgium (36.93%), Turkey (32.76%), and Austria (27.86%)) [16]. The second reason is an extensive network of healthcare facilities providing specialized care, with a high density of specialist doctors in urbanized regions.

Availability of specialist doctors in regions with high urbanization in Ukraine is determined by the patients' economic capacity. According to our data, gross regional product per person is significantly higher in highly urbanized regions, than in regions with low urbanization. Regions with high urbanization due to high gross regional product have fewer financial constraints in the health care system.

A comparison of regions with different levels of urbanization in Ukraine revealed absence of a reliable relation between the level of urbanization, and average life expectancy. All groups did not differ in average life expectancy. In addition, there was no correlation between the level of urbanization and average life expectancy among OECD countries ($p>0.05$). This is because average life expectancy at birth depends on economic development and environmental conditions, lifestyle, and progress in health care [17-19]. According to Nakajima H, Yano K., the main components of mathematical prediction of average life expectancy are availability of significant medical resources, prevention of heart diseases mortality, and prevention of risk factors exposure (alcohol consumption, smoking, obesity, etc.) [18]. According to Johan P Mackenbach et al., the risk factors characteristics of average life expectancy, are smoking (19.8% among men, and 18.9% among women), low income (9.7% and 13.4%), and high body

weight (7.7% and 11. 7%) (19). Ukraine has the lowest average life expectancy compared to OECD countries (71.3 years).

At the same time, a direct relation between the density of GPs and average life expectancy was found in Ukraine. The greater the density of GPs in Ukraine, the greater the average life expectancy of urbanized region is. Such dependence is not typical for OECD countries. It is likely, that dependence of the average life expectancy on the density of GPs in Ukraine is because life expectancy in Ukraine is significantly lower than in OECD countries, and its growth largely depends on the resources of the healthcare system, including personnel and financial ones.

In Ukraine, urbanization affects mortality from circulatory diseases per 1000 people. In regions with low urbanization, this mortality rate is significantly lower ($p<0.05$). Urbanization leads to an increase in cardiovascular diseases due to obesity and type 2 diabetes [3-5, 25]. According to the literature, obesity and diabetes are the main causes of mortality from circulatory diseases [20, 21]. It is likely, that in regions with low urbanization in Ukraine, lower mortality from diseases of the circulatory system is due to lower incidence of these diseases and lesser risk factors effect. This is a probable assumption, which involves a study of urbanization effect on the diseases of the circulatory system incidence in Ukraine.

CONCLUSIONS

When planning healthcare staffing, it is necessary to mind the level of urbanization of the region, and ensure the status of the GP as a leading medical healthcare specialist, responsible for medical care during the first meeting with the patient, and his follow-up.

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ORIGINAL ARTICLE

USING OF CALCULATION MODELS OF THE PENETRATION OF SUBSTANCES THROUGH THE SKIN IN THE ASSESSMENT OF THE RISK OF DERMAL INFLUENCE OF PESTICIDES ON WORKERS

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ABSTRACT

The aim: Quantitative characterization of parameters of penetration of pesticides through the skin and assessment of the risk of their dermal exposure to workers using the basic provisions of diffusion theory and calculation models.

Materials and methods: The penetration coefficient was calculated using the Potts's and Guy's equation: $\log K_{p,m} = -2,8 - 6,0\times10^{-3}MW + 0,74\log K_{o/w}$ ($R^2 = 0.67$). Determination of the absorbed dose was carried out using the maximum flow of the substance per unit area and the area of contact of the pesticide with the skin. Calculations were performed using the Microsoft Excel 2010 computer program package, PubChem information databases, EU Pesticides Database.

Results: It was established that the pyrethroid insecticide bifenthrin and triazole fungicides (prothioconazole, propiconazole, and tebuconazole) penetrate the skin the fastest among the studied substances. The highest value of the absorbed dose is observed in the case of bifenthrin, which creates dangerous conditions during production operations with pesticide formulations based on it and conditions the adoption of necessary management decisions.

Conclusions: The calculation model of Potts and Guy (1992) is sufficiently informative and reliable to determine the coefficient of penetration of pesticides from aqueous solutions in the phase of the steady process of diffusion and allows determining the doses absorbed through the skin and assessing the risk of dermal exposure to workers.

KEY WORDS: pesticides, dermal absorption, penetration coefficient, mathematical modeling, occupational risk

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INTRODUCTION

Quantifying the penetration process and understanding the mechanism of transport of organic substances through the skin is equally important in pharmacology, dermatology, toxicology, and hygiene. The issue of dermal absorption takes on special importance in the regulatory assessment of the probability of systemic exposure of plant protection products (PPPs) when they come into contact with the skin in the conditions of professional use and making relevant decisions within the existing legal framework [1, 2].

Despite the relative availability of experimental determination of dermal exposure doses, quantification of the dose absorbed through the skin is an extremely difficult task due to the influence of many factors on the absorption process (individual skin differences, concentration of the substance in the solvent, physicochemical properties of the substance and solvent, duration and area of exposure, properties of the skin itself, etc.).

The solution to this problem is sought in mathematical modeling based on the understanding of the fundamental mechanisms of the diffusion process, quantitative structure-activity relationships (QSAR), and taking into account that penetration through the skin is not a biological activity, but the result of the process of passive diffusion - quantitative structural permeability relationships (QSPR) or quantitative structure penetration ratios (QSPeR) [3, 4].

Skin modeling has made tremendous progress over the past few decades. A detailed review of the models, their advantages, disadvantages and prospects for use are covered in scientific works [5, 6].

The experience of practical solutions to problems in this direction indicates a very limited and insufficient use of theoretical achievements that open up wide opportunities for quantitative description of the process of penetration and prediction of the behavior of chemical substances when they come into contact with the skin.

Fundamental assets in the field of the theory of penetration through the skin of PPPs in the aspect of quantifying the absorbed dose are not used in any of the exposure models of occupational risk assessment [7, 8].

Along with this, a distinctive feature of the risk assessment methodology adopted by the US EPA is its ability to be adapted to specific tasks, to the possibility of choosing between alternative approaches to assessment, as well as revision of risk assessment guidance materials in connection with accumulated experience and the emergence of new information data. The main task is to master not only the general risk assessment, but also the possibilities of creative approaches inherent in this methodology.

The involvement of fundamental concepts of the phenomenon of mass transfer and thermodynamic interpretations of the diffusion process and mathematical modeling make it possible to calculate the dose of a substance absorbed through the skin and outline current tasks on the way to optimizing risk assessment models.

The application of the basic principles of the theory of isothermal isobaric molecular diffusion in understanding the mechanism of penetration of chemicals through the skin has been known for a long time and is based on Fick's first and second laws of diffusion. From the point of view of thermodynamics, Fick's first law of diffusion establishes the essence of any equilibrium process in the medium (membrane): in the case of a stationary phase of diffusion, the density of the flow of matter penetrating through the membrane (J_{ss}) through a unit of area per unit of time is directly proportional to the penetration coefficient ($K_{p,m}$) and the concentration of the substance in the solution (C). $K_{p,m}$ is the main indicator of the substance's ability to overcome the skin barrier. It makes it possible to determine the flow of a substance through the skin, and with known values of the area and exposure time, the absorbed dose. This indicator describes the chemical substance's affinity for the solvent and the stratum corneum of the skin. A substance that dissolves well in a solvent is more likely to remain in solution than to penetrate the skin.

Theoretically, these data can be used to determine $K_{p,m}$ of chemicals from aqueous solutions using structure-activity principles. Experimentally determined values of $K_{p,m}$ for structurally related biological activity (ability to penetrate through the skin) showed a relationship with some physicochemical properties, in particular, the partition coefficient in the n-octanol/water system ($K_{o/w}$) and molecular weight (MW).

Following this path, an empirical algorithm was developed for obtaining Kr,m values of medicinal products from $K_{o/w}$ values [9]. The results of work [9] were the object of independent statistical analysis by various researchers to assert the objective correspondence of these data to equations that take into account MW and polarity (the latter as $K_{o/w}$).

The most productive, but far from exhaustive, algorithm for determining $K_{p,m}$ is the equation proposed by Potts and Guy: $\log K_{p,m} = -2.8 - 6.0\times10^{-3}MW + 0.74\log K_{o/w}$ [10]. This equation has a solid theoretical basis, averages most of the experimental variability and can be used to determine the penetration coefficient of chemical substances when solving certain applied problems.

Taking into account the bioethical principles of animal treatment, we have shown the possibility of using mathematical models for calculating $K_{p,m}$ for the active substances of PPPs, the risk of percutaneous action of which is quite obvious, taking into account their toxicity and ability to penetrate through intact skin.

THE AIM

Quantitative characterization of the parameters of pesticide penetration through the skin and risk assessment of their dermal exposure to workers using the basic tenets of diffusion theory and calculation models.

MATERIALS AND METHODS

The object of the research was the active substances of PPPs when they were applied by ground rod spraying of agricultural crops. The subject of the study was dermal exposure and absorbed doses.

The algorithm for determining the estimated dermal absorbed dose is based on the use of the penetration flow of the substance, which is formed from the penetration coefficient during the exposure time in the stage of the steady process at an unchanged concentration of the pesticide in the working (aqueous) solution (Fig. 1).

To calculate $K_{p,m}$, we used the regression equation [10], which relates this indicator to MW and $K_{o/w}$. The equation was derived from the analysis of more than 90 organic substances of different classes of chemical compounds, which had MW values from 18 to 750 and $K_{o/w}$ from -3 to +6. The coefficient of multiple determination (R^2) is 0.67, which indicates a good agreement between the selected determinants and the studied indicator.

The exposure dose of the pesticide on the skin is formed due to the settling of aerosol particles formed during spraying. That is why it is important to know the concentration of the active substance of the PPPs in the working solution. The maximum concentration of the pesticide in the working solution was calculated taking into account the content of the substance in the pesticide formulation, the consumption rate of the pes-

Table I. Physicochemical parameters and concentrations of active substances in working solutions under real conditions of application of the plant protection products based on them

Active substance	CAS RN	Chemical class	MW	$LogK_{o/w}$	AOEL, mg/kg	A, g/l	Treated crop	N, g/ha	C, mg/ml
Azoxystrobin	131860-33-8	Strobilurins	403,40	2,50	0,2000	100,0	Sugar beet	1,0	0,330
Acetamiprid	135410-20-7	Neonicotinoids	222,67	0,80	0,0250	60,0	Rapeseed	0,6	0,120
Bifenthrin	82657-04-3	Pyrethroids	422,90	6,00	0,0075	30,0	Rapeseed	0,6	0,060
Imidacloprid	138261-41-3	Neonicotinoids	255,66	0,57	0,0800	200,0	Sunflower	0,25	0,170
Carbendazim	10605-21-7	Benzamidazoles	191,19	1,52	0,0200	300,0	Sugar beet	1,0	1,000
Mesotrione	104206-82-8	Triketones	339,32	0,90	0,0050	55,0	Maize	1,5	0,275
Propiconazole	60207-90-1	Triazoles	342,20	3,72	0,1000	60,0	Winter wheat	1,0	0,200
Prothioconazole	178928-70-6	Triazoles	344,30	3,82	0,2000	60,0	Winter wheat	1,0	0,200
Tebuconazole	107534-96-3	Triazoles	307,80	3,70	0,0300	240,0	Winter wheat	1,0	0,800
Flumioxazin	103361-09-7	Dicarboxamides	354,30	2,55	0,0220	510,0	Soybean	0,12	0,204

Table II. Estimated values of penetration parameters ($K_{p,m}$, J_{ss}) and doses of pesticides absorbed through the skin

Active substance	$K_{p,m}$, cm/h	C, mg/ml	J_{ss}, mg/cm²×h	$D_{abs.}$		
				mg/cm²	mg/kg m.t.*	
					PPE⁻	PPE⁺
Azoxystrobin	$4,36\times10^{-4}$	0,330	$1,44\times10^{-4}$	0,0009	0,0123	0,0012
Acetamiprid	$2,90\times10^{-4}$	0,120	$3,48\times10^{-5}$	0,0002	0,0027	0,0003
Bifenthrin	$1,27\times10^{-1}$	0,060	$7,62\times10^{-3}$	0,0460	0,6290	0,0629
Imidacloprid	$1,20\times1^{0}\text{-}4$	0,170	$2,04\times10^{-4}$	0,0001	0,0014	0,0001
Carbendazim	$1,51\times10^{-3}$	1,000	$1,51\times10^{-3}$	0,0090	0,1230	0,0123
Mesotrione	$6,76\times1^{0}\text{-}5$	0,275	$1,86\times10^{-5}$	0,0001	0,0014	0,0001
Propiconazole	$7,94\times10^{-3}$	0,200	$1,59\times10^{-3}$	0,0100	0,1370	0,0137
Prothioconazole	$9,14\times10^{-3}$	0,200	$1,83\times10^{-3}$	0,0110	0,1503	0,0150
Tebuconazole	$1,83\times10^{-3}$	0,800	$1,46\times10^{-3}$	0,0090	0,1230	0,0123
Flumioxazin	$9,15\times10^{-4}$	0,204	$1,87\times10^{-4}$	0,0001	0,0150	0,0015

Note: * – absorbed dose through the skin, calculated for the surface area of the hands (820 cm²) and unit of mass of the operator's body weight (60 kg); PPE⁻ – absence of personal protective equipment (gloves); PPE⁺ – using of personal protective equipment (gloves).

ticide formulation and the average consumption rate of the working liquid (tractor-mounted/trailed boom sprayer: hydraulic nozzles – 300 l/ha).

Determination of the absorbed dose (D_{abs}) was carried out using the value of the maximum flow of the substance through a unit area (cm²) and the total area of contact of the pesticide with the skin. At the same time, the area of open areas of the skin of the hands (820 cm²), unprotected by personal protective equipment (PPE^{-}) and protected (PPE^{+}) was taken into account [11]. The absorbed dose determined by this algorithm gives an idea of the general danger and characterizes the risk (HQ) associated with the entry of the pesticide into the body of those working through the skin. The risk is considered acceptable if HQ ≤ 1.

Physico-chemical parameters (MW, $logK_{o/w}$) and acceptable operator exposure level (AOEL) for each active ingredient of pesticides are taken from information databases (PubChem, EU Pesticides Database) [12, 13].

The research results were subjected to statistical processing using the Microsoft Excel 2010 computer program package. The work used an information-analytical method, mathematical modeling of the process of penetration through the skin, a risk assessment model, methods of system, comparative and content analysis.

RESULTS

The physico-chemical constants of the studied active substances of PPPs, their permissible levels and maximum concentrations in the working solutions of pesticide formulations during the treatment of agricultural crops by the rod spraying method are given in Table I.

It was established that the investigated substances belong to different chemical classes of organic com-

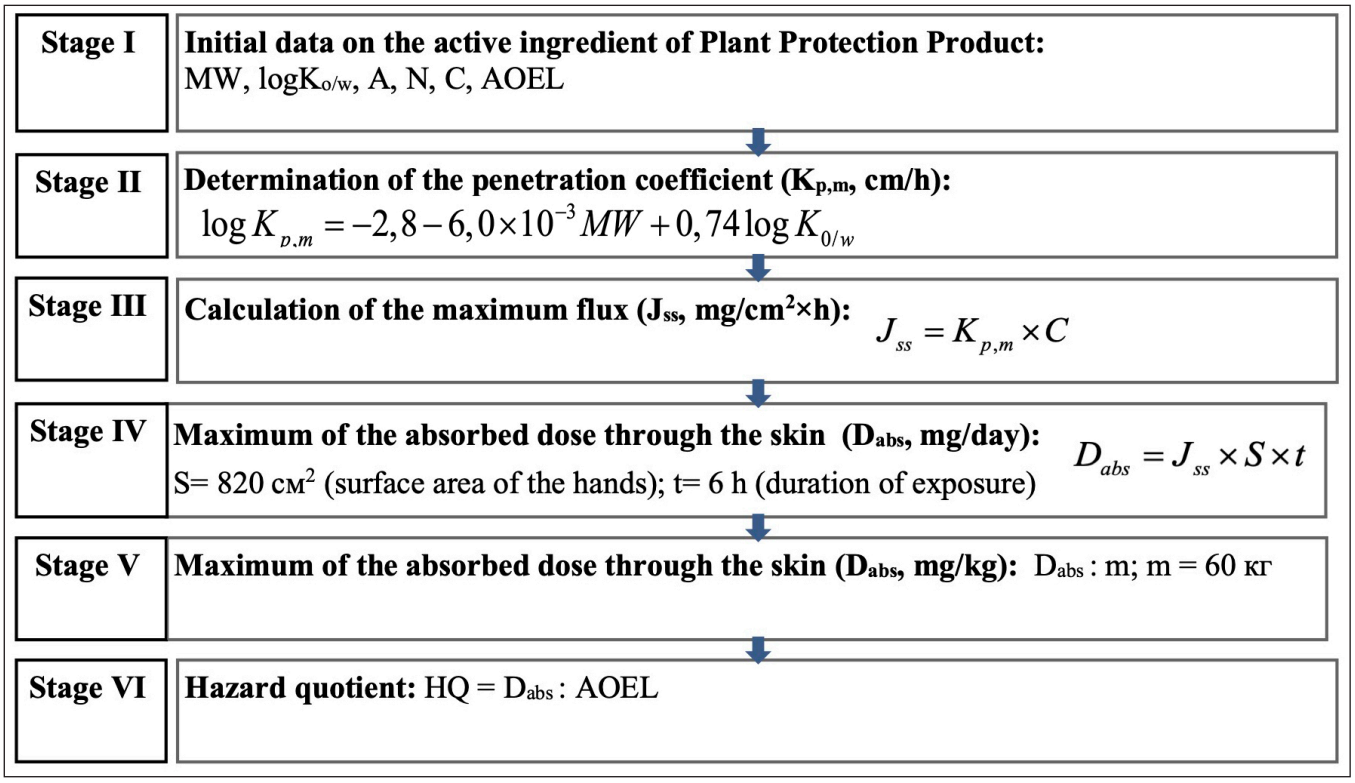

Fig. 1. Algorithm of determining of the dermal absorbed dose of active substances of plant protection products using mathematical modeling of the main parameters of the diffusion process and risk assessment

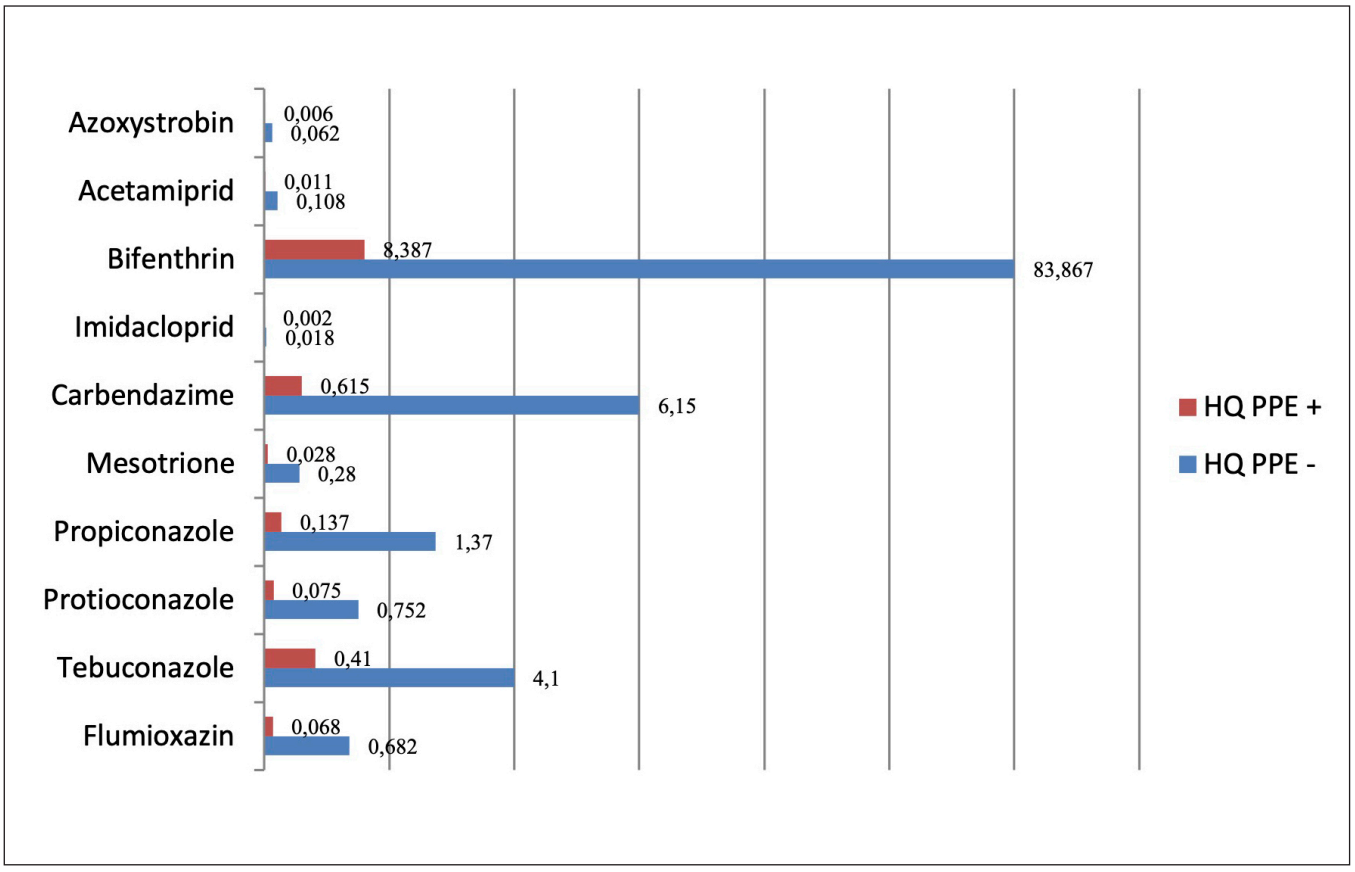

Fig. 2. Quantitative characterization of the risk of dermal exposure of the pesticides

pounds, their MW are in the range of values from 191.19 (carbendazim) to 422.90 (bifenthrin), $K_{o/w}$ – from 0.57 (imidacloprid) to 6.00 (bifenthrin). Thus, the values of the selected determinants for the calculation of $K_{p,m}$ are included in the range of values of the descriptors included in the regression equation [10].

Concentrations of substances in working aqueous solutions increase in direct proportion with an increase in their content in pesticide formulations and consumption rates per unit area of treatment.

The calculated values of the penetration parameters ($K_{p,m}$, J_{ss}) and the dose absorbed through the skin are shown in Table II.

The results of the calculations showed a direct proportional dependence of $K_{p,m}$ on the value of $K_{o/w}$: with an increase in $K_{o/w}$, the rate of entry of substances through trade per unit of time increases. The pyrethroid insecticide bifenthrin ($K_{p,m}$ = 0.127 cm/h) and triazole fungicides (proteoconazole, propiconazole, and tebuconazole) penetrate the skin the fastest; their $K_{p,m}$ are within the same order and range from 1.83×10^{-3} cm/h (tebuconazole) to 9.14×10^{-3} cm/h (proteoconazole). Carbendazim has a similar rate of penetration ($K_{p,m}$ = 1.51×10^{-3} cm/h), which is characterized by both a low $K_{o/w}$ value and a small molecular size (MW = 191.19), which allows the substance easily overcome the skin barrier. Thus, substances with a smaller molecular size and greater lipophilic penetrate the skin faster from aqueous solutions.

The determined concentrations of substances in aqueous solutions and their $K_{p,m}$ made it possible to calculate the flow of the substance through the skin per unit area and the maximum absorbed dose from the exposure area of 820 cm^2 during a work shift lasting 6 hours.

As expected, the highest value of the absorbed dose (D_{abs} = 0.6290 mg/kg) is observed in the case of bifenthrin, due to its high speed of penetration through the skin. The low rate of penetration of mesotrione ($K_{p,m}$ = 6.76×10^{-5} cm/h) and imidacloprid ($K_{p,m}$ = 1.20×10^{-4} cm/h) forms the smallest absorbed dose, which in both cases is 0, 0014 mg.

Quantitative characterization of the risk (HQ) of harmful effects of pesticides when they enter through the skin is a comparison of the absorbed and permissible dose (Fig. 2).

The obtained results of the assessment of the risk of percutaneous action of the investigated pesticides differ significantly. The risk of dermal exposure to azoxystrobin, acetamiprid, imidacloprid, mesotrione, prothioconazole, flumioxazin does not exceed the permissible level: HQ is from 0.018 (imidacloprid) to 0.752 (prothioconazole). This allows us to conclude that the production environment is sufficiently safe for workers if the generally accepted occupational health and safety requirements are observed when working with pesticides. For the rest of the studied active substances, which are characterized by skin resorptive action, the risk of dermal exposure exceeds the permissible level, which requires the adoption of appropriate management decisions.

The use of protective gloves with an exposure attenuation factor of 0.1 makes it possible to reduce the total skin exposure dose, and the risk of dermal exposure to acceptable values.

Manufacturing operations with pesticide formulations based on bifenthrin are especially dangerous. When performing work without the use of PPE (gloves), the risk of potential dermal exposure to bifenthrin to workers may exceed the permissible level by 84 times. The use of gloves will reduce the exposure by an order of magnitude. To reduce the risk of potential exposure to bifenthrin to an acceptable level, it is possible to limit the time: the duration of work with dangerous pesticides should not exceed 4 hours, during which you can actually treat an area of 30 hectares on average, which will reduce the actual costs of the drug by 1.5 times (compared to 50 hectares, which are included in the risk calculation according to the POEM and BVA models) [7].

DISCUSSION

Studies have shown that the developed algorithm for determining the dose absorbed through the skin using the basic provisions of the diffusion theory and the calculation model of Potts and Guy [10] is sufficiently informative in solving the practical problems of hygienic regulation of pesticides and the possibility of conducting a more objective assessment of the adverse effects of pesticides upon their arrival to the body through the skin from working aqueous solutions. Nevertheless, along with the attractiveness due to the simplicity of the solution and the availability of parameters, this model has a number of limitations, the main of which is the possibility of its practical application only in the phase of the stable diffusion process.

At the same time, for most chemicals, the approximate time of onset of the stable phase is almost 2.4 times longer than the lag time, when the time of occurrence of the event (contact with a chemical substance, for example, which has a skin-absorbing effect) can be much shorter. Therefore, calculations of the absorbed dose during this time using this model may significantly exceed the real level of absorption, which will inevitably lead to incorrect conclusions.

This model does not describe the entire diffusion process, especially its unstable phase, which in turn makes

it impossible to analyze the influence of other factors on permeability, for example, co-formulants. Meanwhile, the lost and the lost phases of the diffusion process are equally important for the calculation of absorbed doses during dermal application of compounds.

Absorption occurs faster during the transient phase of the diffusion process, which precedes the lag-time, when the chemical mostly fills the reservoir of the stratum corneum and almost no amount of the substance leaves the stratum corneum. Some time after the lag-time, a steady state of the diffusion process is reached, when the rate at which the amount of substance enters and leaves the stratum corneum is constant.

The barrier resistance provided by the stratum corneum is the inverse of the penetration coefficient. Since the barrier for the penetration of intact skin includes the viable epidermis, the resistance in the stationary phase of the diffusion process is determined by the sum of the resistances in the stratum corneum and the epidermis.

Diffusion in the epidermis is much greater than in the stratum corneum, the magnitude of resistance is often small, and the permeability through the stratum corneum-epidermis barrier is almost equal to the permeability of the stratum corneum itself. The epidermis is much more hydrophilic than the stratum corneum, and the partition coefficient of the absorbed substance between the stratum corneum and the epidermis is similar to the partition coefficient of the substance between lipophilic and hydrophilic solvents such as octanol and water ($K_{o/w}$). Therefore, highly lipophilic compounds with a large value of $K_{o/w}$ will have large resistance values, and the total permeability of the skin ($K_{p,m}$) will be much less than the permeability through the stratum corneum, because the relatively hydrophilic epidermis delays the flow of substances leaving the stratum corneum.

Because many chemicals of environmental concern are highly lipophilic (e.g., pesticides), assessment of dermal absorption must include combined permeability across the stratum corneum-epidermis barrier.

CONCLUSIONS

The application of the basic provisions of the theory of molecular diffusion in understanding the mechanism of penetration of chemical substances through the skin opens up wide possibilities of quantitative description of the process of penetration and prediction of the behavior of chemicals upon contact with the skin.

An integral indicator that characterizes the diffusion of a substance and the speed of penetration through the skin is the penetration coefficient, which shows the ability of the substance to overcome the skin barrier and is important in the quantitative characteristics of the process.

It was established that the calculation model of Potts and Guy (1992) is sufficiently informative and reliable for determining the penetration coefficient of a substance from aqueous solutions in the phase of the steady process of diffusion and allows determining the doses absorbed through the skin and assessing the risk of harmful effects of substances characterized by skin-resorptive action.

Further research will be aimed at determining the dermal absorption of pesticides in the phase of the unsteady diffusion process using the model of the two-layer structure of the skin according to the concept of Cleek and Bunge, based on the amphiphilic properties of the structural elements of the skin - the stratum corneum and the viable epidermis, which appears to be a useful tool for compiling a concentration profile and the formation of the internal depot and the extension of the pesticide action in the post-exposure period.

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The Author declare no conflict of interest.

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ORIGINAL ARTICLE

RATIONAL PHARMACOTHERAPY ON THE BASIS OF PHARMACOECONOMIC JUSTIFICATION AND MARKETING RESEARCH ON THE APPLICATION OF IMMUNOMODULATORY PHYTOPREPARATIONS

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ABSTRACT

The aim: Pharmacoeconomic substantiation and marketing research of immunoprotective phytopreparations in Ukraine to substantiate rational pharmacotherapy of the effectiveness of immunomodulatory drugs of plant origin and pharmaceutical care of patients to strengthen individual immunity.

Materials and methods: Research materials - data from the State Register of Medicinal Products of Ukraine; information content of the Public Health Center of the Ministry of Health of Ukraine; data of the State Register of Wholesale Prices for medicines declared in Ukraine under the international non-proprietary or common name as of 01.01.2023. Research methods: theoretical analysis of scientific sources, systematic, retrospective, descriptive and frequency analysis of information resources of databases; pharmacoeconomic analysis, marketing analysis of positioning in the pharmaceutical market of Ukraine to substantiate rational pharmacotherapy and the effectiveness of immunomodulatory drugs of plant origin to strengthen individual immunity.

Results: Theoretical analysis and pharmacoeconomic substantiation of rational pharmacotherapy of efficiency of application of drugs of immunomodulatory action of plant origin and pharmaceutical care for strengthening of individual immunity of patients is carried out. The algorithm of pharmacoeconomic analysis of the use of immunomodulatory phytopreparations to ensure rational pharmacotherapy and pharmaceutical care of outpatients is substantiated. To substantiate the availability of effective immunomodulatory phytopreparations for patients, marketing research on the use of immunomodulatory phytopreparations in Ukraine has been conducted.

Conclusions: The theoretical analysis shows that the use of immunomodulatory drugs of plant origin is appropriate in rational pharmacotherapy to strengthen the individual immunity of patients, which is especially relevant in an exacerbation of the epidemic situation caused by the spread of infectious diseases of viral origin. An algorithm of pharmacoeconomic substantiation has been developed, which provides an opportunity to confirm the therapeutic efficacy and pharmacoeconomic feasibility of immunomodulatory phytopreparations for rational pharmacotherapy and pharmaceutical care of patients. The results of marketing research provide an opportunity to determine the availability (positioning and price range) for patients of effective immunomodulatory phytopreparations in Ukraine and outline the prospects for pharmaceutical development and registration on the pharmaceutical market of Ukraine of new effective immunomodulatory drugs of plant origin.

KEY WORDS: pharmacoeconomic substantiation, marketing researches, pharmaceutical help to patients, immunomodulatory phytopreparations, combined phytopreparations, plant extracts

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INTRODUCTION

Among the current challenges and threats to the health of the population of Ukraine, one of the most threatening is the spread of infectious diseases of viral origin. With the spread of the COVID-19 epidemic, this challenge poses a threat not only to Ukrainian society, the health care system, but also to the entire European and World community.

The speed and contagiousness of the spread of infectious diseases of viral origin determines the severity of a new challenge to modern society – the formation of social and individual immunity. Under such conditions, the effectiveness of antiviral vaccines is undeniable. However, provided that patients have individual contraindications to vaccination, the presence of systemic diseases, to strengthen individual immunity, it is necessary to find alternative ways of rational pharmacotherapy of patients and pharmaceutical care.

Infectious diseases of viral origin have for many years outweighed the prevalence of all other infectious diseases. According to the Center for Public Health of the Ministry of Health of Ukraine, the annual statistics

of the incidence of infectious diseases of viral origin in Ukraine is 25-30% of the total incidence. With the spread of the COVID-19 epidemic, the number of deaths from complications caused by systemic diseases and ineffective pharmacotherapy of pneumonia caused by SARS-COV-2 infection is increasing [1, 2].

Scientists summarize that the course of acute respiratory diseases combines two interdependent and interdependent processes: the growth of infectious pathology, reduced immunological reactivity of the patient's body. Therefore, in rational pharmacotherapy it is necessary to achieve the optimal therapeutic effect of complex therapy with the use of immunomodulatory drugs [3, 4].

In the context of the spread of the COVID-19 epidemic, the activities of family physicians should also be focused on immunoadaptation – a set of measures aimed at optimizing immune responses in healthy people, but at high risk of developing chronic diseases.

These include immunomodulatory – drugs of natural or synthetic origin, which in therapeutic doses restore the functions of the immune system [5, 6].

Natural immunomodulatory include phytopreparations that are effective and safer than synthetic drugs, have a wide therapeutic range, fewer adverse reactions and less interaction with other pharmaceuticals. In this regard, phytopreparations are currently the safest immunomodulatory, which is acceptable for the adult population and especially acceptable in gerontological and pediatric practice [5, 7].

In general, immunomodulatory drugs of plant origin provide immunomodulatory, anti-inflammatory and hemostatic effects; prevent excessive activation of free radical oxidation and restore the functional activity of the body's natural antioxidant system; increase the body's resistance to the effects of adverse environmental factors, stimulate regeneration processes; increase the phagocytic activity of neutrophils and macrophages, stimulate the synthesis of interleukin-1, the transformation of B-lymphocytes into plasma cells, improve the function of T-helpers. The pharmacologically active biological substances inulin, laevulose and betaine improve metabolic processes. High molecular weight polysaccharide, which belongs to the class of hexose glycosides (which includes glucose, rhamnose, arabinose, mannose, xylose, galactose, uronic acids) provides antiviral action due to inhibition of viral protein synthesis. Ukraine). The vast majority of immunomodulatory drugs of plant origin also have antibacterial and antifungal effects (drugs of Echinacea purpurea, Pinus silvestris). Liquid extract Proteflazid obtained from a mixture of herbs (1:1) Herba Deschampsia caespitosa L. and Herba Calamagrostis epigeios L. (extraction solvent - ethanol 96%), equivalent to at least 0.0035 mg of flavonoids in terms of rutin is a complex of active substances Immunoflazid, in the form of syrups, capsules, Ukraine, which inhibit the replication of DNA and RNA-viruses both in vitro and in vivo. Preclinical and clinical studies have shown inhibitory activity of the drug against influenza viruses and acute respiratory infections, herpes viruses. It is proved that the mechanism of direct antiviral action is to inhibit the synthesis of virus-specific enzymes – DNA and RNA polymerases, thymidine kinase, reverse transcriptase, neuraminidase and induction of endogenous interferon synthesis. It is established that the drug normalizes the synthesis of endogenous α- and γ-interferons to a physiologically active level, which increases the non-specific resistance of the organism to viral and bacterial infections [5,7,8].

Phytoimmunocorrection is relevant in the format of modern medical technologies and standards of appropriate medical care for patients. Therefore, the list of original immunomodulatory phytopreparations and analogues on the Ukrainian pharmaceutical market is growing [6, 9-11].

In comparison with the world practice of immunoprotective phytopreparations the tendency of steady growth of demand of patients to use of medicines of a plant origin is noted [12].

Pharmaceutical manufacturers are expanding the range of immunomodulatory phytopreparations. Some manufacturers specialize in the production of phytopreparations. Thus, in the range of Bionorica drugs registered on regulated markets, the share of immunomodulatory phytopreparations is more than 20% of total sales [13].

THE AIM

Pharmacoeconomic substantiation and marketing research of immunomodulatory phytopreparations in Ukraine to substantiate rational pharmacotherapy of the effectiveness of immunomodulatory drugs of plant origin and pharmaceutical care of patients to strengthen individual immunity.

MATERIALS AND METHODS

Research materials - data from the State Register of Medicinal Products of Ukraine; information content of the Public Health Center of the Ministry of Health of Ukraine; data of the State Register of Wholesale Prices for medicines declared in Ukraine under the international non-proprietary or common name as of 01.01.2023. Research methods: theoretical analysis of scientific sources, systematic, retrospective, descrip-

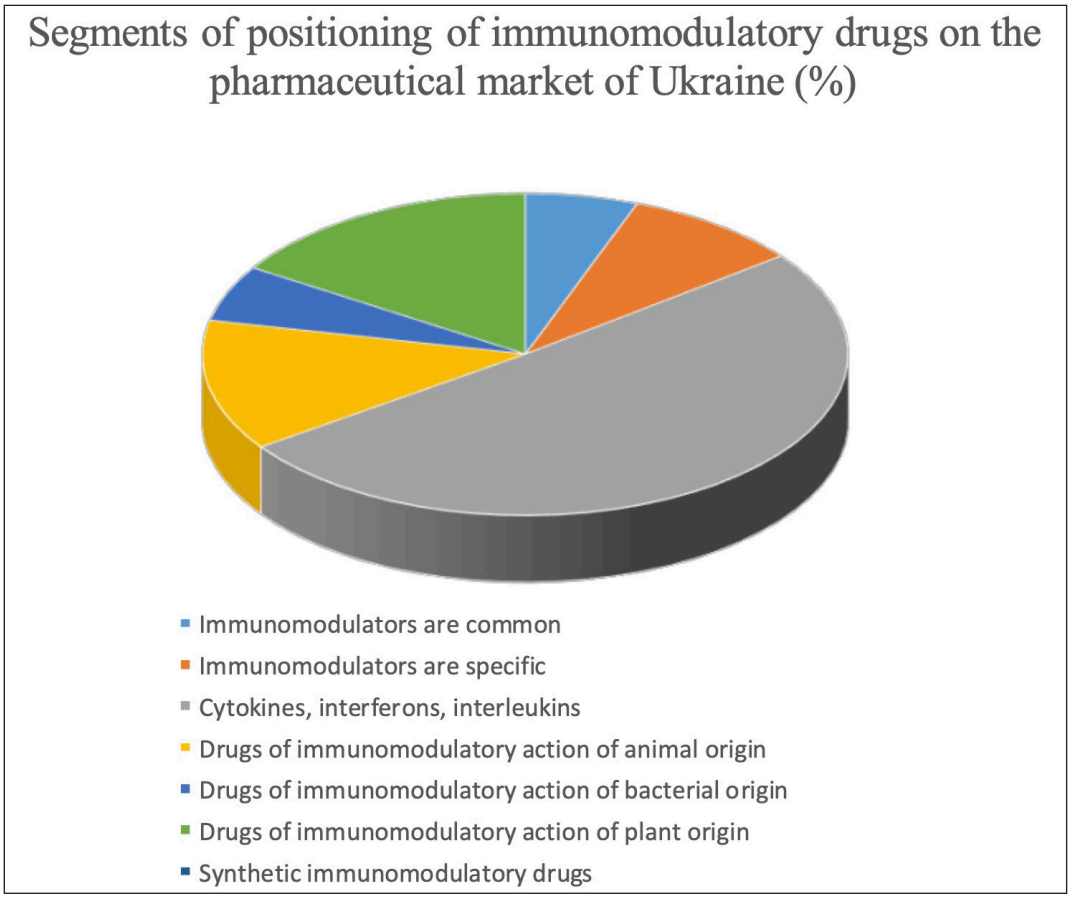

Fig.1. Results of comparative analysis of the share of positioning of immunomodulatory phytopreparations among immunomodulatory in the pharmaceutical market of Ukraine (for the period 2016-2022).

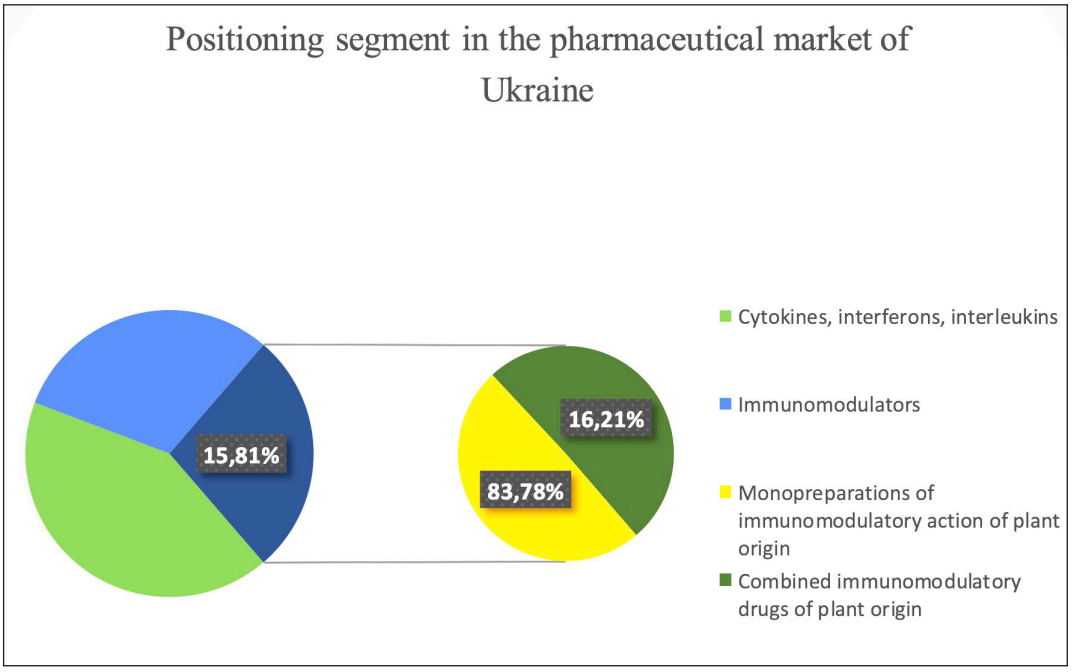

Fig. 2. Distribution of mono and combined phytopreparations with immunomodulatory action.

tive and frequency analysis of information resources of databases; pharmacoeconomic analysis, marketing analysis of positioning in the pharmaceutical market of Ukraine to substantiate rational pharmacotherapy and the effectiveness of immunomodulatory drugs of plant origin to strengthen individual immunity.

RESULTS

To substantiate rational pharmacotherapy and pharmaceutical care of outpatients with immunomodulatory phytopreparations, cost-effectiveness analysis (CEA), which involves comparing the cost and effectiveness (direct and indirect clinical effects) of treatment, is

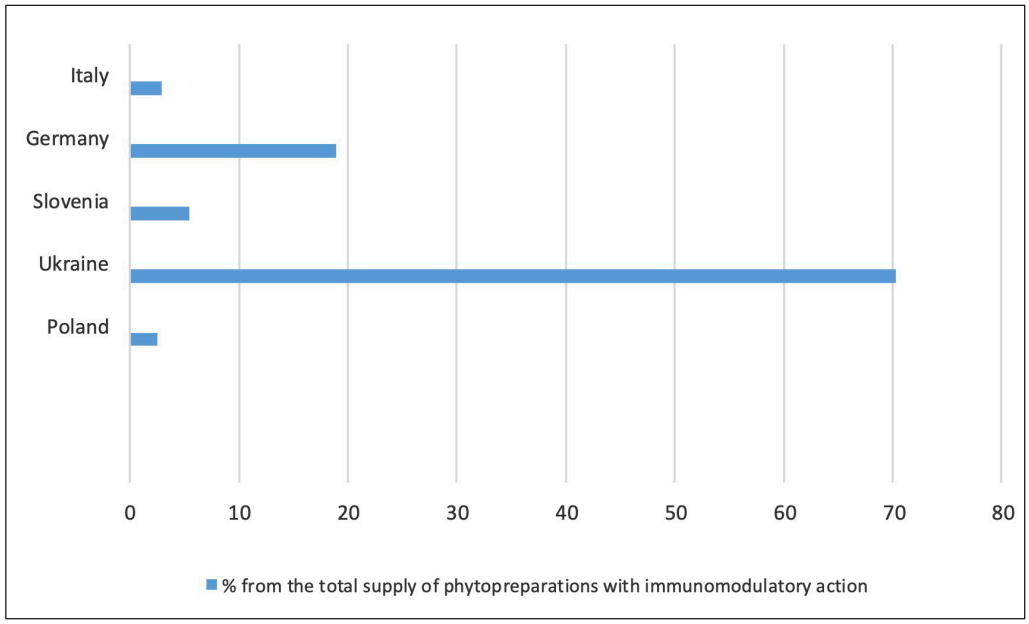

Fig. 3. Distribution of phytopreparations of immunomodulatory action by producer countries on the pharmaceutical market of Ukraine (for the period 2016-2022).

Table I. Algorithm of pharmacoeconomic analysis of immunomodulatory phytopreparations for substantiation of rational pharmacotherapy and pharmaceutical care of outpatients

№	Stages of pharmacoeconomic analysis based on integrated application of methods	Legend
1	Determination of direct costs of pharmacotherapy.	DC_1
2	Determination of indirect costs of pharmacotherapy.	IC_1
3	Determining the total cost of therapy.	COI
4	Determining the cost per unit of efficiency	CER, calculation formula: $CER = \frac{DC + IC}{Ef}$, *(1)*
5	Determination of the usefulness due to treatment	QALY
6	Comparison of the cost-benefit ratio	CUR, calculation formula: $CUR = \frac{DC + IC}{Ut}$, *(2)*
7	Selection of rational purpose of pharmacotherapy with the use of immunomodulatory phytopreparations.	

primarily effective. This analysis allows you to evaluate the effectiveness, in particular to assess the unit cost of treatment. In the end, it is not the cheapest method of treating the disease that is determined, but the optimal one in terms of efficiency and cost. Indicators of the effectiveness of the drug in treatment can be direct clinical effects: changes in physiological, biochemical, physical and other indicators of the patient's body, suppression of symptoms, improvement, well-being, indirect clinical effects (reduction of complications, re-hospitalizations), changes in health in the studied groups of patients, changes in quality of life. Carrying out a cost-effectiveness analysis provides an opportunity to determine the optimal amount of pharmacotherapy for the patient. Determination of the cost-effectiveness ratio (CER), the cost per unit of efficiency according to formula *1*, given in the algorithm in Table I, where CER is the cost-effectiveness ratio; DC – direct costs; IC – indirect costs; Ef – an indicator of the effectiveness of treatment allows you to choose the optimal method of treatment using immunomodulatory phytopreparations.

Therefore, reducing the cost per unit of efficiency in each case has a positive effect on patients, so pharmaceutical care provided by modern masters of pharmacy in pharmacies and medical institutions should be based on proof of therapeutic efficacy and pharmacoeconomic feasibility of immunomodulatory herbal medicines.

It is also effective to use the method of pharmacoeconomic analysis "cost-utility (utilitarianism") - cost-utility analysis (CUA) - a kind of cost-effectiveness analysis, which compares the cost of treatment in monetary terms and its effectiveness in terms of utility (utilitarianism) – treatment outcomes expressed in quality of life indicators. The usefulness index is most often expressed in QALY (quality adjusted life year), but you can use the usefulness index, which is determined by other methods accepted in medicine. The application of

the cost-benefit analysis provides the determination of the most acceptable for the patient method of treatment from the standpoint of cost and benefit, in comparison with the cost-benefit ratio (CUR), the cost per unit of utility of the treatment method 2, given in the algorithm in table I, where CUR is the cost-benefit ratio; DC – direct costs; IC – indirect costs; Ut – utilitarianism. According to the pharmacoeconomic justification, the method of treatment with a lower CUR value is more acceptable for patients. A well-founded algorithm for pharmacoeconomic analysis of the use of immunomodulatory phytopreparations to ensure rational pharmacotherapy and pharmaceutical care of outpatients is shown in Table I.

To substantiate the availability of effective immunomodulatory phytopreparations for patients, marketing research on the use of immunomodulatory phytopreparations in Ukraine (for the period 2016-2021) has been conducted. The results of comparative analysis of the share of positioning of immunoprotective phytopreparations among immunomodulatory in the pharmaceutical market of Ukraine (for the period 2016-2021) are shown in Fig.1. It is established that the share of positioning of immunomodulatory drugs of plant origin is 15.81%.

In turn, phytopreparations with immunomodulatory action are divided into original mono and combined preparations. The distribution of phytopreparations with immunomodulatory action of the original mono and combined preparations is shown in Fig.2. The share of original mono drugs is 83.78%; the share of combined phytopreparations with immunomodulatory action is 16.21%.

To determine the affordability of immunomodulatory phytopreparations for patients, a comparative analysis of marketing research and analysis of the State Register of Medicines of Ukraine and the State Register of Wholesale Prices for medicines declared in Ukraine (for the period 2016-2021) under the international non-proprietary or common name as of 01.01.2023 [14,15].

The distribution of immunomodulatory phytopreparations by producer countries in the pharmaceutical market of Ukraine is shown in Fig.3. It is established that the positioning of immunomodulatory phytopreparations of domestic producers dominates, their share is 70.26%; immunomodulatory phytopreparations of German manufacturers – 18.92%; Italy – 2.86%; Poland – 2.54%; Slovenia – 5.41%.

DISCUSSION

The conceptual basis is the theoretical generalization of scientists about the course of acute respiratory diseases, which combines two interdependent and mutually determined processes: the growth of infectious pathology, the decrease in the immunological reactivity of the patient's body. Therefore, to achieve the optimal therapeutic effect in complex therapy, it is necessary to use immunomodulatory drugs [3-4].

Immunomodulatory are drugs of natural or synthetic origin, which in therapeutic doses restore the functions of the immune system [5-6].

Therefore, in the conditions of an epidemic situation, the use of immunomodulatory drugs of plant origin should be part of a set of measures aimed at optimizing immune reactions in practically healthy people, but with a high risk of developing chronic diseases.

Phytopreparations of immunomodulatory action act effectively and safer than synthetic drugs, have a wide therapeutic range, a smaller number of adverse reactions and a lower level of interaction with other pharmaceutical drugs and are the safest immunomodulatory, acceptable both for the adult population and in gerontological and pediatric practice [5-7].

Acceptability for use in the pharmacotherapy of infectious diseases in patients of various ages is ensured by the fact that immunomodulatory drugs of plant origin have immunomodulation, anti-inflammatory and hemostatic effects; prevent excessive activation of free radical oxidation and restore the functional activity of the body's natural antioxidant system; increase the body's resistance to adverse environmental factors, stimulate regeneration processes [8].

According to the results of the research, it is determined that the range of wholesale and retail prices of immunomodulatory phytopreparations of domestic and foreign manufacturers is acceptable for Ukrainian consumers. However, effective imported phytopreparations of immunomodulatory action of manufacturers in Germany, Italy, Poland, Slovenia are not analogues of domestic products, their original composition provides specific pharmacological activity and therapeutic efficacy. The imported drugs are dominated by combined phytopreparations that provide a complex immunomodulatory effect [10, 14].

Domestic manufacturers supply the pharmaceutical market with original mono- immunomodulatory phytopreparations, dosage forms acceptable for patients of all ages predominate: extracts, tinctures, syrups, hard capsules, tablets [14].

CONCLUSIONS

The theoretical analysis shows that the use of immunomodulatory drugs of plant origin is appropriate in rational pharmacotherapy to strengthen the individual immunity of patients, which is especially relevant in an exacerbation of the epidemic situation caused by the spread of infectious diseases of viral origin.

An algorithm of pharmacoeconomic substantiation has been developed, which provides an opportunity to confirm the therapeutic efficacy and pharmacoeconomic feasibility of immunomodulatory phytopreparations for rational pharmacotherapy and pharmaceutical care of patients.

The results of marketing research provide an opportunity to determine the availability (positioning and price range) for patients of effective immunomodulatory phytopreparations in Ukraine and outline the prospects for pharmaceutical development and registration on the pharmaceutical market of Ukraine of new effective immunomodulatory drugs of plant origin.

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ORIGINAL ARTICLE

PROFESSIONAL RISKS FOR AGRICULTURAL PERSONNEL TREATING BERRIES AND MELON CROPS WITH PESTICIDES

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ABSTRACT

The aim: Hygienic assessment of labour conditions and risks for the Ukrainian agricultural personnel treating berries and melon crops with fungicides, herbicides and insecticides for justification of their safe use regulations.

Materials and methods: Natural studies of labour conditions and risk correspond to the acting laws of Ukraine. The results were statistically treated using IBM SPSS StatisticsBase v.22.

Results: The natural studies of fungicides, insecticides, used for treatment of berries and melon crops, show that labour air environment corresponds to hygienic standards. The authors have established that the hazard index of complex fungicides effect on spray fueling attendants and tractor drivers is 0.110±0.046 and 0.155±0.071, that of herbicides – 0.34±0.025 and 0.380±0.257, that of insecticides – 0.221±0.111 and 0.222±0.110, respectively; hazard index of combined effect of several acting substances makes up– 0.239±0.088 and 0.336±0.140 for spray fueling attendants and tractor drivers, respectively. The statistical analysis shows that the hazard coefficients of inhalation and percutaneous penetration do not differ statistically between spray fueling attendants and tractor drivers ($p>0.05$). The percutaneous risk (%) of various pesticide groups for spray fueling attendants ranges 65.74-97.58 %, for tractor drivers – 50.72-95.23 %.

Conclusions: The analysis has shown that the professional risk of fungicides, herbicides, insecticides, during agricultural treatment of the berries and melon crops does not exceed standards.

KEY WORDS: Fungicides, Insecticides, Herbicides, labour conditions

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INTRODUCTION

Pesticide plant treatment is an obligatory condition of today agriculture [1]. Pesticide treatment has been emphasized recently, which is confirmed by the laws and legal acts on their environmentally conscious application. Preliminary analysis of relation between pesticide treatment and personnel health risks is complicated [2]. Pesticides applied within agriculture may lead to acute poisoning, chronic diseases, neurological disorders, cancer, etc [3-5]. So, the issues of environmental protection and personnel chemical safety are relevant. Assessment of labour conditions makes a necessary component of the pesticides' negative effects risk justification [6].

THE AIM

Hygienic assessment of labour conditions and risks for the personnel dealing with fungicides Kitch, Trinol, Switch, Signum, Sercadis Plus, and Ridomil Gold; herbicides Stomp Aqua, and Herbolex; insecticides Protect, and Vertimek, regarding safe treatment of berries and melon crops in agriculture of Ukraine, and justification of their safe use regulations.

MATERIALS AND METHODS

The authors studied natural labour conditions of the personnel, treating the berries and melon crops with pesticides. The pesticides treatment conditions are represented in table I. The authors hygienically assessed labour conditions and professional risk of the preparations, according to the acting laws of Ukraine [7]. During the treatment manipulations, all personnel were wearing special clothes: synthetic overalls and shoes, rubber gloves and respirators. All personnel were trained and permitted to deal with pesticides and agricultural chemical items. Before and after pesticide treatment procedure, we examined the personnel: measured arterial pressure, pulse, assessed skin condition, noted their general complaints. The climate conditions during pesticide treatment (table II) corresponded to standards [8].

We assessed labour conditions of tractor drivers and pesticide spray filling attendants, treating berries and melon crops with pesticides, by the acting substances content in

Table I. Conditions of pesticide treatment of berries and melon crops in agriculture of Ukraine

Preparation name	Acting substances	Berry/melon crop	Preparation use standards, kg(l)/ha	Liquid use standards, l/ha	Facilities
Fungicides					
Kitch	Fludioxonil Cyprodinil	strawberry blueberry raspberry blackberry	1,0	300	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Trinol	Fenhexamid	strawberry	1,5	300	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Switch	Fludioxonil Cyprodinil	blueberry	1,0	250	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Signum	Boskalid Piraclostrobin	strawberry	1,5	1000	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Sercadis Plus	Difenoconazole Fluxapyroxad	watermelon	1,2	300	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Ridomil Gold	Metalaxyl-M Copper chloride oxide	watermelon	5,0	250	Calibrated sprayer "OPSH 400", tractor DongFang
Herbicides					
Stomp Aqua	Pendimethalin	strawberry	3,5	300	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Herbolex	Glyphosate	melon	8,0	300	Calibrated sprayer "OPSH-500", tractor MTZ-82
Insecticides					
Protect	Spirodiclophen	strawberry	0,6	200	Calibrated sprayer "OPSH-2000", tractor MTZ-82
Vertimek	Abamectin	strawberry	1,0	300	Calibrated sprayer "OPSH-2000", tractor MTZ-82

Table II. Climate conditions during pesticide treatment of berries and melon crops (M±m, n=3)

Preparation	Air temperature, °C	Atmospheric pressure, mm Hg	Relative humidity, %	Air movement speed, m/sec
Fungicides				
Kitch	16±1	764±5	70±5	1,5±0,1
Trinol	20±2	760±7	40±1	2,0±0,4
Switch	20±1	740±4	60±4	1,5±0,2
Signum	17±1	745±3	55±2	1,5±0,1
Sercadis Plus	25±2	740±5	60±5	1,5±0,3
Ridomil Gold	20±1	760±4	60±5	1,0±0,1
Herbicides				
Stomp Aqua	25±3	750±5	59±2	1,0±0,2
Herbolex	23±1	750±4	75±4	1,0±0,1
Insecticides				
Protect	23±2	745±5	41±2	2,0±0,4
Vertimek	22±1	743±2	75±4	2,0±0,1

Notes: 1. M – mean average; 2. m – mean average accuracy; 3. n – number of parallel trials.

labour environment, atmospheric air (in the area of possible preparation dissemination), in washouts from open and covered skin, and in clothes stripes. The absorbing surface represented with three-layer applicators (upper layer – cotton tissue, middle – medical gauze, internal one – "blue filter"), 1 dm^2. Air sampling, preparation and chromatography analysis of samples corresponded to the guides in table III.

To determine exposition inhalation substance dose, we simultaneously collected 2 parallel samples. The study established no penetration of active substances into the respiratory organs of calibrated spraying and filling attendants during preparation of working solution and filling the spray.

Table III. Hygienic standards and margins of acting substances in labour environment air, atmospheric air, soil, washouts from skin and clothes stripes

Acting substance	Study object									
	Working environment air			Atmospheric air				Soil		Washouts, stripes
	TSEL, mg/m³	№ Guid	LOQ, mg/kg³	TSEL, mg/m³	№ Guid	LOQ, mg/m³	TAC, mg/kg	№ Guid	LOQ, mg/kg	LOQ,mg
Fungicides										
Cyprodinil	0.1	82-97	0.02	0.05	82-97	0.02	0.2	65-97	0.05	0.002
Fludioxonil	1.0	48-97	0.1	0.002	430-2003	0.0016	0.2	31-97	0.2	0.002
Fenhexamid	2.0	605-2005	0.2	0.005	605-2005	0.004	0.65	604-2005	0.1	0.002
Difenoconazole	0.2	294-2001	0.1	0.001	294-2001	0.0008	0.3	6147-91	0.02	0.002
Boskalid	1.5	484-2004	0.5	0.01	484-2004	0.008	0.4	453-2003	0.1	0.002
Piraclostrobin	1.0	484-2004	0.5	0.01	484-2004	0.008	0.6	453-2003	0.1	0.002
Metalaxyl-M	0.5	138-99	0.25	0.01	138-99	0.008	0.05	206-2000	0.05	0.002
Fluxapyroxad	0.7	1208-2012	0.25	0.01	1208-2012	0.008	0.3	1238-2013	0.1	0.002
Copper chloride oxide	0.5	4823-88	0.004	0.003	3865-85	0.001	3.0	4770.6:2007	0.1	0.0003
Herbicides										
Pendimethalin	0.5	2781-83	0.025	0.002	562-2005	0.0013	0.2	139-99	0.01	0.002
Glyphosate	1.0	4379-87	0.25	0.01	4379-87	0.001	0.5	4363-87	0.07	0.001
Insecticides										
Spirodiclophen	0.2	970-2009	0.01	0.0007	970-2009	0.00056	0.4	1023-2010	0.02	0.001
Abamectin	0.04	1106-2011	0.001	0.0002	1106-2011	0.00016	0.3	1108-2011	0.01	0.00005

Notes: 1. Guid – Guidelines; 2. LOQ – limit of quantification; 3. TSEL – Tentatively safe exposure levels; 4. TAC – Tentatively allowable concentration.

Table IV. Air content of fungicides during agricultural treatment of berries and melon crops (M±m, n=6)

Preparation	Acting substance	Air within respiration environment, mg/m³		Air above the processed environment (field center), mg/m³, after				Possible disseminated area, 300m from the field borders (side affected by wind), mg/m³, after			
		At	T	1 hour	3 hours	3 days	7 days	1 hour	3 hour	3 days	7 days
Fungicides											
Kitch	Fludioxonil	<0.1*	<0.1*	<0.1*	-	<0.1*	<0.1*	<0.016*	-	<0.016*	<0.016*
	Cyprodinil	<0.02*	<0.02*	<0.02*	-	<0.02*	<0.02*	<0.02*	-	<0.02*	<0.02*
Trinol	Fenhexamid	<0.2*	<0.2*	<0.2*	-	<0.2*	<0.2*	<0.004*	-	<0.004*	<0.004*
Switch	Cyprodinil	<0.02*	<0.02*	<0.02*	<0.02*	<0.02*	<0.02*	<0.02*	<0.02*	<0.02*	<0.02*
	Fludioxonil	<0.1*	<0.1*	<0.1*	<0.1*	<0.1*	<0.1*	<0.016*	-	<0.016*	<0.016*
Signum	Boskalid	<0.5*	<0.5*	<0.5*	<0.5*	<0.5*	<0.5*	<0.008*	-	<0.008*	<0.008*
	Piraclostrobin	<0.5*	<0.5*	<0.5*	<0.5*	<0.5*	<0.5*	<0.008*	-	<0.008*	<0.008*
Sercadis Plus	Difenoconazole	<0.1*	<0.1*	<0.1*	<0.1*	<0.1*	<0.1*	<0.0008*	<0.0008*	<0.0008*	<0.0008*
	Fluxapyroxad	<0.25*	<0.25*	<0.25*	<0.25*	<0.25*	<0.25*	<0.008*	<0.008*	<0.008*	<0.008*
Ridomil Gold	Metalaxyl-M	<0.25*	<0.25*	<0.25*	-	<0.25*	<0.25*	<0.008*	-	<0.008*	<0.008*
	Copper	<0.004*	<0.004*	<0.004*	-	<0.004*	<0.004*	<0.001*	-	<0.001*	<0.001*
Herbicides											
Stomp Aqua	Pendimethalin	<0.025*	<0.025*	<0.025*	<0.025*	<0.025*	<0.025*	<0.0013*	<0.0013*	<0.0013*	<0.0013*
Herbolex	Glyphosate	<0.25*	<0.25*	<0.25*	<0.25*	<0.25*	<0.25*	<0.001*	-	<0.001*	<0.001*
Insecticides											
Protect	Spirodiclophen	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.01*	<0.00056*	-	<0.00056*	<0.00056*
Vertimek	Abamectin	<0.001*	<0.001*	<0.001*	-	<0.001*	<0.001*	<0.00016*	-	<0.00016*	<0.00016*

Notes: 1. – At.– Pesticide Filling Attendant; 2. T – tractor driver; 3. «*» - below the limit of quantification (tab. 3); 4. «-» - the study was not held; 5. M – mean average; 6. m – mean average accuracy; 7. n – number of parallel trials.

Table V. Potential risk of hazard effect of fungicides for agricultural personnel treating berries and melon crops

Preparation	Acting substance	Hazard coefficients				Hazard indices				Percutaneous risk, %	
		percutaneous		inhalation		complex		combined			
		At*	T	At**	T	At***	T	At/	T	At//	T
Kitch	Fludioxonil	0.043	0.042	0.026	0.051	0.068	0.093	0.122	0.173	62.56	45.398
	Cyprodinil	0.029	0.028	0.026	0.051	0.054	0.079			53.020	35.662
Trinol	Fenhexamid	0.005	0.005	0.013	0.026	0.018	0.030	-	-	27.285	15.595
Switch	Cyprodinil	0.040	0.028	0.026	0.051	0.066	0.079	0.124	0.138	61.249	35.662
	Fludioxonil	0.057	0.057	0.001	0.003	0.059	0.059			97.827	95.684
Signum	Boskalid	0.016	0.016	0.002	0.007	0.018	0.023	0.046	0.056	90.604	70.045
	Piraclostrobin	0.026	0.026	0.001	0.005	0.028	0.033			95.400	84.716
Sercadis Plus	Difenoconazole	0.320	0.318	0.045	0.096	0.364	0.414	0.429	0.514	87.750	76.882
	Fluxapyroxad	0.032	0.032	0.032	0.068	0.064	0.100			50.466	31.769
Ridomil Gold	Metalaxyl-M	0.142	0.141	0.319	0.638	0.461	0.779	0.476	0.799	30.830	18.148
	Copper	0.010	0.010	0.005	0.010	0.015	0.020			66.151	48.330
Risk values, M±m		0.065± 0.028	0.064 ± 0.028	0.045 ± 0.028	0.091± 0.055	0.110± 0.046	0.155± 0.071	0.239± 0.088	0.336± 0.140	65.741± 7.468	50.717± 8.189

Notes : 1. At – spray fueling attendant; 2. T – tractor driver; 3. * – no reliable difference between hazard coefficients of percutaneous effect for spray fueling attendants and tractor drivers by Student test, p>0.05 (df=20); t= 0.040; 4. ** – no reliable difference between hazard coefficients of inhalation effect foron spray fueling attendants and tractor drivers by Student test, p>0.05 (df=20); t= -0.750 ; 5. *** – no reliable difference between hazard coefficients of complex effect for spray fueling attendants and tractor drivers by Student test, p>0.05 (df=20); t= -0.533; 6. / – no reliable difference between hazard coefficients of complex effect for spray fueling attendants and tractor drivers by Student test, p>0.05 (df=8); t= -0.584; 7. // – no reliable difference between percutaneous risk for spray fueling assistants and tractor drivers by Student test, p>0.05 (df=20); t= 1.356.

Table VI. Potential risk of hazard effect of herbicides for agricultural personnel treating berries and melon crops

Preparation	Acting substance	Hazard coefficients				Hazard indices		Percutaneous risk, %	
		Percutaneous		Inhalation		total			
		At*	T	At**	T	At***	T	At/	T
Herbicides									
Stomp Aqua	Pendimethalin	0.362	0.110	0.006	0.013	0.369	0.123	98.271	89.599
Herbolex	Glyphosate	0.128	0.127	0.191	0.510	0.319	0.637	40.068	19.963
Risk values, M±m		0.245 ±0.117	0.11 ±0.009	0.09 ±0.093	0.262 ±0.249	0.34 ±0.025	0.380 ±0.257	69.17 ±29.102	54.781 ±34.818
Insecticides									
Protect	Spirodiclophenv	0.325	0.318	0.006	0.013	0.331	0.331	98.074	96.145
Vertimek	Abamectin	0.107	0.106	0.003	0.006	0.110	0.112	97.095	94.327
Risk values, M±m		0.216 ±0.109	0.212 ±0.106	0.005 ±0.002	0.010 ±0.004	0.221 ±0.111	0.222 ±0.110	97.58 ±0.490	95.23 ±0.909

Notes : 1. At – spray fueling attendant; 2. T – tractor driver; 3. * – no reliable difference between hazard coefficients of percutaneous effect for spray fuel attendants and tractor drivers by Student test, p>0.05 (df=6); t= 0.78; 4. ** – no reliable difference between hazard coefficients of inhalation effect for spray fuel attendants and tractor drivers by Student test, p>0.05 (df=6); t= -0.63 ; 5. *** – no reliable difference between hazard coefficients of complex effect for spray fuel attendants and tractor drivers by Student test, p>0.05 (df=6); t= -0.135; 6. / – no reliable difference between percutaneous risk for spray fuel attendants and tractor drivers by Student test, p>0.05 (df=6); t= 0.36.

The variance analysis and comparison of mean variables was performed by parametric and non-parametric tests, using software IBM SPSS StatisticsBase v.22 та MS Excel.

RESULTS

Natural studies of labour conditions of tractor drivers and spray filling attendants during pesticide treatment of berries and melon crops showed that the acting substances

content in the air above the treated area and area of possible dissemination was less than the quantitative margin value (table IV), and approved levels of pesticides in labour environment and atmospheric air (table III).

During and after manipulations, the personnel had no health problems, with arterial pressure within standards. and no changes of skin and eye mucosa.

The authors observed no face, neck, and hand open skin contamination in the respondents during calibrated spraying (below quantitative margin (table III)), as the skin surface of the personnel was permanently protected with special clothes, and gloves during all manipulations.

The washouts from skin under special clothes showed no studied substances. The washouts from the gloves of spray filling attendants preparing the solution contained: cyprodinil (Kitch) - 0.0035 mg, fenhexamide – 0.003 mg, cyprodinil (Switch) – 0.0045 mg, fludioxonil – 0.003 mg, boskalid – 0.006 mg, pyraclostrobin – 0.002 mg, fluxapyroxad – 0.0041 mg, copper – 0.0013 mg, pendimethalin – 0.009 mg, spirodiclophen – 0.002 mg. The content of fungicides, herbicides, and insecticides in clothes stripes of calibrated spraying personnel was below the limit of quantification.

The hazard inhalation effect coefficients of fungicides were (0.045±0.028) and (0.045±0,028), herbicides – (0.09±0.093) and (0.262±0.249), and insecticides – (0.005±0.002) and (0.010±0.004), for the spray fueling attendants and tractor drivers respectively. The hazard percutaneous effect coefficients of fungicides were (0.065±0.028) and (0.064±0.028), herbicides – (0.245±0.117) and (0,11± 0.009), insecticides – (0.216±0.109) and (0.212±0.106), for the spray fueling attendants and tractor drivers respectively. No reliable difference was found for the hazard inhalation effect and hazard percutaneous effect coefficients of the spray fueling attendant and tractor drivers ($p>0.05$) (table V – VI).

Pesticides percutaneous risk (%) for spray fueling attendants ranged 65.74-97.58 %, for tractor drivers – 50.72-95.23 %.

The combined fungicide inhalation and percutaneous penetration during agricultural calibrated spraying occurs within the permitted hazard index of complex (simultaneous action of acting substance with different ways of penetration) and combined (simultaneous action of several active substances) effect (<1). The analysis shows no reliable difference between inhalation and percutaneous effect hazard coefficients for spray fueling attendants and tractor drivers ($p>0,05$).

DISCUSSION

The results evidence about necessity of individual protection during treatment of berries and melon crops with pesticides.

Similar results were obtained before, during natural studies of pesticides used to treat strawberries, which established that the combined hazard for the personnel is 0.45, and it does not exceed the margin [9]. For pesticides used to treat potatoes, the percutaneous risk was 56.3±7.3 % for spray fueling attendants, and 43.9±7.3 % for tractor drivers. The hazard indices of complex and combined effect were within the standards [10].

The studies of professional risk of new agricultural treatment methods revealed that the combined risk values are reliably higher for tractor drivers than for spray fueling attendants. The values of the combined risk of the pilot were significantly lower than operator of nmanned aerial vehicle. The combined risk for all professional groups during various operations did not exceed the standard, making up approximately 0.46±0.02 [11].

It was established that the hazard coefficient ranged from 0.5×10^{-4} to 10.0×10^{-4} during inhalation exposure on workers of insecticide Oberon Rapid, which includes two active substances spiromesifen and abamectin for garden crops treatment. Inhalation hazard coefficient was for ten times higher than percutaneous exposure, which was 0.04×10^{-4}– 1.5×10^{-4}. The combined risk was less than allowable (less than 1) to 7.8×10^{-4} for the operator and for the tractor driver – 11.1×0^{-4} [12].

It was shown according to the results of research carried out during treatment oil crops in the agro-industrial sector with the fungicides Akanto, Retengo, Amistar Gold, the indices of the harmful effects of active substances of picoxystrobin, pyraclostrobin, azoxystrobin, and difenoconazole in the case of complex intake by inhalation and dermal exposure under the conditions of ground and aviation processing are less 1 [13].

In the given literature emphasizes the use of personal protective equipment during working with pesticides. The use of personal protective equipment during working with pesticides is the most effective preventive measure [9-13].

The experience of many countries has shown that prevention of health risks for worker's health caused by pesticides is technically feasible and economically beneficial for individuals and society as a whole. Proper risk assessment and management of pesticide use is an important component of prevention of occupational poisoning and diseases [14].

In addition, the use of appropriate and well-maintained spraying equipment, with taking all necessary ruelses of using at all stages of treatment of plants by pesticides, can minimize human exposure to pesticides and their potential negative impact on the environment [15].

CONCLUSIONS

1. The article shows that treatment of berries and melon crops with different pesticides is not associated

with exceeded hygienic standards, if agrotechnical and hygienic standards are kept.

2. The authors have established that hazard index of complex effect of fungicides on spray fueling attendants and tractor drivers is respectively 0.110±0.046 and 0.155±0.071, that of herbicides – 0.34±0.025 and 0.380±0.257, that of insecticides – 0.221±0.111 and 0.222±0.110; hazard index of combined effect of several acting substances is 0.239±0.088 and 0.336±0.140. The authors have proven, that the professional risk of chemicals does not exceed the standards.
3. Statistical analysis shows, that the hazard coefficients of inhalation and percutaneous penetration do not differ statistically between spray fueling attendants and tractor drivers, by Student test ($p>0,05$). The percutaneous risk of various pesticides for spray fuel attendants ranges within 65.74-97.58 %, tractor drivers – 50.72-95.23 %.
4. Obtained results will be useful for prediction of hazards during treatment of other agricultural plants with the studied pesticide groups and classes, and further monitoring is recommended.

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REVIEW ARTICLE

EXPERIENCE OF INTEGRATED MANAGEMENT OF PATIENTS WITH DIABETIC RETINOPATHY (EXAMPLE OF ANALYSIS OF PERFORMANCE INDICATORS OF A MULTI PROFESSIONAL HEALTHCARE FACILITY)

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ABSTRACT

The aim: Conducting an analysis of indicators of the dynamics and prevalence of the main classes of chronic non-infectious diseases of the contingent attached to a multidisciplinary health care institution of the population contingent, to determine the main predictive trends of morbidity for the formation of a strategy for the prevention of diabetes complications, in particular, one of the most dangerous complications - diabetic retinopathy.

Materials and methods: In our work, we used the bibliosemantic method and structural-logical analysis. During the research, we analyzed individual indicators of the health status of patients over 18 years of age, who are attached for medical care to the State Scientific Institution «Scientific and Practical Center of Preventive and Clinical Medicine» of the State Administrative Department. Our main focus is on the prevalence of diabetes and its complications.

Conclusions: The stability of the dynamics of the general morbidity indicators for the most common nosological forms of diseases of the main rating classes of diseases indicates the effectiveness of measures for the prevention and early diagnosis of diseases among the attached contingent. The levels of coverage of dispensary supervision of patients of SIS «SPC PCP» SAD are quite high (more than 90%). Performing preventive dynamic observations of patients with diabetes and diabetic retinopathy and observing the basic principles of integrated management allows to improve the results of treatment and the prognosis of the course of the disease, because the onset of retinopathy often occurs without obvious symptoms. An important factor is the constant updating and implementation of medical and technological documents for the constant improvement of the quality of medical care.

KEY WORDS: population morbidity, chronic non-infectious diseases, endocrine pathology, diabetic retinopathy, retinal pathology, integrated patient management, quality of medical care

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INTRODUCTION

According to the definition of the World Health Organization (WHO), diabetes is an urgent global medical and social problem of our time. This pathology occupies a leading position among such a class of diseases as diseases of the endocrine system, nutritional disorders and metabolic disorders [1].

That is why solving the problems of prevention of complications related to diabetes is one of the priority tasks of national health care systems both in Ukraine [2] and in other countries [3].

Such a situation is due not only to the increase in the number of patients with diabetes, but also to the extremely high risk of developing its complications, which are the causes of disability, disability, and mortality of this category of patients. According to the researchers of this issue, diabetic retinopathy appears in patients with diabetes in 90% of cases, and complete blindness occurs 25 times more often in patients with diabetes than in healthy people [4].

It is worth noting that the vast majority of patients with diabetic retinal lesions are patients with type 2 diabetes. When a diagnosis of type 1 diabetes is made, diabetic retinopathy is rarely detected at the time of diagnosis, but already 15-20 years after the onset of the disease, according to numerous researchers, retinopathy occurs in almost all of these patients, and in 70% it is in the proliferative stage. Diabetic retinopathy is inextricably linked with the course of diabetes, hyperglycemia, and hypertension and is accompanied by the development of diabetic macular edema (DMA), which is diagnosed in 7% of patients with diabetes [5-6].

During 2015–2019, the global prevalence of diabetic retinopathy in patients with diabetes was 27.0%, including 25.2% nonproliferative diabetic retinopathy, 1.4% proliferative diabetic retinopathy, and 4.6% diabetic

macular edema. In 2020, the total number of adult patients with diabetic retinopathy worldwide was estimated at 103.12 million [7]. In 2021, the prevalence of diabetic retinopathy was 536.6 million people, and the expected number of such patients worldwide will increase to 783.2 million people in 2045 [8].

THE AIM

To analyze the indicators of the dynamics and prevalence of the main classes of chronic non-infectious diseases of the contingent attached to a multidisciplinary health care institution of the contingent of the population, to determine the main predictive trends of morbidity for the formation of a strategy for the prevention of diabetes complications, in particular, one of the most dangerous complications — diabetic retinopathy.

MATERIALS AND METHODS

In our work, we used the bibliosemantic method and structural-logical analysis. When conducting the research, we analyzed individual health indicators of patients over the age of 18, who are attached for medical care to the State Institution of Science «Research and Practical Center of Preventive and Clinical Medicine» State Administrative Department (hereinafter referred to as SIS «SPC PCP» SAD) (form No. 12) from 2011 to 2022 inclusive, their dynamics [9]. Our main focus is on the prevalence of diabetes and its complications.

REVIEW AND DISCUSSION

SIS «SPC PCP» SAD provides medical assistance to the attached contingent of the population - civil servants and other sections of the population on contractual terms. In SIS «SPC PCP» SAD, as of 01.01.2023, 34,838 (in 2022, this indicator was 33,698) adults are receiving medical services, of which 20,847 (in 2022 – 20,483) persons are over 60 years old (59 .8%). Such a feature of the age structure of the attached contingent is characteristic of SIS «SPC PCP» SAD, which distinguishes it according to the distribution of the permanent population of the city of Kyiv by age, in which the specific weight of persons of retirement age, according to official statistics, is about 30%.

For the possibility of conducting a more detailed analysis of population morbidity and prevalence of diseases among the population attached to the service of the SIS «SPC PCP» SAD, we used statistical data for 2022.

In the structure of the prevalence of diseases in 2022, the first five ranking places were occupied by diseases of the circulatory system (1082.8 per 1000 population), diseases of the digestive organs (685.5 per 1000 population), diseases of the endocrine system, nutritional disorders and metabolic disorders (444 .9 per 1,000 population), respiratory diseases (233.6 per 1,000 population) and diseases of the genitourinary system (210.2 per 1,000 population).

In the structure of morbidity in 2022, classes of diseases were located as follows: diseases of respiratory organs (125.9 per 1000 population), diseases of the genitourinary system (33.9 per 1000 population), diseases of the eye and its accessory apparatus (21.9 per 1000 population) , diseases of the endocrine system, nutritional disorders and metabolic disorders (13.3 per 1000 population), neoplasms (12.5 per 1000 population), diseases of the circulatory system (5.3 per 1000 population).

In the structure of diseases of the endocrine system, nutritional disorders and metabolic disorders among the adult population, diabetes is the most common pathology.

Among SIS «SPC PCP» SAD patients with diseases of the endocrine system, eating disorders, metabolic disorders with diabetes, one in five patients. Among the population of Kyiv, this indicator is 36.8%, respectively. The dynamics of the primary incidence of diabetes among the adult population of Kyiv and the population over 18 years of age attached to the SIS «SPC PCP» SAD for medical services is presented in Fig. 1

When conducting an analysis of the dynamics of the general and primary incidence of diabetes, both of the first and second type, we obtained results that indicate a stable decrease in the primary and general incidence of diabetes among the population of Kyiv (the approximation probability indicators are quite high - 0, 97 and 0.8, respectively), which indicates a decrease in the number of public appeals and/or a low rate of establishing the primary diagnosis of this pathology [9].

In 2022, 49 patients with type I diabetes and 2,495 patients with type II diabetes were registered with an endocrinologist (Table I).

Diabetic retinopathy (DR), cataracts, and glaucoma are the most frequent complications of diabetes mellitus. This complication develops gradually and depends directly on the course of the underlying disease.

The development of occlusion of small vessels and their pathological permeability (diabetic retinopathy) occurs in patients with diabetes 5-7 years after the onset of the disease, and loss of vision as a result - in 8-15% of cases. In patients with insulin-dependent diabetes mellitus, 5-7 years after the onset of the disease, clinically significant symptoms appear in 15-20% of cases, after 10 years - in ¬50-60%, and after 30 years in almost all patients. With non-insulin-dependent diabetes mellitus,

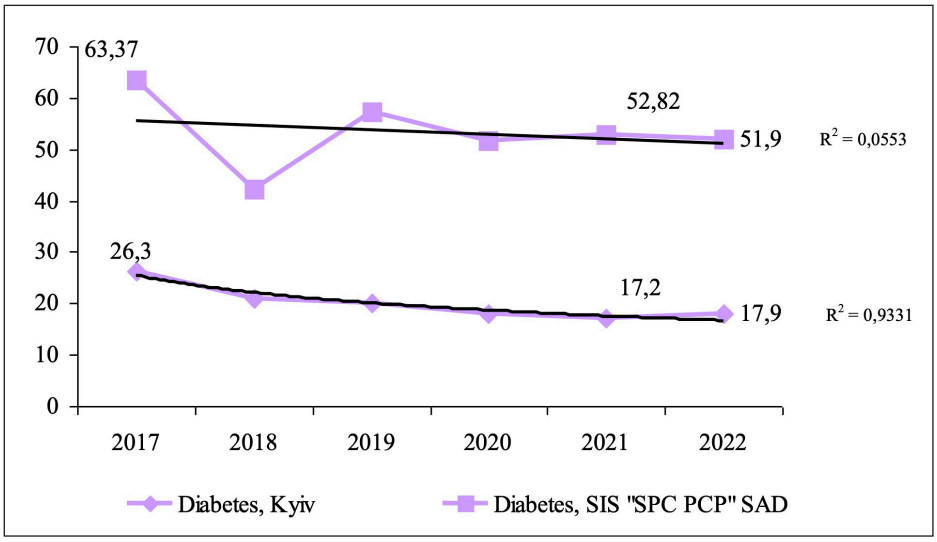

Fig. 1. Primary incidence of diabetes among the population over 18 years of age attached for medical care to the SIS «SPC PCP» SAD and among the adult population of Kyiv (per 10,000 adult population)

Table I. The number of patients with type 1 and type 2 diabetes mellitus attached to the service in SIS «SPC PCP» SAD

Type I diabetes (number of registered patients, abs.)	Scheduled visits to the endocrinologist (number of patients, from registered)		Type II diabetes (number of registered patients, abs.)	Scheduled visits to the endocrinologist (number of patients, from registered)	
	abs	%		abs	%
49	22	44,9	2495	714	28,62

Table II. Dynamic supervision by an ophthalmologist of patients with diabetes in 2022

	Type I diabetes mellitus		Type II diabetes mellitus	
	n	%	n	%
The number of patients registered	49		2495	
Planned visits to the endocrinologist were carried out (number of patients, from registered ones)	22	44,9 %	714	28,6 %
Consultation of an ophthalmologist (comprehensive examination by an ophthalmologist (visiometry, refractometry, tonometry, biomicroophthalmoscopy) was carried out	19	86 %	605	84,7 %
Computer perimetry	19	86 %	605	84,7 %
Fundus examination with a Goldman lens	19	86 %	605	84,7 %
Optical coherence tomography of the retina	19	86 %	605	84,7 %
Optical retinal angiography	19	86 %	605	84,7 %
Retinal angiography is fluorescent	8	36,4 %	247	34,6 %
Referred to the consultation of related specialists (nephrologist, cardiologist and vascular surgeon)	2	9,1 %	18	2,5 %

due to late diagnosis, diabetic retinopathy is detected in 15-30% of cases, after 10 years - in 50-70%, and after 30 years in almost 90% of patients.

For the dynamic monitoring of patients with diabetes, local medical care protocols "Type 1 diabetes" and "Type 2 diabetes" have been developed and implemented in the work practice of the SIS "SPC PCP" SAD. These medical-technological documents describe all stages of providing medical assistance to such patients - from the moment of diagnosis to further actions in case of complications.

When conducting active monitoring of patients with diabetes, we apply the principles of continuity and interaction between doctors of various branches of medical care to ensure high-quality medical care and the maximum possible avoidance (postponement) of the development of complications.

One of the important links of work with such patients (in accordance with the medical and technological regulations of SIS "SPC PCP" SAD) is a consultative examination by an ophthalmologist. The examination includes visiometry, refractometry, tonometry, biomicroophthalmoscopy, fundus examination with a Goldman lens, computer perimetry, optical coherence tomography retina, if additional examinations are necessary, retinal

angiography (optical and fluorescent) is performed and additional consultations of a nephrologist, cardiologist, and vascular surgeon are scheduled.Among patients with diabetes who underwent routine examinations by an endocrinologist in 2022, about 80% were referred for examination to an ophthalmologist (Table II).

Based on the results of the consultative reviews, individual tactics of integrated management were developed for each of the patients with diabetes.

There is strong evidence that the use of regular screening for early detection and clinical surveillance of diabetic retinopathy is critical to improving patient outcomes and prognosis, as the onset of retinopathy is often asymptomatic.

Research into the pathogenesis of diabetic retinopathy continues, updated data on the clinical signs of this disease, risk factors for its development, and methods for determining the features of retinal pathology are constantly appearing. Some of them turned out to be quite progressive in the understanding of pathogenesis and provoked the creation of new therapeutic methods [10].

According to Cochrane meta-analyses, angioprotectors, vitamins and antioxidants are unable to prevent the progression of diabetic retinopathy. The most effective way is constant control of blood sugar and blood pressure. Therefore, until recently, doctors were only forced to observe the progression of diabetic retinopathy in order to establish the moment of inevitable appointment of laser photocoagulation of the retina, however, this intervention is often unsuccessful and has a very high risk of complications. Therefore, one of the priority directions in treatment today is the prevention of the progression of diabetic retinopathy [11].

During the last decade, the complex interdependence between diabetic retinopathy and dyslipidemia has been actively discussed, as well as questions about the possible positive effect of hypolipidemic therapy on the development and course of diabetic retinopathy [10-12].

CONCLUSIONS

The stability of the dynamics of the general morbidity indicators for the most common nosological forms of diseases of the main rating classes of diseases indicates the effectiveness of measures for the prevention and early diagnosis of diseases among the attached contingent. The levels of coverage of dispensary supervision of SIS «SPC PCP» SAD patients are quite high (over 90%).

Performing preventive dynamic observations of patients with diabetes and diabetic retinopathy and observing the basic principles of integrated management allows to improve the results of treatment and the prognosis of the course of the disease, because the onset of retinopathy often occurs without obvious symptoms. An important factor is the constant updating and implementation of medical and technological documents for the constant improvement of the quality of medical care.

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REVIEW ARTICLE

SOME ASPECTS OF MEDICAL REHABILITATION IN UKRAINE AND PROSPECTS FOR CHANGES IN REHABILITATION SERVICES IN THE WORLD

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ABSTRACT

The aim: To assess the situation, relevance and opportunities for providing medical rehabilitation services in Ukraine and to determine the current trends in the development of medical rehabilitation in the world.

Materials and methods: An analysis was made of WHO data on the prospects for the development of rehabilitation services, as well as the legal framework of Ukraine and data from the National Health Service on medical rehabilitation.

Conclusions: Demand for rehabilitation services is growing. Ukraine is following the path of active adaptation and implementation of world documents from medical rehabilitation to practical health care, taking into account the dynamics of population aging, the prevalence of non-communicable diseases, and as a component of the strategy of improving the quality and availability of medical care, adequacy to the realities of the times.

KEY WORDS: medical rehabilitation, package of medical services

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INTRODUCTION

Universal coverage of medical care should become the main strategy for the development of any health care system in the world, and this strategy is clearly reflected in the Sustainable Development Goals. [1]. Universal coverage of medical care also provides for the possibility of receiving high-quality rehabilitation care without additional financial burden anywhere and anytime without any restrictions.

The importance of rehabilitation measures is emphasized in the Alma-Ata Declaration of the WHO [2], where it is defined as an important component of primary health care.

However, according to the WHO, among many health care systems today, rehabilitation is not fully and effectively integrated into primary health care [3].

The needs for the development of rehabilitation services tend to grow. It is determined that the main reason for this situation is the aging of the population in all countries; prevalence of non-communicable diseases; disability; an increase in the level of injuries; migration and resettlement of people; emergency situations (including outbreaks of infectious diseases, humanitarian crises, natural disasters, etc.) [4].

THE AIM

To assess the situation, relevance and opportunities for providing medical rehabilitation services in Ukraine and to determine the current trends in the development of medical rehabilitation in the world.

MATERIALS AND METHODS

An analysis was carried out of: the regulatory and legal framework of Ukraine on issues of ensuring medical rehabilitation measures; data dashboards of reports of the National Health Service of Ukraine on the results of providing medical care in accordance with the Program of Medical Guarantees; WHO data on the prospects for the development of rehabilitation services.

REVIEW AND DISCUSSION

According to the WHO, the countries of the European region have the oldest population among six regions of the world [5]. Thus, among the twenty-five countries with an elderly population, twenty-two countries belong to the European region, and the number of the population over the age of 60 has an upward trend: from 23.9% in 2015 to

34.2% in 2050 [6]. The increase in the age of the population is combined with multimorbidity, a combination of diseases and an increase in functional disorders, as a consequence of diseases, which leads to limitation of movement or self-care, communication or mental disorders [7], limitation of participation in community life, labor and social activity, can cause isolation or impoverishment. The WHO also includes the incidence of COVID-19 as an emergency situation today, which, as a consequence, also requires multidisciplinary rehabilitation interventions [8, 9].

Currently, about 2.4 billion people worldwide suffer from pathological conditions for which rehabilitation is indicated. Due to changes in health and population demographics, the need for rehabilitation around the world is projected to continue to grow [8,9].

According to WHO, in many regions of the world, these growing needs for rehabilitation are largely unmet. In some low- and middle-income countries, more than half of people who needed for rehabilitation services do not receive them.

The World Health Organization identifies a number of factors that contribute to unmet rehabilitation needs. It:
- low priority level of rehabilitation, insufficient funding, lack of policy or plans in the field of providing rehabilitation services at the national level;
- lack of access to rehabilitation services outside urban areas and long waiting times;
- a high level of public spending on rehabilitation services and the absence or insufficiency of financial support mechanisms;
- shortage of qualified specialists in the field of rehabilitation;
- shortage of resources, including auxiliary technologies, equipment and consumables;
- low level of scientific work and data collection on rehabilitation;
- ineffective or insufficiently used mechanisms for directing patients to receive rehabilitation services [10].

Strengthening the medical rehabilitation system is relevant for Ukraine as well. Medical rehabilitation, as a type of medical care, is defined by the Law of Ukraine "On Health Care", which defines and substantiates to whom, in what cases and how this type of medical care should be provided [11].

It is also determined that Medical Rehabilitation is prescribed for patients: after the end of the acute period of the disease in the presence of life restrictions; with congenital and hereditary pathological conditions, acquired disorders of the locomotor and speech apparatus, visual and hearing impairments; in case of permanent incapacity (disability).

In accordance with the Law, medical rehabilitation is carried out free of charge by state and communal health care institutions, with which contracts for public health care have been concluded, upon referral according to the medical indications of a state or communal health care institution in which the patient was provided with secondary (specialized) or tertiary care (highly specialized) medical care.

Given the relevance of the development of the rehabilitation system in Ukraine, the Law of Ukraine "On Rehabilitation in the Health Care Sector" (2021) came into force. [12]. This document defines the state policy on rehabilitation in the field of health care, the rights and obligations of persons who receive rehabilitation, the principles of providing rehabilitation services, rehabilitation subjects, providers and recipients of rehabilitation services.

According to the classification of the World Bank (2022), Ukraine belongs to countries with income below the average. The data used by the WHO show that among the population of Ukraine (44042432), almost half (47.33%) of people have at least one disease for which it would be possible to use rehabilitation services. In some other countries of the European region, this percentage of people is: in Great Britain 43.16%; Sweden - 41, 48%; Switzerland 44.98%; Poland 48.23%; Germany 45.32%; Belarus 45.25%; Latvia 46.88%; Lithuania 47.09%; Turkey 31.79%; Uzbekistan 26.62%; Italy 44.96% [5].

According to WHO (2019), the sex-age structure of the population, which provides for the introduction of rehabilitation measures in Ukraine, is presented in table I.

Conditions requiring rehabilitation services include: diseases of the musculoskeletal system (65.5%), sensory disorders/sense organs (8.6%); neurological disorders (9.0%); mental disorders (3.3%); chronic diseases of the respiratory tract (1.9%); neoplasms (0.6%); cardiovascular diseases (1.1%).

Issues related to medical rehabilitation are reflected in the service packages of the medical guarantee program of the National Health Service of Ukraine (NHSU). The service packages were formed on the basis of the work of experts in the development of draft specifications and conditions for the provision of medical care, which will be provided under the Program of Medical Guarantees in the relevant areas of medical care.

The mission of NHSU is universal medical coverage, when the patient can receive affordable and high-quality medical care without significant financial costs. NHSU procures safe and high-quality medical services necessary for patients, taking into account the possibilities of the state budget.

So, today it is envisaged to provide / carry out medical rehabilitation activities for patients in the subacute and recovery period in the conditions of providing medical

Table I. Distribution of the population of Ukraine, which provides for the introduction of rehabilitation measures, by sex and age structure (2019)

age categories	0-14 years		15-64 years		Older than 65 years	
gender	female	male	female	male	female	male
absolute indicators / %	299166 (47,44%)	331374 (52,55%)	6793912 (47,91%)	7384164 (52,08%)	3907313 (64,73%)	2128900 (35,27%)
in general / %	630540 (3,07%)		14178076 (68,02%)		6036213 (28,96%)	
all in Ukraine	20844829					

services begins from outpatient basis at the patient's place of residence / stay if there are medical indications.

The grounds for providing rehabilitation services are the referral of a doctor (treating physician, GP/family doctor) or self-referral to a doctor with whom a patient with a chronic disease is under medical supervision.

Today, the specifications and conditions for the purchase of medical services under the Program of Medical Guarantees provide for the following medical rehabilitation packages in the following areas [13]:

- medical rehabilitation of babies who were born prematurely and/or sick during the first three years (package of services No. 25);
- medical rehabilitation of adults and children from three years of age with lesions of the musculoskeletal system (package of services No. 26);
- medical rehabilitation of adults and children from three years of age with damage to the nervous system (package of services No. 27).

These packages of services provide for an examination, establishing a diagnosis and the need for measures, conducting laboratory studies, conducting instrumental studies, providing services by a multidisciplinary team, providing counseling for the child by doctors of various specialties according to nosology and condition, drawing up an individual work program, providing recommendations (to the patient/family /parents), psychological support, referral to institutions of specialized/highly specialized medical care, assessment of the condition regarding the possibilities of transition to another stage of rehabilitation.

The requirements for the provision of these types of services are the presence of a license to conduct economic activity in medical practice in the specialty of physical and rehabilitation medicine, orthopedics/ traumatology, psychology, psychiatry.

According to the analytical data of the NHSU for 2022, it was established that the total amount of payments for rehabilitation service packages is UAH 3,626,701,520. At the same time, package No. 26 "Medical rehabilitation of adults and children from 3 years of age with damage to the musculoskeletal system" was the most popular and possible to implement, which is confirmed by a significant percentage of payments for this particular package among the packages of rehabilitation services, which is 58. 89%, against 32.14% of payments under package No. 27 "Medical rehabilitation of adults and children from 3 years old with damage to the nervous system" and package No. 25 "Medical rehabilitation of babies who were born prematurely and/or sick during the first 3- x years of life" (8.97%).

Kyiv, Dnipropetrovsk and Lviv regions are among the regions with a high level of implementation of this rehabilitation package (No. 26). These same regions, according to the dashboards of the National Health Service, have the largest number of contracts for medical care and the largest total number of groups of services implemented.

Prospects for the development of rehabilitation services in the world.

Rehabilitation interventions are cost-effective and have the best health outcomes. Rehabilitation interventions avoid costly hospitalizations, reduce hospital stays, reduce readmissions, and reduce the risk of complications from health problems.

The importance of updating rehabilitation services for health care systems is emphasized by numerous publications of the World Health Organization, which identify ways to solve existing problems.

So, rehabilitation is an important health care service, along with prevention, treatment and palliative care. However, in many countries, people do not have access to the rehabilitation services they need. And the best way to ensure that rehabilitation services reach all those who need them is to integrate rehabilitation at all levels of the health care system as part of overall health care coverage. In particular, it is important that rehabilitation is integrated at the primary care level, bringing services closer to the community, thereby reducing costs and improving the equity and timeliness of service delivery.

It is emphasized that rehabilitation cannot be expanded on its own, rather the health system as a whole needs to be strengthened to better deliver rehabilitation. This includes strengthening the various components that make up the health system, namely: leadership and management; financing; delivery service; workforce; auxiliary technologies; and information.

In many countries, there is limited integration of rehabilitation into health financing schemes, and this has resulted in relatively small budget allocations and a further gap between what is funded and available compared to what the population needs [9]. When public investment in rehabilitation is low, service users are forced to pay more out-of-pocket and, unfortunately, rehabilitation is often out of reach for many people who need it. In addition, in many countries there is a dependence on funding from external development partners, which leads to problems with the long-term delivery and sustainability of rehabilitation services.

The Rehabilitation 2030 initiative proposed by WHO specifically draws attention to the deep unmet need for rehabilitation worldwide and emphasizes the importance of strengthening health systems to enable rehabilitation [9]. The initiative marks a new strategic approach for the global rehabilitation community, emphasizing that:

- Rehabilitation should be available to the entire population at all stages of life.
- Efforts to strengthen rehabilitation should be aimed at supporting the health care system as a whole and integrating rehabilitation at all levels of health care.
- Rehabilitation is an important health service and crucial to achieving universal health care coverage.

The Rehabilitation 2030 initiative was launched in February 2017 and presented a "call to action" encouraging stakeholders to take concerted and coordinated global action to scale up rehabilitation efforts [9].

For this purpose, 10 priority areas of activity were determined, which can be adapted and implemented to the health care systems of different countries:

1. Building strong leadership and political support for rehabilitation efforts at sub-national, national and global levels.
2. Strengthening rehabilitation planning and implementation at the national and subnational levels, including in the framework of emergency preparedness and response.
3. Improving the integration of rehabilitation into the health care sector and strengthening intersectoral relations to effectively meet the needs of the population.
4. Inclusion of rehabilitation in the general coverage of medical care.
5. Creation of complex models of providing rehabilitation services to gradually achieve fair access to quality services, including auxiliary items, for the entire population, including residents of rural and remote areas.
6. Developing a strong multidisciplinary rehabilitation workforce appropriate to the country context and promoting rehabilitation concepts throughout health workforce education.
7. Expansion of rehabilitation funding through appropriate mechanisms.
8. Collection of rehabilitation-related information to improve health information systems, including system-level rehabilitation data and information on functioning using the International Classification of Functioning, Disability and Health (ICF).
9. Building research capacity and expanding the availability of reliable evidence for rehabilitation.
10. Creation and strengthening of networks and partnerships in rehabilitation, especially between low-, middle- and high-income countries.

Also, the World Health Organization (WHO) has prepared the document "Rehabilitation in the health care system: a guide for action" to assist governments in strengthening health care systems to provide the population with the necessary rehabilitation services. This guide recommends that governments undertake the task of strengthening rehabilitation services in the following four stages: (1) assessment of the rehabilitation situation; (2) strategic planning; (3) development of the concept of monitoring, evaluation and review; (4) implementation of the strategic plan (6).

Rehabilitation is one of the most important health care strategies aimed at ensuring people's participation in education, work and social life; however, rehabilitation needs often remain unmet due to a shortage of skilled rehabilitation workers [14].

The resource that should solve the problem of qualification of rehabilitation specialists is the proposed system of rehabilitation competencies of the WHO [14]. It is consistent with WHO strategic approach to workforce competencies, detailed in the WHO Global Competency Framework (2020), and should provide a basis for the development of context-specific competency frameworks and standards that are needed to improve education and training, regulation and quality improvement health care services. This system, proposed in the WHO document, can also be used in the development of educational programs, in the establishment of practice standards, and in the creation of tools for evaluating the effectiveness of rehabilitation services. The proposed competencies are considered as part of the implementation of the WHO Initiative "Rehabilitation 2030".

The deepening of medical rehabilitation programs and the expansion of services is relevant both for the European community and for Ukraine in view of global trends, such as the aging of the population and the spread of non-infectious diseases, as well as

specific problems of the country, such as significant population migration and numerous consequences of military actions.

In 2023, the Medical Guarantee Program provides for 39 service packages. Medical rehabilitation is expected to be one of the priorities in 2023. In this way, the country will have an incentive to create powerful rehabilitation facilities, where the patient will be able to receive comprehensive rehabilitation services.

Special attention is paid today to psychological help. In particular, a package of psychological support services is being introduced at the primary level, which is proposed for implementation since 2022.

The WHO strategies for the development of medical rehabilitation, the stages of strengthening rehabilitation services, and the requirements for the competencies of rehabilitation specialists are important for Ukrainian society in the context of reforming the health care system and are on the way to ratification and adaptation to modern requirements.

Further analysis of the development of the medical rehabilitation system, inclusion of this type of assistance in the package of medical guarantees in Ukraine, as well as scientific justification of the optimal volume of rehabilitation services with the involvement of scientific institutions is necessary.

CONCLUSIONS

Global analytics determine that the demand for rehabilitation services is growing. The reasons are: the aging of the population, the spread of non-infectious diseases, injuries, natural disasters, etc.

The problems of improving the medical rehabilitation system are relevant in the world, which is confirmed by a number of analytical and recommendatory documents of the WHO. The documents determine the strategy for the development of rehabilitation services and the competencies of medical workers who provide rehabilitation services, and determine effective intervention algorithms.

Ukraine is following the path of active adaptation and implementation of world documents of medical rehabilitation to practical health care, taking into account the dynamics of population aging, the prevalence of non-communicable diseases, and as a component of the strategy of improving the quality and availability of medical care, adequacy to the realities of the times.

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REVIEW ARTICLE

MAGNETIC RESONANCE IMAGING DETERMINATION OF STRUCTURAL DISORDERS OF ARTICULAR CARTILAGE: MODERN DIAGNOSTIC TECHNOLOGIES AND RESEARCH PROSPECTS

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ABSTRACT

The aim: To present enhanced (with the contrast) and non-enhanced MRI techniques, provide an update on the physical principles of the main and latest techniques, and describe the advantages and disadvantages of each technique. The information obtained can provide an opportunity to diagnose changes at the structural level of the articular cartilage, thereby improving the early diagnosis of OA and optimizing the tactics of further treatment of patients.

Materials and methods: We retrospectively reviewed publications published in the PubMed and Embase databases up to February 2023 using the following terms: "MRI cartilage", "MRI osteochondral lesion", "T2 mapping cartilage", "dGEMRIC", "DWI cartilage", "DTI cartilage", "sodium MRI cartilage", "gagCEST", "T1rho cartilage". A manual search for review references was also carried out.

Comparative, analytical, as well as the method of meaningful analysis was used.

Conclusions: Modern methods of MRI examination of the articular cartilage make it possible to assess its structure more accurately, in comparison with only a morphological assessment. In most cases, the components of the ECM, namely PG, GAG and collagen, are evaluated. Among the available methods, the most common, informative and accessible technique is T2 mapping. T1ρ and dGEMRIC are also fairly common methods, but require longer acquisition times. DWI/DTI, sodium MRI, gagCEST, and T1ρ are promising methods because they do not require the administration of a contrast agent and are quite specific for assessing PG and GAG. However, the available methods of MRI research already provide more detailed information about the state of the articular cartilage, which has a positive effect on the treatment of patients in this group.

KEY WORDS: osteochondral lesion, osteoarthritis, rapid imaging

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INTRODUCTION

Damage to the articular cartilage may be the result of degenerative changes in the joint, or be traumatic. The most common joint disease is osteoarthritis (OA), which in turn occupies a leading position among the causes of disability in the world [1-4]. Changes in cartilage structure occur in the early stages of degenerative joint disease and are the first signs of OA. Such structural changes occur much earlier than changes in the thickness of the articular cartilage [5]. Articular cartilage is built from a cellular component and an extracellular matrix (ECM). Chondrocytes (cellular component) synthesize and secrete the components of the extracellular matrix. The extracellular matrix, in turn, mainly consists of water, collagen, and proteoglycans (PG)/glycosaminoglycans (GAG) [6].

Currently, the following options for visualizing articular cartilage damage are available: radiography (detection of narrowing of the joint space, but without the image of the cartilage itself), computer tomography (CT), arthrography, ultrasound diagnostics, and magnetic resonance imaging (MRI) [7-9].

MRI has the highest sensitivity for detecting articular cartilage damage. Traditionally, in clinical practice, a morphological assessment is carried out, namely, a change in the thickness of the articular cartilage, a change in signal intensity, and the detection of a diffuse or focal nature of the lesion [10]. Modified Outerbridge or Noyes scales (with arthroscopic gradation) are used to assess articular cartilage damage [11, 12].

However, morphological MRI lacks specificity precisely in pathophysiological changes in the composition of articular cartilage, although these changes precede changes in cartilage thickness and signal intensity, which in turn leads to the need to study and use the latest MRI methods [13-15].

These MRI techniques include delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), T2 relaxation time mapping, diffusion-weighted imaging (DWI), diffusion tensor imaging (DTI), sodium MRI, chemical exchange saturation transfer imaging of GAG (gagCEST), and T1ρ.

An ideal MRI study of articular cartilage should visualize the thickness, diameter, volume, and area of the lesion, display morphological changes in the cartilage surface, change in cartilage signal intensity, assess the condition of the subchondral bone, and provide information about the very physiology of the articular cartilage (ECM condition).

THE AIM

This review will present enhanced (with the contrast) and non-enhanced MRI techniques, provide an update on the physical principles of the main and latest techniques, and describe the advantages and disadvantages of each technique. The information obtained can provide an opportunity to diagnose changes at the structural level of the articular cartilage, thereby improving the early diagnosis of OA and optimizing the tactics of further treatment of patients.

MATERIALS AND METHODS

We retrospectively reviewed publications published in the PubMed and Embase databases up to February 2023 using the following terms: "MRI cartilage", "MRI osteochondral lesion", "T2 mapping cartilage", "dGEMRIC", "DWI cartilage", "DTI cartilage", "sodium MRI cartilage", "gagCEST", "T1rho cartilage". A manual search for review references was also carried out.

Comparative, analytical, as well as the method of meaningful analysis was used.

REVIEW AND DISCUSSION

DGEMRIC (DELAYED GADOLINIUM-ENHANCED MRI OF CARTILAGE)

A non-invasive MRI technique that allows you to determine the amount of GAG in cartilage. GAG have a large number of negatively charged sulfate and carboxyl groups. This technique uses the contrast agent gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA2-), which is negatively charged [16]. The contrast agent (Gd-DTPA2-) can be administered intra-articularly or intravenously.

However, intravenous injection (double dose) is a more attractive option, since it makes it impossible for the development of infectious complications in the joint [16]. After injection of a contrast agent, Gd-DTPA2- is distributed within the articular cartilage in a manner inversely proportional to the content of negatively charged GAGs (distributed in higher concentration in those areas where the content of glycosaminoglycans is low, and in areas where the content of glycosaminoglycans is higher, the contrast agent is distributed in more low concentration) [17]. Long T1 relaxation times are found in intact articular cartilage, while shorter T1 relaxation times are found in diseased cartilage due to the high amount of infiltrated Gd-DTPA2-.

The disadvantages of this technique include the need to enter an exogenous contrast agent. The filtration time of Gd-DTPA2- through the synovial membrane and penetration into the cartilage takes more than 60 minutes. It is necessary to obtain a specific MRI sequence with multiple inversion times (TIs) in order to properly quantify the articular cartilage T1 time reduction, similar to the T1 mapping technique.

Experimental studies have been carried out on the application of the dGEMRIC method in vitro and ex vivo, with satisfactory results in the assessment of articular cartilage in animals and humans [18]. Experimental studies were carried out to determine the required type of contrast agent to obtain the best image. There are also discussions regarding the penetration rate of ionic and non-ionic contrast agents, but the general recommendation now is to use an ionic contrast agent [15].

The dGEMRIC technique is an important method for evaluating cartilage composition, monitoring the effectiveness of the treatment of articular cartilage damage and osteoarthritis. Those areas where the concentration of GAG is preserved will not absorb Gd-DTPA2-, since the negatively charged sulfate and carboxyl groups prevent significant diffusion of the contrast agent into the articular cartilage. However, areas where there is a loss of GAG (and their negative charges) will allow Gd-DTPA2- molecules to penetrate the articular cartilage (Fig. 1) [19].

T2 RELAXATION TIME MAPPING

MRI is characterized by the excitation and relaxation (returning back to equilibrium) of water molecules. This process is called the relaxation time T1 and T2, and it is constant for the selected tissue at a given magnetic field strength. Changes in relaxation time are the result of pathological changes in tissues or the introduction of a contrast agent.

The reduction in relaxation time T2 occurs due to the interaction of collagen fibers (component of the ECM) with water protons. The T2 relaxation time depends on

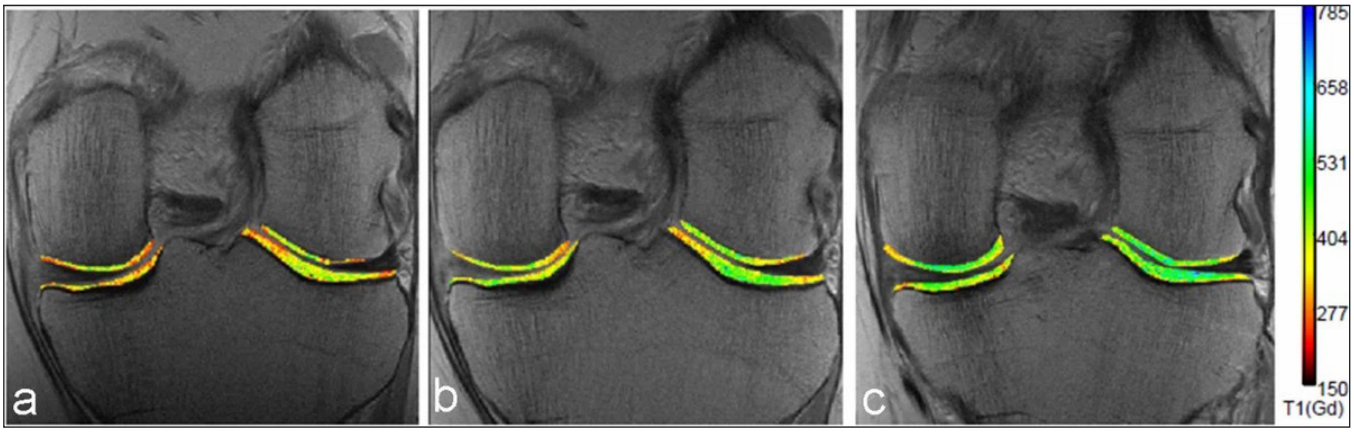

Fig. 1. dGEMRIC, magnetic resonance imaging of the knee joints, contrasting with Gd-DTPA2-. (a) Before, (b) 3 months, and (c) 1 year after meniscal repair surgery. These images demonstrate the potential to show changes in the molecular state of articular cartilage. dGEMRIC provides the ability to monitor the recovery of articular cartilage after injury or intervention aimed at improving the biomechanical condition of the joint [19]

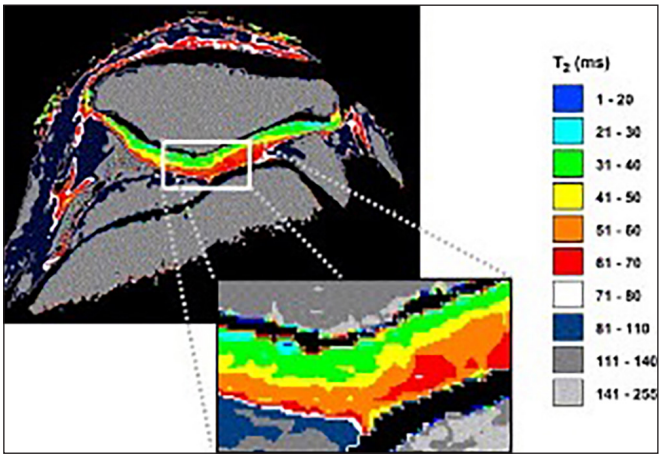

Fig. 2. Distribution of T2 relaxation time of the articular cartilage [21]

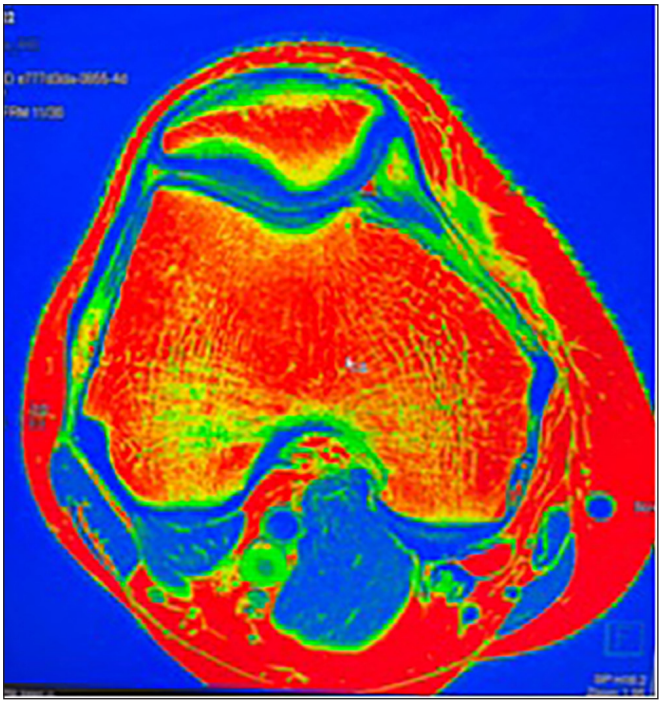

Fig. 3. T2 mapping. Intact articular cartilage

the water content of the articular cartilage as well as the integrity of the ECM. The study showed a direct correlation between T2 relaxation time and water proton content, as well as an inverse correlation with collagen fiber density in cartilage. An increase in the relaxation time T2 is associated with a decrease in the concentration of collagen in the articular cartilage [20]. The T2 relaxation time image is then created with a color or gray map representing the relaxation time (Fig. 2) [21].

A study was conducted that shows an increase in the T2 relaxation time of damaged cartilage, compared with healthy cartilage, due to changes in the composition of the extracellular matrix and a decrease in the concentration of collagen in it (Fig. 3) [22].

Violation of the composition of the ECM and a decrease in the content of collagen increases the total content of water protons in the articular cartilage, which leads to an increase in the relaxation time T2. This indicator is affected by damage to all components of the extracellular matrix (including GAG and PG), but the most specific change is precisely the change in the concentration of collagen. Also, the disadvantages include the fact that the change in the relaxation time T2 is not sufficiently indicative in the deep layers of the articular cartilage [23]. The superficial layers of cartilage may have a longer T2 relaxation time (due to certain spatial variations) compared to the deeper layers. T2 mapping can be done at 1.5 and 3 T.

T2 mapping provides an opportunity to detect changes in the articular cartilage even before the displayed morphological changes. A positive correlation was also found between T2 relaxation times and articular cartilage damage.

Like other methods, T2 mapping can be used for postoperative assessment of articular cartilage repair. Studies have been published that, during long-term follow-up of patients after surgical restoration of articular

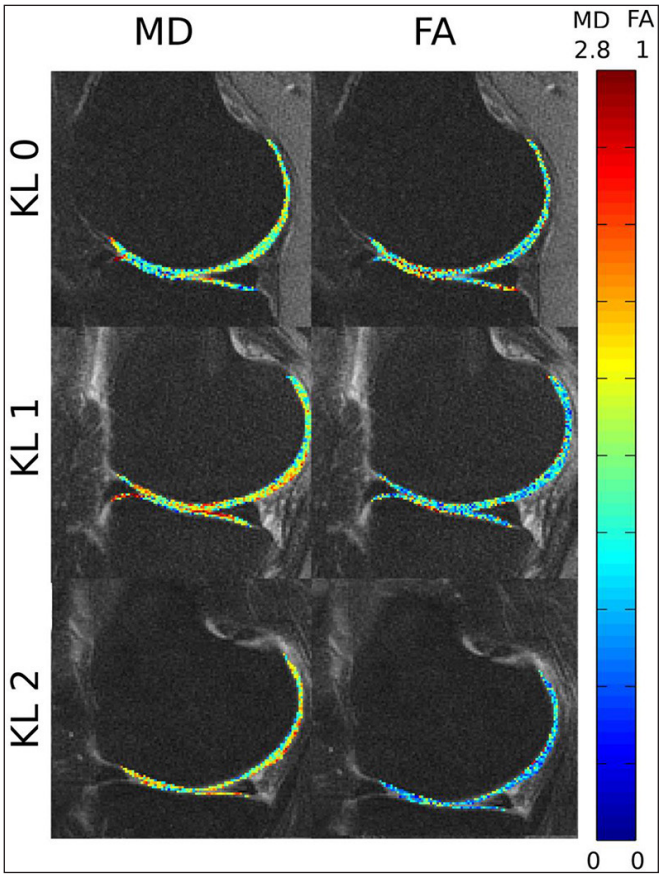

Fig. 4. An example of MD and FA maps depending on the Kellgren-Lawrence stage. Shown is an increase in MD and a decrease in FA with increasing Kellgren-Lawrence stage. [31]

cartilage, demonstrate normalization of T2 relaxation time, and approaching healthy cartilage [24, 25].

DWI/DTI (DIFFUSION-WEIGHTED IMAGING, DIFFUSION TENSOR IMAGING)

DWI is a promising diagnostic tool because it is sensitive to early degradation of articular cartilage. In human tissues, water molecules are constantly in random motion (due to thermal energy and interaction with macromolecules) [26]. The DWI method measures the microscopic movements of water molecules, to obtain information about the tissue, and the average movement of water molecules, to obtain information about the organization of the tissue microstructure, along the direction of diffusion for a certain time (diffusion time) [27]. Measurements are made by the gradients that sensitize diffusion. ECM has the ability to limit diffusion, and DWI, based on the movement of water molecules, has the ability to assess the integrity of ECM. ADC map (apparent diffusion coefficient) - diffusion level map (built with and without gradients). ADC is not a bulk water diffusion coefficient, but decreases with long diffusion times due to water being restricted by articular cartilage components (most commonly due to a network of collagen fibers). This indicator is also used to measure the average motion of water molecules in mm^2/s [28]. Since cartilage is 75% water, so the ADC value is from 1.4 to 1.6×10^{-3} mm^2/s, and damage to the articular cartilage leads to less resistance to water diffusion, and as a result, an increase in the ADC value.

To obtain data on the tissue itself, diffusion is measured in six non-colinear directions (the diffusion tensor model is used) [29]. Thanks to this model, diffusion is described as a symmetrical tensor. DTI allows you to get the FA (fractional anisotropy) parameter, which in turn is an index of tissue organization, and MD (mean diffusivity) which is the average of the three main eigenvalues (displaying the magnitude of each direction of water molecules in the tissue). The described parameters provide information about the structure of collagen fibers (due to FA), and information about PG (due to MD) [28].

However, DWI also has certain disadvantages. The T2 relaxation time is in the range of 10-50 ms, so echo time (TE) must be short for optimal articular cartilage signaling. Gradients that sensitize diffusion increase TE, and make the sequence sensitive to motion.

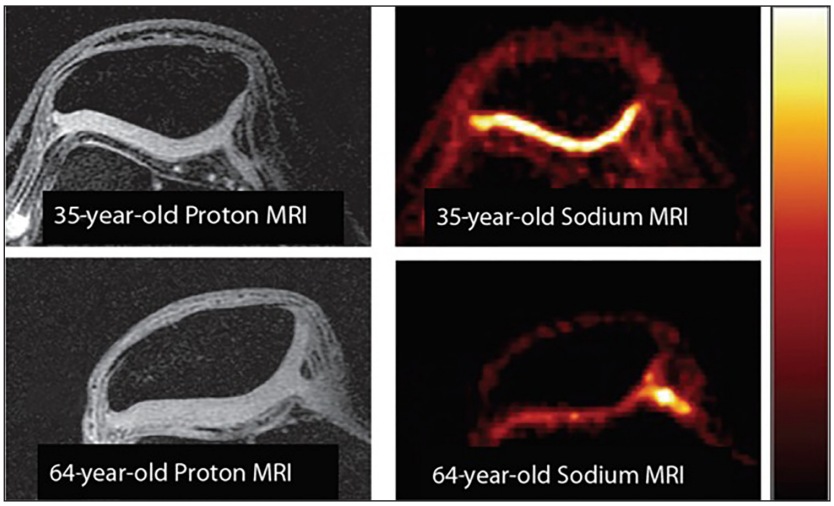

Fig. 5. Detected changes in PG concentration (optical resolution 7 Tesla) in the knee joint. There is signal reduction (right) in an older patient (64 years old) compared to a proton image (left) in an older patient (64 years old) [34]

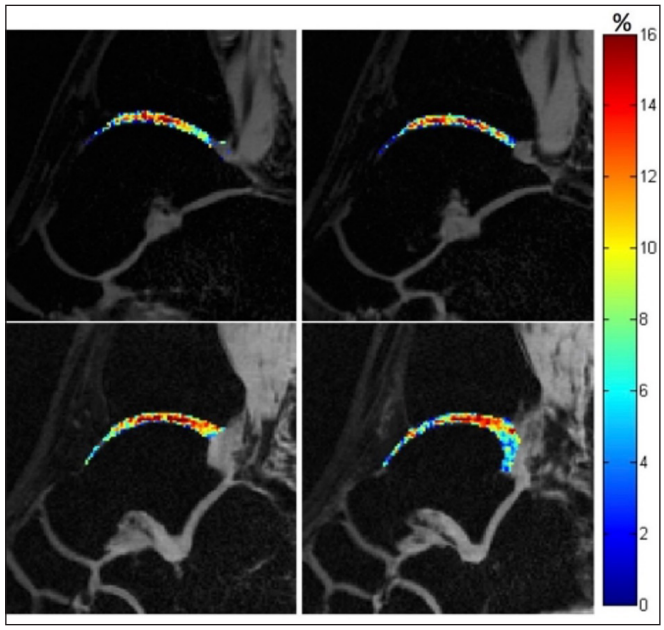

Fig. 6. GagCEST map of the articular cartilage of the calcaneal-ankle joint [36]

Studies have been conducted where PG were enzymatically cleaved, which led to an increase in the MD parameter, but did not affect the FA index, which reflects the ability to distinguish changes at the structural level of ECM (collagen fibers and proteoglycans) (Fig. 4) [30, 31].

DWI/DTI provide information about changes in the structure of articular cartilage (changes in collagen and proteoglycans) and can be used for early diagnosis of articular cartilage damage.

SODIUM MRI

Atoms containing an odd number of protons/neutrons have nuclear rotational momentum. In most cases, MRI detects and characterizes ^{1}H protons, but tissues also contain other compounds, such as ^{+23}Na. ^{+23}Na, which has a positive charge, and PG, which have a negative charge, establish an electromagnetic equilibrium with a direct correlation between both compounds. ^{+23}Na is useful for displaying articular cartilage. The Larmor frequency of ^{+23}Na corresponds to 11.262 MHz/T, while for 1H this figure is 42.575 MHz/T, at 1.5 T the resonant frequency of +23Na is 16.9 MHz, for 1H it is 63 MHz. The concentration of ^{+23}Na in normal human cartilage is approximately 320 μM, and the T2 relaxation time is from 2 to 10 ms [32].

This technique for the study of articular cartilage is very promising, since it makes it possible to image areas of PG depletion. The ^{+23}Na atoms are associated with a high fixed charge density present in the sulfate and carboxylate groups of proteoglycans [33]. A decrease in the amount of PG leads to a decrease in ^{+23}Na in the articular cartilage, since the sulfate and carboxyl groups of PG are associated with ^{+23}Na (Fig. 5) [34].

However, this technique also has its drawbacks, namely poor image quality due to low signal-to-noise ratio (SNR), as well as low optical resolution. To overcome these shortcomings, special coils (transmitting and receiving) with a long scan time must be used to obtain a satisfactory SNR.

Clinical studies have shown the existence of FCD (fixed charge density) in cartilage due to the existence of a balance between ^{+23}Na and GAG. FCD provides an opportunity to determine the concentration of GAG in articular cartilage. Studies have been carried out on animal models that reflect the change in the concentration of ^{+23}Na with damage to the articular cartilage with a linear dependence [35].

Although this method is rarely used in clinical practice, due to these shortcomings, sodium MRI remains an indicative method for changes at the structural level of articular cartilage.

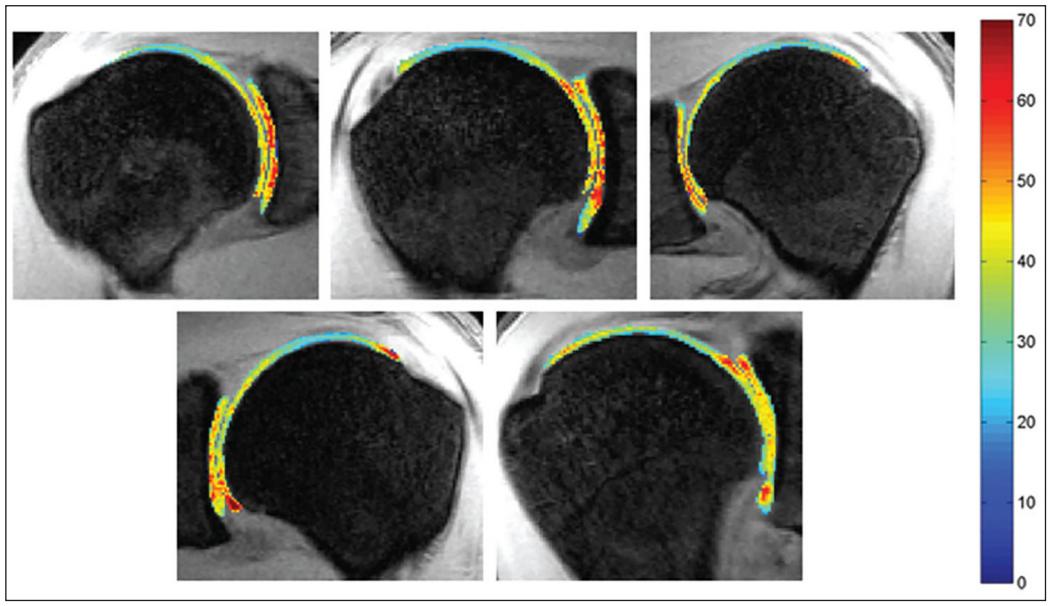

Fig. 7. T1ρ coronary maps of the shoulder joint. Five healthy individuals (mean age 27.4 years; range 24-30 years) without prior dislocation. T1ρ mapping is sensitive to the concentration of proteoglycans in articular cartilage [40]

GAGCEST (CHEMICAL EXCHANGE SATURATION TRANSFER IMAGING OF GAG)

GagCEST is an improvement on conventional magnetization transfer (MT) sequences. MT evaluates the contribution of protons that are part of unbound water molecules (bulk) to the MRI signal. This method evaluates the increase in contrast between free and bound water, and also evaluates the energy exchange between these water pools. A selective radiofrequency (RF) pulse excites the exchangeable protons of GAG, a chemical exchange with protons of free water occurs, and as a result, a decrease in the magnetization of the free water pool occurs. In GAG, the sulfate and hydroxyl groups are the targets, which allow determining the concentration of GAG in the articular cartilage (Fig. 6) [36].

A number of studies have been carried out to tune the radiofrequency pulse to saturation of GAG with exchangeable protons. Studies have also been conducted to evaluate differences in gagCEST asymmetry between 3 and 7 T. The findings indicate that gagCEST asymmetry at 3 T is deficient, so 7 T is the best option for increasing asymmetry (increasing tissue contrast between diseased and healthy articular cartilage).) [37].

Currently, this method is rarely used in clinical practice, due to its technical difficulties and requirements for the examination. However, studies have been conducted where a loss in the concentration of GAG in damaged articular cartilage was revealed [38].

T1P

It is a promising method in modern diagnostics of articular cartilage. This image evaluates the relaxation of spins under the influence of an RF pulse, and is indicative of a decrease in the concentration of PG. At T1ρ, the magnetization is tilted into the transverse plane, and due to the constant RF pulse, spin blocking occurs. Studies have been conducted reflecting the dependence on the exchange of protons with PG/GAG (namely, amide and hydroxyl groups) [39]. In this technique, the interaction between water and ECM components is similar to T2 mapping, however T1ρ mapping requires a system that is capable of generating a specific RF pulse to achieve "spin blocking". Also, if we compare the time required to obtain an image, then for T1ρ it is longer.

T1ρ is used to detect early cartilage degeneration, determines changes in the composition of the ECM (decrease in the concentration of PG), and this technique is also able to distinguish between intermediate and progressive articular cartilage degeneration and does not require the use of a contrast agent (Fig. 7) [40].

MRI is a fairly relevant and informative method for diagnosing articular cartilage damage. Morphological imaging has made remarkable progress in terms of study time, optical resolution, and contrast. This makes it possible to create detailed maps of the articular cartilage, to carry out its best assessment (determination of volume, thickness). Significant changes have also been achieved in terms of early diagnosis of articular cartilage injuries. Now we have the opportunity to determine changes in the concentration of ECM components (PG, GAG, collagen) at the structural level, which allows us to diagnose the disease at an early stage, as well as to choose the most effective tactics of surgical and medical treatment.

However, MRI diagnostics of articular cartilage still needs to be improved. Now one of the most common and informative methods for diagnosing articular cartilage damage is dGEMRIC, which in turn requires the introduction of an exogenous contrast agent into the joint cavity, which can lead to complications after the examination. Also, certain research methods require a lot of time to conduct it (dGEMRIC, sodium MRI, T1ρ), which leads to certain inconveniences for the patient and the doctor. GagCEST could be a viable alternative, but this technique has technical difficulties in conducting research, so it has not yet gained wide popularity. Issues of low image quality and low optical resolution still remain unresolved.

The ideal solution to these problems would be to combine the advantages of each method to obtain the most effective morphological and physiological assessment of articular cartilage.

CONCLUSIONS

Modern methods of MRI examination of the articular cartilage make it possible to assess its structure more accurately, in comparison with only a morphological assessment. In most cases, the components of the ECM, namely PG, GAG and collagen, are evaluated. Among the available methods, the most common, informative and accessible technique is T2 mapping. T1ρ and dGEMRIC are also fairly common methods, but require longer acquisition times. DWI/DTI, sodium MRI, gagCEST, and T1ρ are promising methods because they do not require the administration of a contrast agent and are quite specific for assessing PG and GAG. However, the available methods of MRI research already provide more detailed information about the state of the articular cartilage, which has a positive effect on the treatment of patients in this group.

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REVIEW ARTICLE

DIABETIC NEPHROPATHY: NOVELTY ABOUT THE DIABETIC NEPHROPATHY TREATMENT IN CHILDREN

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ABSTRACT

The aim: To analyze and discuss the main aspects of the DN treatment in children.

Materials and methods: Basic and modern data about the new aspects of the DN treatment analyzed in current review paper.

Conclusions: DN is a major healthcare challenge and is a major cause of irreversible kidney damage. The DN course and progression leads to severe cardiovascular complications and early death. Treatment of DN is complicated clinical issue and requires individual and complex approach, including renoprotection, antihypertensive treatment. Nowadays, we are able to provide additional medications that can enhance the benefits of the renin-angiotensin-aldosterone (RAAS) blocking, Further search of neproprotective medicines for early DN correction in pediatric patients is still of high importance.

KEY WORDS: kidney damage, diabetic nephropathy, treatment, correction

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INTRODUCTION

T1DM increased by 4.8% year from 2002 to 2015, according to the Centers for Disease Control and Prevention, and it increased by 1.9% annually in children and adolescents under the age of 20 [1]. End-stage renal disease (ESRD) in adults is primarily brought on by DM worldwide. One in five persons with diabetes have diabetic nephropathy (DN). Incidence of DN in pediatric population has significantly increased in 2013 as compared to 2002 (1.16% to 3.44%) [1,2].

Diabetic nephropathy is a prominent side effect of both type 1 and type 2 diabetes. One in three adults who have diabetes also have diabetic nephropathy. The best ways to prevent or delay the formation of diabetic nephropathy include maintaining a healthy lifestyle, managing diabetes and high blood pressure, and exercising regularly [2]. From 2002 to 2015, the prevalence of type 1 diabetes (T1D) and the associated insulin-resistant phenotype increased annually in children and adolescents by 1.9% and 4.8%, respectively. Additionally, compared to adults, children and adolescents face a more aggressive clinical course of diabetes, which is defined by a muted response to current treatments as well as a faster loss of beta-cell activity, progression of insulin resistance, and development of end-organ issues. DN is becoming more common among kids and teenagers as a result [1-5].

Early detection and adequate treatment can halt or slow the progression of the disease while reducing the chance of complications. Kidney failure, also referred to as end-stage kidney disease, can result from DN. Kidney failure is a condition that can be fatal. The only treatments available at this time are dialysis or a kidney transplant. Positively, a number of pharmacological techniques are now available for the management of diabetes and have been shown to enhance cardiorenal outcomes. The goal of this review is to discuss and summarize the approaches available nowadays for DN treatment.

THE AIM

The aim of the paper was to analyze and discuss the main aspects of the DN treatment in children.

MATERIALS AND METHODS

Novel references reviewed. Basic and modern data about the aspects of the DN treatment analyzed in current paper.

REVIEW AND DISCUSSION

DIABETIC NEPHROPATHY. BASIC DATA

Hyperglycemia is a key disorder in diabetic nephropathy. It has many damaging effects including the following meta-

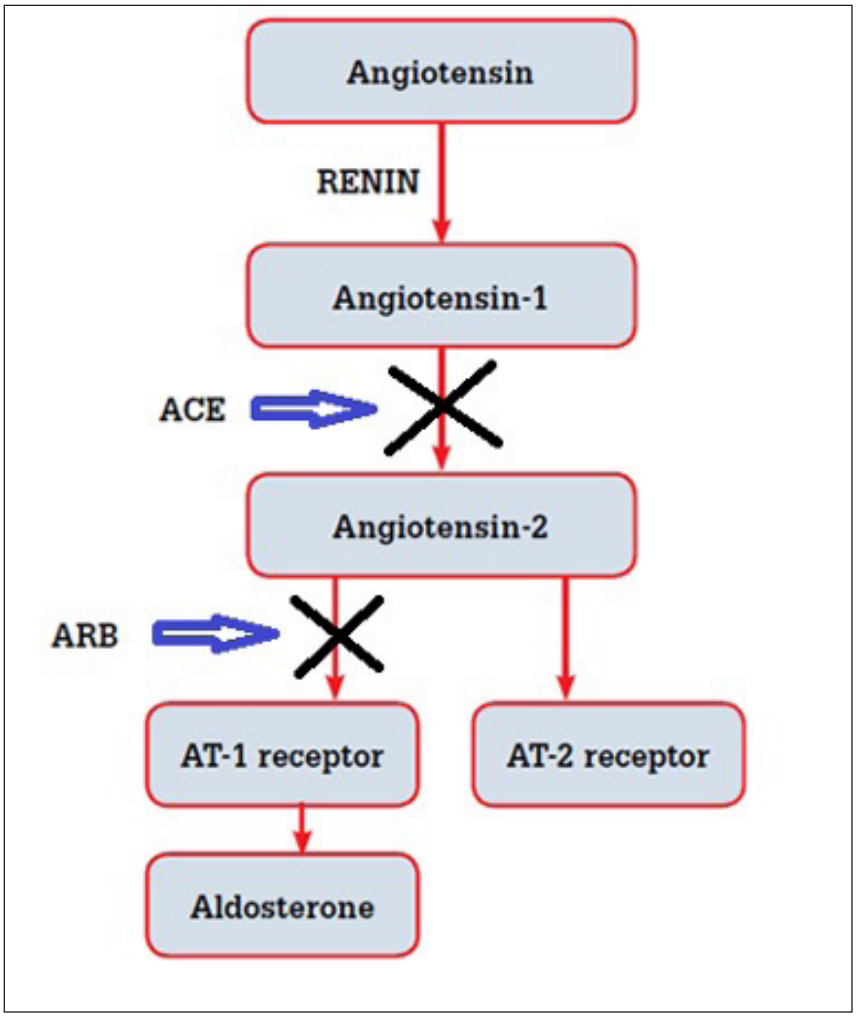

Fig. 1. Pathophysiological stages of DN

bolic changes, i.e. oxidative stress, activation of advanced glycation end products formation (AGE) etc. The latter disorders are dealing with inflammation. Development of inflammation associated with production of cytokines, growth factors, vasoactive substances (IL-6, MCP-1, transforming growth factor-beta, vascular endothelial growth factor. These events lead to fibrosis and vascular damages. Moreover, a podocytopathy has place under the hyperglycemic conditions. Beside these events intraglomerular hypertension and epithelial-mesenchymal cell transformation are activated. The outcome of these damages is fibrosis and chronic tubular disorders [3].

Stages of DN in patients with diabetes mellitus type:

• **stage 1** (hyperfiltration stage) - increased glomerular filtration rate (GFR) and capillary glomerular pressure possibly due to renal hypertrophy

• **stage 2** (silent stage) - usually normal GFR (dropped from stage 1) and no albuminuria, but with renal morphological changes, such as basement membrane thickening and mesangial expansion

• **stage 3** (microalbuminuria stage or stage of incipient nephropathy) - increased urinary albumin excretion rate (in range of 20-200 mcg/minute or 30-300 mg/day). Usually occurs 5-15 years after diagnosis of type 1 diabetes, but has been reported ≤ 2 years of diagnosis in younger patients. Persistent microalbuminuria (confirmed microalbuminuria at least twice at 3-6 months apart) is reported to be associated with widespread advanced glomerular structural changes. Microalbuminuria may be transient and reversible especially if short duration and in patients with glycated hemoglobin < 8%, systolic blood pressure < 115 mm Hg, and low cholesterol and triglyceride levels

• **stage 4** (macroalbuminuria stage) - urinary albumin excretion rate > 200 mcg/minute or > 300 mg/day

- usually occurs 10-15 years after diagnosis of type 1 diabetes
- reported association with arterial hypertension in two-thirds of patients
- highly predictive of progression to renal failure if untreated

• **stage 5** (renal failure) - development of uremia and end-stage renal disease

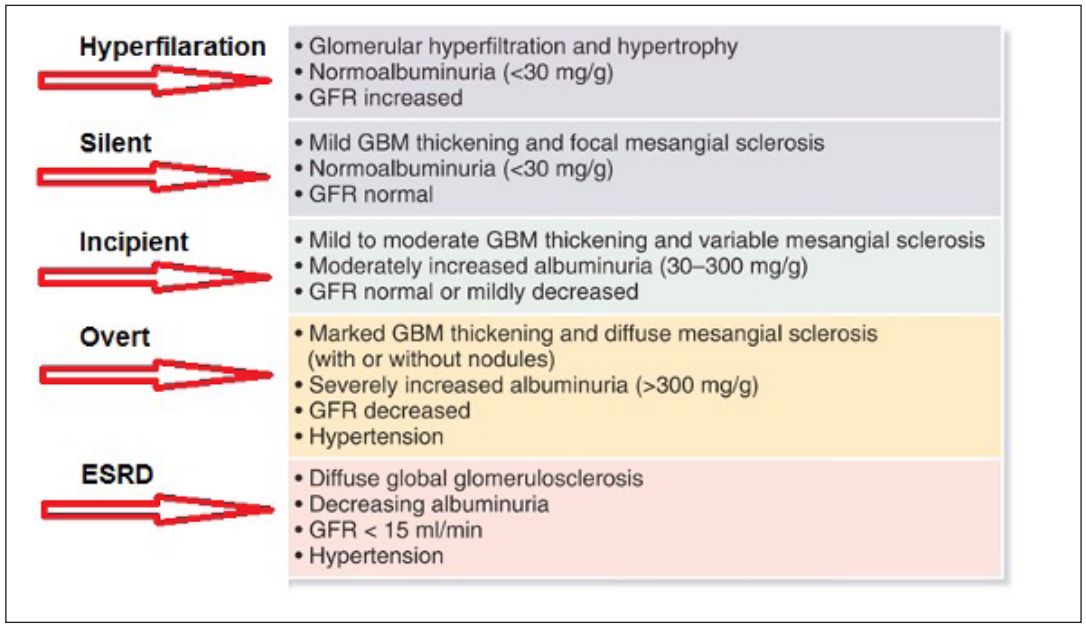

Fig. 2. Basic scheme of the renin–angiotensin–aldosterone system (RAAS) action and the mechanism of action of angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB).

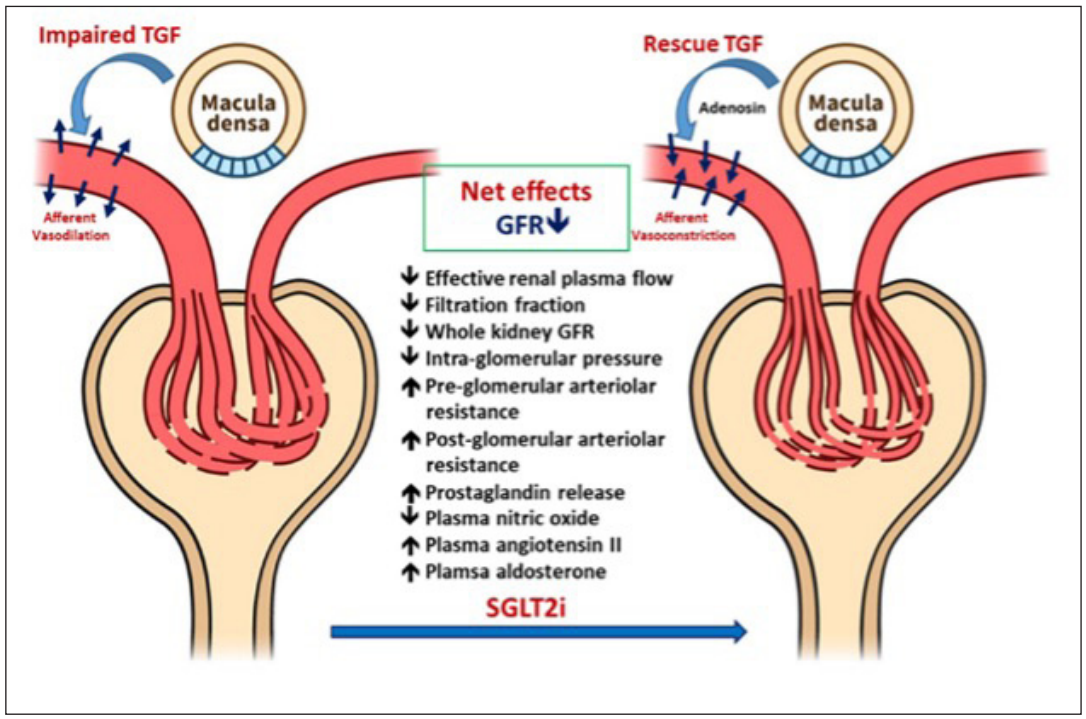

Fig. 3. Scheme of the topical action of SGLT2 inhibitors

oreported in up to 40% of patients

orequires dialysis or renal transplantation

Currently albuminuria categories which we use in practiceis following:

• A1 - albumin excretion rate (AER) < 30 mg/24 hours, albumin:creatinine ratio (ACR) < 30 mg/g (3 mg/mmol) (normal-to-mildly increased)

• A2 - AER 30-300 mg/24 hours, ACR 30-300 mg/g (3-30 mg/mmol) (moderately increased compared to young adult level)

• A3 - AER > 300 mg/24 hours, ACR > 300 mg/g (30 mg/mmol) (severely increased [including nephrotic syndrome]) [3-5].

Pathophysiological stages of DN described on Fig 1.

GFR and intraglomerular capillary pressure (PGc), glomerular hypertrophy, and microalbuminuria are the first steps in the progression of clinical diabetic nephropathy. Poor glycemic management and high systolic blood pressure make the condition worse by forcing the development of proteinuria, nodular glomerulosclerosis, tubulointerstitial damage, a decline in GFR, and ultimately ESRD (BP). It is generally agreed upon that the cumulative effects of a number of metabolic and hemodynamic factors lead to diabetic nephropathy. Kidney damages are brought on by the production of cytokines and growth factors as a result of

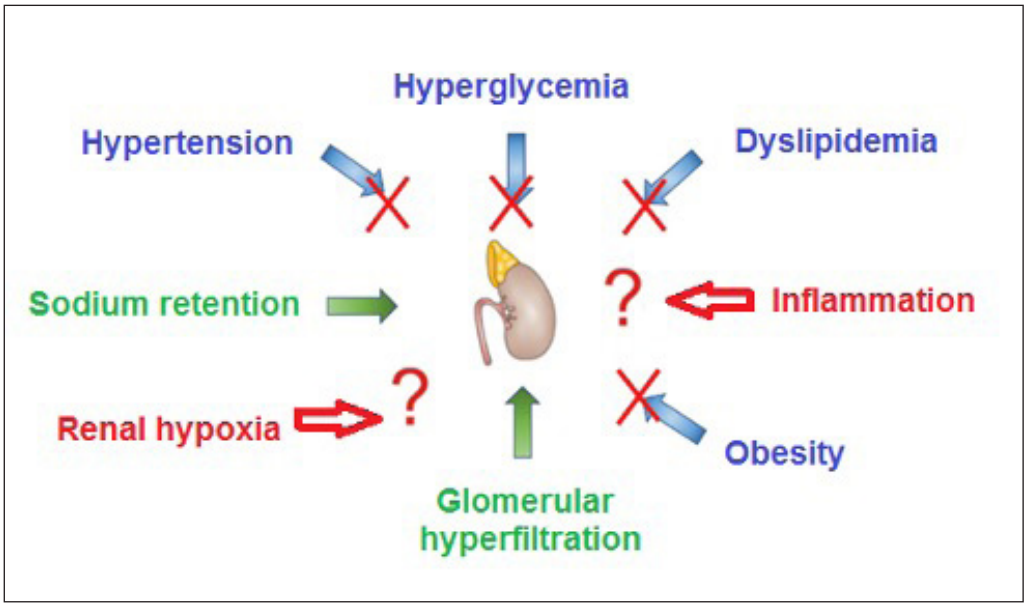

Fig. 4. Scheme illustrating mechanisms of GLP-1 agonists

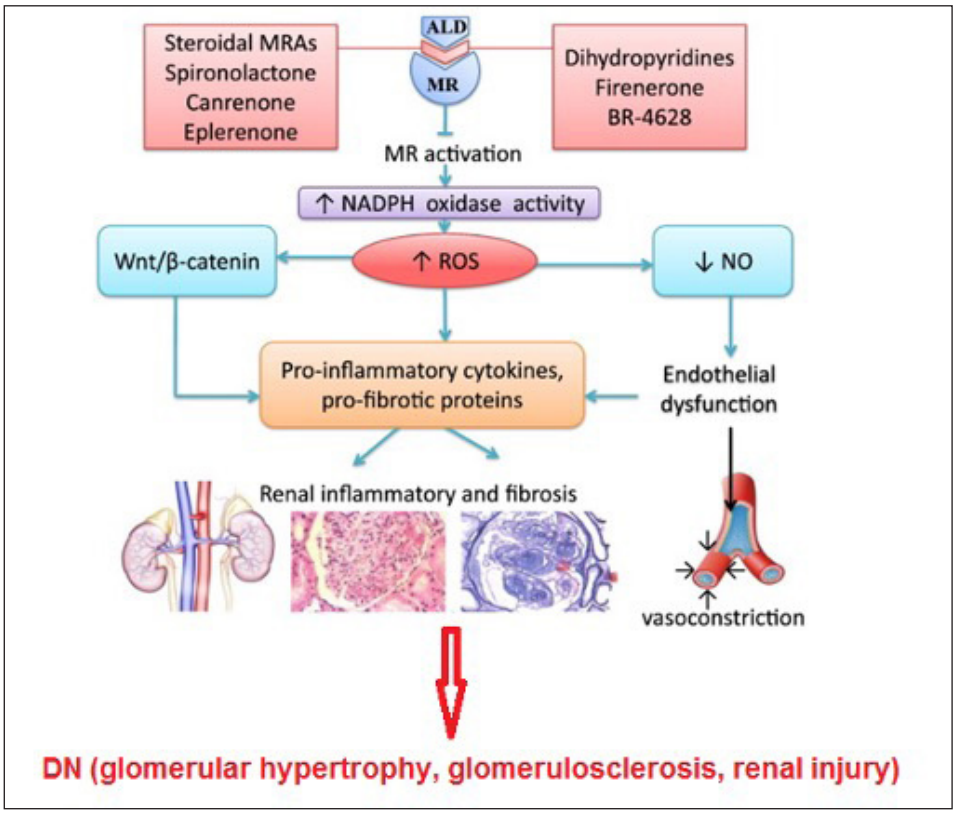

Fig 5. Mechanisms of MRAs nephroprotective effect

these common intracellular signaling pathways being activated [6].

CURRENT VIEW OF DIABETES NEPHROPATHY TREATMENT IN CHILDREN

DIETARY AND LIFESTYLE INTERVENTIONS

Increased physical activity promotion and dietary education, such as calorie counting, carbohydrate tracking, and eating foods with a low glycemic index, are all components of current treatment guidelines and are all associated with improved glycemic control. However, these strategies continue to be only marginally effective. When developing dietary recommendations for children, it's also important to consider the considerable prevalence of disordered eating behavior in young individuals with diabetes, which is connected to worse glycemic control and more detrimental consequences [7].

The American Diabetes Association (ADA) recommendations also recommend weight management, particularly for young T2D patients. However, com-

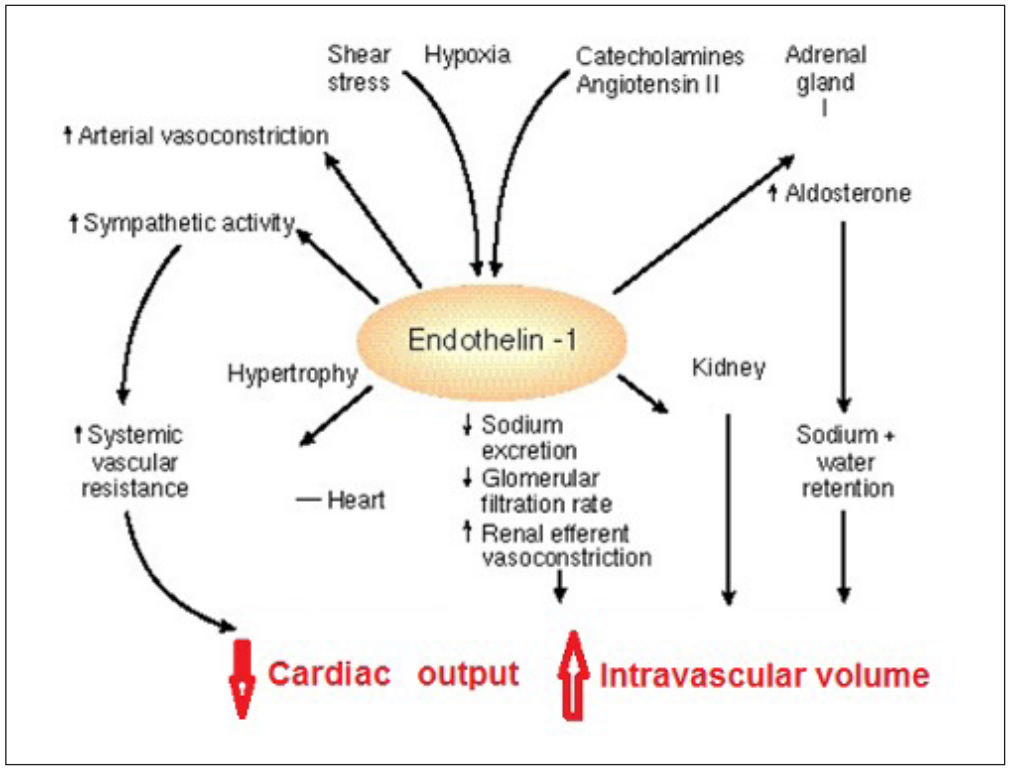

Fig. 6. Pathological effects of endothelins

prehensive lifestyle intervention programs with goals for food and exercise have not yet been successful in helping adolescents with T1D significantly enhance their glycemic control. In addition, decreasing weight and exercising are part of the treatment for diabetic nephropathy Gonzalez et al [7,8].

PHARMACOLOGICAL MANAGEMENT

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM (RAAS) BLOCKADE (ACE-I AND ARB)

Kidney and heart disease have a strong association with the renin-angiotensin-aldosterone system. Angiotensin I is a vasoactive substance which is converted to angiotensin II. This is ongoing with angiotensin-converting enzyme (ACE). ACE has a plenty of effects, i.e., activation of inflammation, fibrosis [9]. Moreover, angiotensin II increases sympathetic activity, sodium and chloride absorption in tubuli and production of increases aldosterone. It is known that bradykinin metabolism is related to ACE activity too [9-13]. (Fig 2).

Patients with kidney and heart disorders have shown benefit from ACE inhibition and angiotensin blocking in the form of ACE inhibitors and angiotensin receptor blockers. As early as 1983, the effects of angiotensin on renal auto-regulation were documented. Numerous investigations conducted in the ensuing ten years shown a reduction in albuminuria [6] as well as reno-protective effects of RAAS blockage [13,14].

SGLT2 INHIBITORS

Nowadayd a new class of medication is widely used and called a sodium-glucose co-transporter-2 (SGLT-2). The key action of these medications is that they have capacity to inhibit the SGLT-2 proteins. The latter are located in cells renal proximal convoluted tubules of humans. Their key role is to prevent the absorbtion of filtered glucose from the tubular lumen. Currently, medical doctors allowed to use following medications: canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin. Each of those medications has an individual way of prescribtions (dose, regimen). They are high effective in type 2 diabetes mellitus (DM) treatment in addition to diet and adequate physical activity [15-17].

It is known that human proximal convoluted tubules have SGLT-2 proteins localized in their cells. The main role of the SGLT-2 proteins is to reabsorb the glucose from tubular filtrate. It is shown that SGLT-2 inhibitors lead to decreased reabsorption of glucose from tubular filtrate, increase excretion of glucose as a result.

Moreover, SGLT-2 causes the increased excretion of sodium form distal tubuli. In addition to inhibiting the renin-angiotensin-aldosterone system, this is also thought to control a number of physiological processes, including lowering renal intraglomerular pressure, enhancing tubuloglomerular feedback, decreasing sympathetic activity, and lowering preload and afterload in the heart.

Due to enhanced urine glucose excretion, SGLT2 inhibitors were first studied for their potential to help

patients with type II diabetic mellitus (T2DM) better control their blood sugar levels [18].

SGLT2 can reduce glomerular hyperfiltration. This is due to inhibition of SGLT2. In turn this leads to a natriuretic effect and realization of tubulo-glomerular feedback [18]. RAAS administration leads to decrease the glomerular pressure and as a result slows down the kidney damage. .

In addition to regulation of glomerular pressure SGLT2 inhibitors enhances glucose uptake in kidney and regulate extracellular matrix formation [19]. Moreover, SGLT2 inhibitors provide an antioxidant and anti-inflammatory activity and in turn decrease fibrosis, inflammation [20].

One more link says that SGLT2 inhibitors induce the low ketotic state. This is due to ketones synthesis and lowering their excretion. It is known that ketones can be oxidized which leads to oxidative stress in kidney and vessels.

Data show that cardiovascular and kidney effects of SGLT2 inhibitors are very effective in CKD prevention and in proteinuric states as well.

Dapagliflozin was authorized by the European Commission in March 2019 as an adjuvant treatment for type 1 diabetes. The use of SGLT2 inhibitors increases the incidence of DKA in people receiving insulin, according to prior studies. Dapagliflozin does not, however, appear to raise the risk of DKA in the near term, according to the current findings (24 weeks) [21].

GLP-1 AGONISTS

In response to meal consumption and an increase in plasma glucose, L-cells in the lower stomach produce the incretin hormone glucagon-like peptide-1. These incretin hormones promote the release of insulin from pancreatic ß islet cells, inhibit the release of glucagon, postpone the emptying of the stomach, and increase satiety. The lungs, stomach, and kidneys are only a few of the other organs that have GLP-1 receptors in addition to the pancreas [22,23].

Additionally, GLP-1 has been shown to have a variety of kidney-protective effects, including the ability to reduce albuminuria, glomerular hyperfiltration, glomerular hypertrophy, and mesangial matrix expansion in animal models. It has also been shown to reduce oxidative stress and inhibit albuminuria (Fig 4)., as well as an ability to ameliorate albuminuria, glomerular hyperfiltration, glomerular hypertrophy and mesangial matrix expansion in animal models [23,24].

MINERALOCORTICOID RECEPTOR ANTAGONISTS

The mechanisms of action of the mineralocorticoid receptor (MR) go beyond their antagonistic effects on the epithelial sodium channels (ENaC) in the collecting tubules. Numerous tissues, such as the vascular, cardiac, and colonic tissues, express MR. MRs contribute significantly to the adaptive response to damage in addition to fluid and ion transport [25]. Reactive oxygen species and inflammation have been demonstrated to rise with the activation of these receptors, and renal hypertrophy has been linked to the overexpression of this receptor.

The most commonly used mineralocorticoid receptor antagonists are spironolactone and eplerenone. Meta-analyses report data that steroidal MRAs are effective in lowering proteinuria rates in patients especially those treated with RAAS inhibitors. However, these drugs are still accurately used in patients with CKD, due to their side effects - hyperkalemia and effect on GFR [26,27].

Non-steroidal MRAs were first introduced, with finerenone being the most famous. They had great promise for perhaps improving cardiac and proteinuric conditions while having less of an impact on causing hyperkalemia. The tissue distribution of finerenone, the way it inactivates MR, and other pharmacologic characteristics are just a few of the characteristics that set it apart from steroidal MRAs [28].

Finerenone, which promises the similar advantages of steroidal MRAs with less side effects, is a welcome addition to our toolbox. Numerous ground-breaking studies showing the therapeutic potential of finerenone for DKD.

ENDOTHELIN ANTAGONISTS

Endothelin-1 (ET-1) is a 21 amino acid peptide and is the most potent vasoconstrictor in the human body. ET-1 is produced in almost all kidney cells. Most of the production of ET-1 in going in tubular cells, primarily principal cells of the inner medullary collecting duct [29].

There are substantial clinical evidence for increased plasma endothelin-1 (ET-1) levels in patients with diabetes mellitus, leading to endothelial dysfunction. The endothelin system consists of three isoforms - ET-1, ET-2, and ET-3. ET-1 is a potent vasoconstrictor peptide that plays a key role in controlling cell proliferation and regulating the accumulation of extracellular matrix and inflammatory cells. These events lead to fibrosis.

Endothelin receptors are expressed in the kidney [30], and diabetics have been shown to have an overexpression of these receptors. The renal endothelin system has been demonstrated to play a crucial role in normal renal function, and derangements of this system are involved in the onset and progression of DN [31].

It has been demonstrated that endothelin receptor antagonism enhances renal microcirculation and that it can decrease urine protein excretion [32].

Trials have been done to evaluate the benefits of endothelin antagonists in the treatment of DKD patients in light of this evidence of possible renal benefit.

CONCLUSIONS

DN is a major healthcare challenge, complicating the course of many people who live with diabetes, and is a major cause of ESRD. The DN course and progression leads to severe cardiovascular complications and early death. Prognosis of DN is quite different and depends on presense of kidney damage, i.e. albuminuria and hypertension. Treatment of DN is complicated clinical issue and requires individual and complex approach, including renoprotection, antihypertensive treatment. These may prevent early death. Literature data and reports from different research groups agreed on necessity of individual approach.

We were only able to prescribe patients with DN one treatment option for many years: RAAS inhibition with ACE-I and ARBs. These medications continue to be the key effectors in managements of DN patients. Nowadays, we are able to provide additional medications that can enhance the benefits of RAAS blocking.

SGLT2 inhibitors are revolutionizing nephrology thanks to their undeniable protective advantages that go beyond DN. According to the first KDIGO guidelines, GLP-1 agonists are now the preferred oral medications for treating diabetes in CKD patients. As we approach a medical therapy for DN that follows guidelines and includes an ACE-I or ARB, MRA, SGLT2 inhibitors, and maybe an SGLT3 inhibitor. These medications are very effective addition to our conventional treatment. The future of DN management may involve a more individualized strategy, where each patient can receive a treatment plan that is specific to their genetic and biomarker profile. Further search of neproprotective medicines for early DN correction in pediatric patients is still of high importance.

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ABSTRACT BOOK

SCIENTIFIC AND PRACTICAL CONFERENCE WITH INTERNATIONAL PARTICIPATION, DEVOTED TO WORLD HEALTH DAY 2023 AND WHO'S 75TH ANNIVERSARY

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APRIL 6, 2023, BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

IMPACT OF PROLONGED SELF-ISOLATION DURING THE COVID-19 PANDEMIC ON ANXIETY

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Introduction: The quarantine measures during the COVID-19 pandemic meant that millions of people were forced into social distancing for months. Although there has been some research on people's mental health in lockdown, there are not enough studies that look at the difference in anxiety levels between people with different levels of social distancing. Studying the differences in levels of anxiety among people in different countries can help improve the global strategy for managing quarantine measures.

The aim: Our study examined the relationships between the forced sedentary lifestyle of people observing quarantine conditions and their psychological health.

Materials and methods: Our study, PsycO-Social Evaluation of soclal Distancing effects ON PHysical ACTivity (POSEIDON-PHACT), included 2,029 participants (72% women), mean age 31.95 (SD=14.34) from 54 countries, including 904 (45%) individuals from Ukraine. All participants completed a questionnaire that included informed consent, demographic and anthropometric data, physical activity and health data, and the State-Trait Anxiety Inventory for Adults to measure state anxiety levels. We evaluated the effects of quarantine adherence on anxiety scores, adjusted for gender, age, ethnicity and body mass index using generalised linear model in *R-studio*.

Results: In the POSEIDON-PHACT study, 34.8% (n=704) of participants reported that they self-isolated, while 65.2% (n=1,321) did not adhere to self-isolation; 76.5% (n=1,549) of respondents self-quarantined and 23.5% (n=476) did not quarantine. We compared the anxiety scores of respondents who did and did not self-isolate, defining that the self-isolating group experienced higher anxiety levels (OR=1.05 [95%CI 1.01-1.10]; p=0.044). This difference remained significant in the 18-27 age group (p=0.018). There was no difference in anxiety scores between those who quarantined and those who did not quarantine (OR=1.02 [95%CI 0.97-1.06]; p=0.490). At the same time, the both models were significant (p<0.001).

Conclusions: We report that prolonged self-isolation during the COVID-19 pandemic is associated with higher anxiety levels in the general population across diverse ethnicities. The effect of social isolation factors on individual well-being should be considered when developing quarantine regulations and designing population-based studies.

KEY WORDS: COVID-19, multinational study, anxiety, social isolation

ESTIMATION OF THE PREVALENCE OF CHRONIC LIVER DISEASES AMONG URBAN ADULTS

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Introduction: The prevalence of hepatobiliary diseases and their burden on healthcare systems are increasing worldwide. There is no reliable epidemiological data on the prevalence of chronic liver diseases in Ukraine. According to most international clinical guidelines, ultrasound is the first-choice non-invasive method to examine the liver and biliary tract, and with certain limitations, it allows to identify main prerequisites for liver disorders. Fatty liver disease, alcoholic liver disease, and mildly symptomatic chronic viral hepatitis are the main causes of diffuse changes in the liver and can naturally progress to cirrhosis and hepatocellular carcinoma, the treatment technologies for which are expensive and insufficiently effective. The registered scopes of medical services partially reflect the prevalence of liver diseases, covering only cases with obvious clinical manifestations. We have not found any up-to-date publications on the assessment of the prevalence of diffuse liver changes among the Ukrainian population based on the results of large-scale radiological studies of the liver.
The aim: Estimation of prevalence of diffuse liver disorders based on the results of the ultrasound examinations and open data of health care statistics.
Materials and methods: We examined 3438 adult city residents aged 19-74 (uneven age distribution, the median is 51) in 2019-2021. Ultrasound examinations were performed after standard preparations. Patients who received chemotherapy for any oncological disease were not included in the study. Indications that we considered as signs of diffuse liver changes in the B-mode gray scale: increased echogenicity of the liver parenchyma compared to the kidney cortex, decreased visibility of the vascular system of the liver, decreased visualization of the diaphragm and deeper areas of the liver parenchyma (decreased sound conductivity). All patients were examined according to the standard protocol for the abdominal examination. Data from public statistical reporting of licensed medical service providers by form № 20 and data from the National Health Service under ICPC-2 code D97 for 2021 were also studied.
Calculations were made using the MedStat software.
Results: According to the Ukrainian National Health Service, 76428 patient visits to primary care physicians for causes of different liver diseases grouped under ICPC-2 code D97 in 2021. During the year, 8170 patients (10,6% of all requests) received specialized medical care. Over the same time, 25127 patients with liver cirrhosis (mortality rate of 22,5%) and 10799 patients with various chronic hepatitis completed inpatient treatment.
Among the patients examined by us with ultrasound, women predominated – 62,6%, which can be explained by the fact that women traditionally request medical services more frequently as well as by population gender imbalance, especially in older age subgroups. Among women (2155), the median age was 55, diffuse liver changes were found in 1222 (57,7%). Among men (1283), the median age was 51, diffuse changes were found in 1035 (80,6%). The prevalence of diffuse liver changes was significantly higher than the prevalence of chronic liver diseases according to the data of doctor visits and the frequency of hospitalizations, which requires further research for clinical certainty and the selection of patients with a risk of progression of fibrosis and the formation of liver cirrhosis.
Conclusions: Diffuse changes in the liver are much more common according to the results of the ultrasound, while the statistics of the diseases that cause them demonstrate a much lower prevalence of this pathology. It is necessary to improve the clinical patient's pathway with the wider implementation of non-invasive testing to identify patients at risk of progression of liver fibrosis and perform medical interventions timely.

KEY WORDS: liver disease, hepatitis, cirrhosis, ultrasound diagnostics.

FORECASTED MORBIDITY TRENDS OF ELDERLY PERSONS – PATIENTS OF MULTIDISCIPLINARY HEALTH CARE FACILITY

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Introduction: The development and implementation of effective management solutions in the healthcare system, disease prevention measures, effective treatment and diagnostics is not possible without forecasting various phenomena and processes. Identifying trends, predicting their development prospects is an important task of forecasting. The result of the forecast is the determination of priority issues regarding the preservation and strengthening of the health of the population as a whole and in its individual groups.

The aim: Determining morbidity trends of elderly people who are served at multidisciplinary health care facilities and forecasting their morbidity in the future.

Materials and methods: Based on the data collected from statistical report form "Report on diseases registered in patients who live in the service area of a medical and preventive institution", an analysis of the morbidity of the elderly population served in a multidisciplinary health care institution for 2009-2021 was carried out. With the help of the extrapolation method, prognostic calculations of the morbidity of this contingent until 2026 were made.

Results: An analysis of data on the morbidity of elderly patients treated in a multidisciplinary health care facility showed that over the period 2009-2021, the primary morbidity overall decreased by 25.6%, and the prevalence of diseases decreased by 4.7%. This can be explained by the availability and quality of medical care in a health care facility, as well as the possibilities of integrating medical care in a multidisciplinary facility. Despite the positive dynamics of the reduction of morbidity rates in general, negative trends are observed for a number of diseases.

High rates of increase in primary morbidity over thirteen years are observed for some infectious and parasitic diseases (by 6.6 times), diseases of the ear and mastoid process (by 6 times), diseases of the skin and subcutaneous tissue (by 2.5 times), diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (by 21%). The prevalence of some infectious and parasitic diseases in 2009-2021 among the elderly treated in a multidisciplinary health care facility increased by 2.8 times, endocrine, nutritional and metabolic diseases – by 94.7%, diseases of the ear and mastoid process – by 56.3%, diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism - by 35.4%.

Forecast calculations of the incidence and prevalence of diseases among the specified contingent until 2026 indicate that compared to 2021, the primary incidence of all diseases among elderly people will increase by 36.0%, the prevalence by 2.9%, and the patient contingent by almost by 10.0%. As for certain classes of diseases, a significant rate of increase in primary morbidity is predicted for diseases of the endocrine system, nervous system, diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, diseases of the ear and mastoid process, diseases of the eye and adnexa. At the same time, in the future, the incidence of diseases of the circulatory system, diseases of the digestive and respiratory system is expected to decrease.

According to forecast data, by 2026, the prevalence of diseases of the ear and mastoid process, diseases of the musculoskeletal system and connective tissue, injury, poisonings and some other consequences of external causes will grow at the fastest rate. At the same time, a decrease is expected in the prevalence of diseases of the nervous system, diseases of the circulatory system, diseases of the respiratory system, diseases of the genitourinary system, diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism.

Conclusions: Forecast data are a powerful basis for the adoption and development of measures to preserve and strengthen the health of the elderly, provide an opportunity to determine the priorities of providing medical care, establish resource needs, including staffing.

KEY WORDS: morbidity, classes of diseases, elderly people, predictive trends.

SUBSTANTIATION OF CONTENT OF THE EDUCATIONAL DISCIPLINE «HEALTH SYSTEMS» IN THE TRAINING COURSE OF MASTER OF PUBLIC HEALTH

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Introduction: Since the public health system got into the integral part of the health system, knowledge of the basic organization, financing and management of the health system is an important prerequisite for the implementation of the Masters of Public Health in the Essential Public Health Operations.
The aim: To substantiate the program and educational content of the academic discipline «Health Systems» in frame of master students of public health education.
Materials and methods: Bibliographic, semantic, information-analytical methods were used. The requirements of the Standard of Higher Education of Ukraine of the second master's level in the specialty «public health», the ASPHER`s European Program of Core Competences for the Public Health Professionals analyzed. The best experience of the public health personnel training of 50 universities worldwide studied.
Results: Based on the results of the study, a syllabus was developed, the working program of the academic discipline «Health Systems» was substantiated, and its educational and methodological support was created. The purposes of studying the academic discipline «Health Systems» is to obtain the necessary knowledge about the organization and functioning of health systems and to learn related components. The latter includes public health systems, as well as skills and competencies of their practical application in the process of research, analysis and evaluation of health systems, development of recommendations for further implementation of their work in order to prevent disease, promote health and extend life expectancy.
The program competencies were determined for the educational and professional program of the specialty «Public Health», the formation of which is ensured in the study of the discipline «Health Systems». Several competencies are included into the program. Among them are the following: the ability to prioritize and assess public health needs in a certain situation; the ability to develop concerns for strategies, policies and to identify individual interventions aimed to maintain and strength the health of the population and to evaluate their effectiveness; the ability to analyze public health strategies, policies and interventions and propose measures to improve the efficiency of the use of available funds.
The program of the discipline includes the following topics: main parameters (goals, values) and functions of health systems (service delivery, financing, resource generation, management); types of health care systems (Beveridge, Bismarck, liberal); modern trends in the development of healthcare systems; national healthcare system of Ukraine.
Particular attention is paid to the issues of evaluation criteria and the world ranking of health systems; advantages and disadvantages of individual models; peculiarities of ensuring the functioning of the public health system in individual models; approaches to ensuring accessibility and quality of health care services; problems of overall coverage of the population with health services; the main directions of reforming health care systems.
Conclusions: The content of the academic discipline «Health Systems» includes a wide range of issues related to the goals, parameters, functions of health systems, their models, the advantages and disadvantages of each of them, their rating, features of reform, etc. Assimilation the provisions of the academic discipline will end-up in a comprehensive vision of public health professionals of existing problems and approaches to their solution within the framework of specific models of health care systems.

KEY WORDS: public health, master's education, training program, health systems.

ANALYSIS OF THE BEHAVIOUR OF THE BALANCE VALUES OF COSTS, QUALITY, AND COMFORT OF MEDICAL SERVICES DEPENDING ON INDIVIDUALISED DEMAND ELASTICITIES

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Introduction: The patient's ability to assess the quality and comfort of medical services and their proportionality to payments is crucial for optimising healthcare services, in particular because of the possibility of strengthening the monopsony power of the collective patient as a counterargument to the monopolistic competition of the manufacturer.
The aim: Econometric assessment of market efficiency of medical services to gynaecological patients.
Materials and methods: A combined (retrospective+prospective) study of 150 case histories of patients treated in gynaecological departments at Vinnytsia city hospitals over 2017-2022 years was performed.
Econometric model of Dranove and Satterthwaite, 1992 was used to check for market efficiency.
Power analysis of Satorra & Sarris, 1985 *undertaken* to determine the sample size to support statistical tests of two main hypotheses: a) an increase in the healthcare costs leads to an increase of quality and comfort; b) a decrease in the individual demand elasticities by price, quality and comfort due to lack of patient awareness leads to a decrease in the equilibrium values of costs, quality and comfort
Given hypotheses were tested by parameters of structural equations (Dranove and Satterthwaite, 1992).
Results: A theoretical model was developed for the study. The theoretical model is based on the behaviour of a provider who tries to maximise profits within certain limits (set by demand) by manipulating three important attributes: price (p), quality of service (ql) and comfort (cm).
In order to relate the theoretical model to the data, we make the following obvious assumptions: (i) both quality and comfort are not directly observable (latent factors), but instead are described by a number of observable variables; the same applies to information noise; (ii) all measurements are stochastic in nature with their own variances; (iii) the nature of the relationship is directional or covariate; and (iv) the balance values of price, quality and comfort are observed and determined simultaneously. These assumptions are consistent with the capabilities of structural equation modelling.
The structure is supported by three latent factors: information noise (F1), quality of hospital services (F2), and comfort (F3), F1 is loaded (correlated) with patient age, duration of illness, interventions, education, and employment. F2 has loadings from the length of hospital stay, duration of intervention, complications due to intervention and anaesthesia. Another load of F2 is derived from the experience and qualifications of medical staff, which is an auxiliary latent factor F with loadings from physician position, length of service, and category. The latent factor F3 is determined by loadings from treatment regimen violations, patient complaints, type of ward (specialised, hotel, single, double), length of hospital stay, duration of intervention, complications due to intervention, and anaesthesia. In addition to the latent factor variables, the design included exogenous variables such as price/cost and insurance plan. According to the theoretical model, costs modify latent factors F2, F3 and in turn depend on latent factor F1. Given the process under study, costs also depend on the insurance plan. The latent factor of patient experience (F1) influences the latent factors F2 and F3 according to Hypothesis 2, while the latent factors F2 and F3 have a common variation (cov effect).
Conclusions: We have established that:
• the balance sheet values of expenditures on medical services are significantly higher with better awareness of patients, i.e. higher with an increase in the individual elasticity of demand at the price of ;
• higher balance sheet values of healthcare expenditures result in significantly higher quality of healthcare services, which correlates with higher complexity of services according to factor loadings;
• at higher balance values of healthcare costs, the comfort of healthcare services is significantly higher, with discomfort correlating with more complex pathology and the need for higher complexity and volume of services.
Thus, the structural model of the Dranove and Satterthwaite system can be used to analyse shifts in the balance of costs, quality, and comfort of healthcare services, in particular, depending on individual elasticities of demand.
However, the most important thing is that the organisation of inpatient obstetric and gynaecological care for the nosologies under consideration meets the optimisation conditions, on the basis of which the theoretical model and system of structural dependencies were developed, and therefore is market-based and cost-effective.
Estimates of correlation matrix of three latent factors showed that
- correlation between balance values of awareness factor and quality of healthcare services provision factor is positive (r=0.283), however, proving reliability of the relationship requires more units of observations;
- correlation between balance values of awareness factor and discomfort factor of healthcare provision is inverse (r=-0.289), proving reliability of relationship requires more units of observations;
- there is a significant inverse correlation between balance values of quality factor and discomfort with healthcare provision factor (r=-0.920).

KEY WORDS: co-payments, medical services, quality and comfort of healthcare services.

EPIDEMIOLOGICAL EFFECTIVENESS COVID-19 VACCINES, UKRAINE, 2021-2022

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Introduction: Vaccination is one of the most effective means of preventing the occurrence of cases of the coronavirus disease (COVID-19). Worldwide, as of Dec 27, 2022, 13.15 billion doses of COVID-19 vaccines have been administered. In Ukraine, since the beginning of the vaccination campaign, as of Dec 22, 2022, 15,403,937 people received two doses of the COVID-19 vaccine, 16,222,706 people received one dose, and 194,503 people received a second booster dose.
The aim: To study and analyze indicators of the epidemiological effectiveness of the vaccination against COVID-19 in Ukraine from Oct 04, 2021 to Dec 22, 2022.
Materials and methods: Epidemiological and statistical research methods were used in the work. The data was obtained from the websites of: State institution "Public Health Center of the Ministry of Health of Ukraine", Vaccination against COVID-19, Ministry of Health of Ukraine, Our World in Data. Calculations were made in the Microsoft Office Excel computer program.
Results: COVID-19 vaccines used in Ukraine are AstraZeneca (Covishield and AstraZeneca-SKBio), Pfizer-BioNTech (Comirnaty), Sinovac Biotech (CoronaVac), Spikevax/ Moderna. The mass use of COVID-19 vaccines in the world began only in the second half of 2020, in Ukraine - from June 2021. As of Dec 22, 2022, 5,357,941 cases of COVID-19 were detected, including 509,751 people who were vaccinated with at least the 1st dose of the vaccine against COVID-19. The vaccination efficiency rate of the total population was 70.6%. The weekly incidence rate of COVID-19 among the vaccinated total population ranged from 0.3 per 100,000 population to 124.9 per 100,000 population, and the average value was 19.3 per 100,000 population. The weekly rate of incidence of COVID-19 among the unvaccinated aggregate ranged from 2.4 per 100,000 population to 601.3 per 100,000 population, and the average value was 111.2 per 100,000 population. That is, the morbidity rate among vaccinated cases of COVID-19 was on average 5 times lower than among unvaccinated ones, which generally indicates a moderate effectiveness of vaccinations against the COVID-19 in Ukraine for the period from Oct 04, 2021 to Dec 22, 2022. The decrease in vaccination efficiency rate can most likely be explained by the change of the Delta-variant of the pathogen to the Omicron variant. Accordingly, during this period there was a trend towards a moderate increase in the incidence of both vaccinated and unvaccinated cases of COVID-19.
Conclusions: The results of the study of the effectiveness of vaccinations against COVID-19 of the total population in Ukraine indicate that it is generally moderately effective.

KEY WORDS: public health, COVID-19 vaccines, mass vaccination, immunization

MANAGERIAL STYLES ASSOCIATED WITH PUBLIC HEALTH LEADERSHIP COMPETENCIES

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Introduction: Modern challenges (the COVID-19 pandemic, war activities, economic crisis, etc.) require a high level of professionalism in solving public health problems. At the same time, the importance of leadership at all levels of health care is increasing, both in the provision of individual medical services and in ensuring population health.
Leadership competencies in public health can be influenced by various factors, especially educational ones. Our previous studies have shown that management styles can be considered as factors affecting overall management effectiveness, so our next step was to determine their connections with the corresponding competencies.
The aim: To identify leading managerial styles that are associated with having public health leadership competencies.
Materials and methods: A study on self-assessment of managerial styles was conducted on a sample of 192 healthcare workers, healthcare managers and students of higher medical education. Leading management styles were evaluated according to the methodology of the World Health Organization (https://apps.who.int/iris/handle/10665/205407), in which 12 distinct managerial styles are distinguished: supportive, rescuing, normative, prescriptive, problem-solving, task-obsessive, innovative, bohemian, resilient, sulking, assertive, aggressive
Managerial styles are interrelated with management functions and overall managerial effectiveness score. Using general information about the respondents and their score of overall management efficiency, the surveyed were divided into groups with a sufficient level of public health leadership competencies (n=109) and without it (n=83).
Processing of the obtained results was carried out using methods of logistic regression and factor analysis (varimax rotation of normalized data) using TIBCO Statistica™ Trial Download for Windows (https://www.tibco.com/resources/product-download/tibco-statistica-trial-download-for-windows) software.
Results: Among the leading management styles, in which the largest share of respondents with a sufficient level of public health leadership competencies was observed - supportive (56.0%) and problem-solving (33.9%), while none with the aggressive (0%) or sulking (0%) styles as dominant ($p<0.001$).
The conducted logistic regression analysis showed that the chances of having a sufficient level of public health leadership competencies increase with the use of a supportive management style (OR=1.49; 95% CI 1.23-1.80), problem-solving style (OR=1.43; 95% CI 1.13-1.81) or normative style (OR=1.22; 95% CI 1.04-1.41).
As a result of the factor analysis, four factors were selected from the general list of managerial styles, which determined the total variance by 65.6%. The first factor, which accounted for 31.3% of the total variance, included supportive style and problem-solving style (the second one had a higher factor loading), allowing it to be defined as "support in problem-solving". The second factor included three managerial styles (listed in order of decreasing factor loading) – prescriptive, aggressive and task-obsessive. According to the content, this factor was defined as «practical ingenuity», its influence on the total variance is 14.5%. The third factor, accounting for 10.6% of the variance, consisted of only flexible managerial style and therefore was named «flexibility». The fourth factor was formed by two styles – bohemian and innovative, which have the generation of new ideas in common, so they were united in the factor which is called «ideas generation».
Conclusions: The leading managerial styles associated with public health leadership competencies are supportive, problem-solving, and normative styles. Since every leader uses a different combination of managerial styles, with the help of factor analysis it was determined that the leading factors related to management and contributing to the acquisition of a sufficient level of public health leadership competencies include: support in problem-solving, practical ingenuity, flexibility and ideas generation (total factor loading = 65.6%).
Leadership competencies in public health, which are formed under the influence of these factors, can be formed based on the natural abilities of the individual, with the help of targeted influence, both of the person himself (self-improvement, self-study, etc.) and with the help of the system of formal and informal education.

KEY WORDS: public health, leadership competencies, managerial styles

OPTIMIZATION OF PREVENTIVE MEASURES FOR DENTAL DISEASES IN CHILDREN IN THE CONDITIONS OF WARTIME IN THE KHARKIV REGION

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Introduction: Maintaining a child's dental health is a global task of primary prevention. According to modern views on this problem, the factors that lead to the development of dental pathology and the level of risk for the patient should be identified at first. Based on these data, taking into account the child's age, the doctor is able to make an individual plan of preventive measures. However, because the provoking factors may change, the child needs regular visits to control and correction of the prescriptions. Currently, there is a situation in the region where most patients are limited in their ability to visit a dentist. That is why it is important to provide an opportunity to receive support as part of the primary prevention of dental diseases.
The aim: Optimization of individual preventive measures by identifying and eliminating the factors of dental pathology in children of the Kharkiv region during wartime.
Materials and methods: Individual consultations on the condition of the oral cavity using video from the devices available to and the selection of preventive measures were conducted for primary patients. Also for children, who received treatment at the Pediatric Dentistry and Implantology Department of KhNMU before the beginning of hostilities. A total of 28 children aged 2 to 10 were consulted.
Because patients were unable to visit the dentist for various reasons, the communication between the patient and the doctor was carried out on distance. Online consultations for patients were held to determine the factors of dental pathology development. The questionnaires used were created in the form of Google forms and developed taking into account changes in the environment and living conditions of children due to the hostilities in the Kharkiv region.
Results: The consultations provided information about the ability to perform oral hygiene care and about the availability and types of hygiene tools and items. Factors such as changes in diet and the possibility and duration of being outdoors were not neglected. On the basis of these data, new and adjusted previously recommended individual plans for the prevention of dental diseases were made. Parents were also instructed on how to determine their child's oral hygiene, explained the role of bad habits, and provided links to useful online resources.
Conclusions: Prevention has always been a significant part of the work of a pediatric dentist. First of all, given the age aspect, preventive measures need to be monitored and corrected, especially in the period of childhood. In wartime, when direct visits to dental clinics are quite limited, non-standard approaches to doctor-patient communication are a solution to the situation and allow to solve a number of issues that at first glance seem unattainable.

KEY WORDS: preventive measures, dental diseases, children.

GLOBAL HEALTH DIPLOMACY: CONTEMPORARY CHALLENGES AND PROSPECTS FOR UKRAINE

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Introduction: The UN General Assembly, in its resolution of Nov. 26, 2008, A/RES/63/33, recognized the close relationship and interdependence between foreign policy and the health of the world's population, and also called on member states to take health issues into account when developing foreign policy. In contemporary world, the diplomatic component is an integral part of the global health management system. Global Health Diplomacy (GHD) brings together practices by which governments and non-governmental organizations coordinate and organize global policy decisions to improve public health. In the course of countering the spread of the COVID-19 pandemic, GHD became an integral part of geopolitics for the first time. With the beginning of the large-scale Russian invasion of Ukraine, general geopolitical changes are taking place that affect all areas of public life. This requires new concepts of international relations for the formation of global policies in the management of health care.

The aim: To analyze directions of development of GHD taking into account global socio-economic and geopolitical trends.

Materials and methods: The research methodology was based on the application of bibliosemantic, information-analytical method, system approach and analysis.

Results: The full-scale Russian aggression created a number of difficult challenges for Ukrainian health care system, which survived despite the losses incurred. During the year of the war, the Russians killed 106 healthcare workers, completely destroyed 174 healthcare facilities, and seriously damaged 1,106. The total amount of damages exceeded USD 1.5 billion. Active hostilities on a long front, missile attacks and drone attacks, mining of about 30% of the territory also caused an increase in the need for specialized medical assistance, provision of modern effective and high-quality medicines and medical products for both the civilian population and wounded defenders. Overcoming the challenges faced by the Ukrainian health care system is based on relevant systemic solutions involving all available mechanisms corresponding to the seven dimensions of GHD (I.Kickbusch, A.Liu, 2022): negotiating health promotion as a prime priority; creation of new management mechanisms to support health; creating alliances to support public health; building and managing relationships with donors and stakeholders; responding to public health crises; improving relations between countries through health care; promoting peace and security. Communication with the ministers of health of the partner states, in particular, Belgium, Czech Republic, Great Britain, Greece, Germany, France, Poland, Romania, USA, the leadership of WHO, UNICEF, PIC/S and other influential international organizations regarding coordination has become unprecedentedly intense regarding their provision of specialized assistance to Ukraine, the elimination of the possibility of the spread of Russian influence and the exclusion of the Russian Federation from international agreements and alliances.

In September 2022, for the first time in history, the Minister of Health of Ukraine was elected to the WHO Executive Board, which is not only a recognition of Ukraine's role in the international arena, but also another effective tool of the GHD.

At the initiative of the President of Ukraine, the UNITED24 fundraising platform was launched, thanks to which more than UAH 1 billion was raised for health care needs, and more than 9,000 units of medical and other equipment and transport were used for the purchase.

Another important direction of GHD was the prioritization of the receipt and distribution of humanitarian aid received from more than 30 countries of the world, from international organizations, business representatives and medical institutions of other countries. During the period of martial law, a total of 10,500 tons of medical humanitarian aid for the total amount of UAH 12.8 billion arrived in Ukraine.

In order to provide specialized medical care in partner countries since the beginning of the invasion, the Ministry of Health of Ukraine and the European Commission have organized the medical evacuation of more than 2,600 Ukrainians. With the involvement of international aid, over the past 12 months, 186 health care facilities have been completely rebuilt, and another 297 are in the process of being rebuilt.

Diplomatic aspects of global health are also taken into account in the preparation of the project Strategy for the Development of the Health Care System until 2030, developed in accordance with the Decree of the President of Ukraine No. 369/2021 of 18.08.2021, taking into account the WHO and EU strategic documents, as well as the best practices of the EU countries, Great Britain, USA and other countries.

Conclusions: Thus, we concluded that there is a need for concerted, consolidated activities aimed at developing the mechanisms of global health diplomacy. Such activities will contribute to the productive renewal and reconstruction of the Ukrainian health care system, its reform and development in accordance with the EU integration vector of development and modern world standards.

KEY WORDS: Global Health, Public Health, geopolitics, health diplomacy.

COUNTERFEITING DIETARY SUPPLEMENTS BY ADDING UNDECLARED ACTIVE PHARMACEUTICAL INGREDIENTS OR THEIR ANALOGUES TO THEIR COMPOSITION IS A NEW THREAT TO THE HEALTH OF THE POPULATION AND A CHALLENGE TO THE NATIONAL HEALTH CARE SYSTEM

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Introduction: One of the public health challenges is the counterfeition of dietary supplements by adding undeclared active pharmaceutical ingredients or their analogues into their composition in order to obtain illegal commercial advantages.
The aim: To draw attention to the problem of falsification of dietary supplements, as well as to propose chemometry methods to solve this problem.
Materials and methods: Visible and ultraviolet spectroscopy and chemometric method of reverse calibration were applied for the model mixtures with numerous DS-s to determine undeclared API-s or their analogues.
Results: It is no exaggeration to say that with the development of mankind and medicine, a tendency to prevent disease become stronger. So Benjamin Franklin wrote the famous words that became a proverb: «An apple a day keeps the doctor away.» The meaning of these words in Franklin's time was that vitamin C contained in an apple prevented one of the most terrible diseases of that time - scurvy. The role of this apple in the modern world is played by dietary supplements (DS), which contain such food ingredients (vitamins, minerals, amino acids, etc.), the lack of which in the diet leads to the occurrence of certain disease states. However, any good business can be ruined by unscrupulous people, such as the undeclared introduction of DS intended for weight loss (by creating a feeling of satiety or improving intestinal motility) of synthetic substances (once being active pharmaceutical ingredients (API)) such as sibutramine or phenolphthalein, or adding of undeclared phosphoesterase type 5 inhibitors such as sildenafil, vardanafil, etc. in dietary supplements designed to improve men potency can lead to serious health desorder and even death (we will further refer to such APIs or their analogues as counterfeiters). Reports of this kind of fraud grew up as snowball, leading to the release of a General Chaptersdietary Supplements (2251) Screening For Undeclared Drugs And Drug Analogues) In 2017.
In the general USP article, methods for undeclared ingredients detecting are divided into targeted, used when the analytes (i.e. counterfeiters) are known, and non-targeted, which are aimed to detect any undeclared ingredients. Both types of methods have their advantages and disadvantages and can complement each other harmoniously.
In our opinion, spectrophotometry in the visible and ultraviolet regions of the spectrum, along with chemometric methods, provides a good basis for developing of non-target methods for undeclared APIs detecting. Thus, the use of the chemometric method of reverse calibration made it possible to detect with a high level of reliability a large number of APIs in model mixtures with numerous DSs (and, moreover, to quantify these APIs if DSs if they were included in the calibration set).
This approach is currently being developed using the principal components method and some innovations, and we hope that in the near future it will lead to the creation of an express inexpensive method for controlling the DS market for the presence of undeclared APIs or their analogues, which will allow us to answer the challenge indicated in the title.
Conclusions: The threat of falsified dietary supplements is one of the many threats to human health that can lead to a serious deterioration of the quality of human life. Research in the field of chemometric identification methods is promising for solving both this problem and related ones, such as API standardization, and, according to the authors of this thesis, deserve the attention of the scientific community.

KEY WORDS: healthcare; chemometrics; standartization; dietary supplement.

SYSTEM-EXPERT ANALYSIS OF THE PROSPECTS FOR THE DEVELOPMENT OF PRIVATE HEALTHCARE INSTITUTIONS IN UKRAINE IN CONDITIONS OF HIGH UNCERTAINTY

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Introduction: In the current realities, due to the Russian-Ukrainian war, the issue of taking into account probable risks in strategic planning for the development of private healthcare institutions *(PHI)* has become particularly relevant. However, the war can also open up new opportunities for the development of both PHI and state-owned healthcare institutions. Therefore, having knowledge and skills to timely assess and analyze potentially attractive trends in the market for the provision of medical services to the population acquires new importance.

The aim: System-expert analysis of the opportunities, limitations, and prospects of PHI activities in conditions of high uncertainty in the medical market of Ukraine. Such an assessment contributes to the preparation of targeted recommendations for this category of medical institutions in the medical services market regarding their development strategy, funding, and effectiveness enhancement in conditions of war.

Materials and methods: For the study we used literature review, analysis of the official websites of PHI in Kyiv, survey method, expert-business communication with leading experts and PHI executives, system and SWOT analysis.

Results: The conducted complex system study allowed to determine the following risks for PHI:

- Insufficiency of medical resources due to increase of the volume of work;
- Economic crisis: increasing unemployment, migration of the population and specialists, high mortality rate of working-age population, rising prices for drugs, equipment, etc;
- Power outages, air raids, and the danger of destroying healthcare institutes due to shelling or missile and bomb strikes.

The opportunities that exist and may open up for PHI are as follows:

- Changes in the demand structure and expansion of the spectrum of medical services: increasing demand for rehabilitation and neurology, occupational therapy, and prosthetics;
- Changes in the evaluation of the Ukrainian healthcare system compared to European and US systems, with a greater willingness of the population to receive paid medical services;
- Development of telemedicine and acceleration of digitalization;
- Intensification of medical tourism after the end of the war due to the increased investment potential of Ukraine, and so on.

Conclusions: War poses a major challenge to private medicine in Ukraine; However, PHI have significant potential for development in conditions of high uncertainty due to their flexibility in responding to the challenges of the wartime medical environment. To succeed, PHI must consider the risks mentioned for the development and implementation of the strategy, and the results mentioned can help medical regulators make more balanced management decisions regarding the healthcare sector's development.

KEY WORDS: strategic planning, healthcare systems, uncertainty.

THE MORBIDITY OF MALIGNANT NEOPLASMS OF THE BODY OF WOMB IN UKRAINE DURING LOCKDOWN RESTRICTIONS

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Introduction: A number of factors influence the medical care of patients with oncologic pathology. In the last few years the COVID-19 pandemic and lockdown restrictions have limited patient access to health care institutions. As a result, planned specialized interventions have been forced to be postponed, preventive measures have been significantly reduced.
The aim: To analyze the morbidity rate of malignant neoplasms (MN) of the body of womb during lockdown restrictions.
Materials and methods: The data of the National Cancer Registry of Ukraine for the years 2015-2021, excluding temporarily occupied territories, has become the information base for statistical analysis. A statistical method has been used - the analysis of statistical series.
Results: In Ukraine, during 2015-2019, there was an increase in the prevalence of MN of the body of womb from 363.3 to 419.5 (+15.5%), morbidity from 32.9 to 35.9 (+9.1%), and a decrease in mortality from 8 .2 to 8.1 (-1.2%) per 100,000 female population. These indicators correlate with global trends. Thus, in 2019, the mortality rate from MN was somewhat higher in the countries of Eastern Europe (in Lithuania – 10.0, in Poland – 10.3 per 100,000 female population) and lower in the G7 countries (in the USA – 7.0 , in Canada – 6.9, in Great Britain – 7.4, in Germany – 6.3, in Japan – 6.1 per 100,000 female population).
During the COVID-19 pandemic in 2019-2021, in general, in Ukraine, the rate of growth of the prevalence of MN of the body of womb slowed down slightly from 419.5 to 453.9 (+8.2%), the morbidity decreased from 35.9 to 31.8 (- 11.4%) and mortality from 8.1 to 7.2 (-11.1%) per 100,000 female population. However, the part of patients with MN of the body of womb detected during preventive examinations also decreased (-19.5%), which is due to a decrease in the number of women applying for preventive examinations. At the same time, the part of patients with I-II stages according to the TNM classification decreased (-2.8%) and increased with III (+8.2%) and IV (+27.5%) stages. A similar trend can be observed in some regions of Ukraine, where the number of patients with MN of the body of womb during preventive examinations has significantly decreased.
In the future, this trend may have a negative impact on the survival rate of patients and the increase in mortality among patients with MN of the body of womb.
Conclusions: The obtained data indicate a certain trend that has formed during the COVID-19 pandemic. In the conditions of lockdown measures during the COVID-19 pandemic, there is a negative trend towards an increase in the percentage of detection of patients in III and IV stages of MN of the body of womb. One of the factors of its development is the decrease in the detection of patients with MN of the body of womb during preventive examinations.

KEY WORDS: malignant neoplasms of the body of womb, the COVID-19 pandemic, preventive examinations.

DISSECTING THE EFFECT OF SHINGLES INFECTION ON RECURRENT MISCARRIAGE IN DIVERSE EUROPEAN POPULATIONS

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Introduction: The burden of non-communicable diseases, the decline in the fertility index, and the ageing of the population pose create new challenges to preventing the threat of depopulation. Therefore, reproductive health research is one of the priority areas of modern medicine. The frequency of miscarriage in the structure of total reproductive losses is 10-25%, and the study of the causes of this pathology is important for maintaining the population's reproductive potential.

The aim: We investigated the causality between infection from the herpes zoster virus (shingles) and subsequent risk of recurrent pregnancy loss (RPL) and recurrent miscarriage (RM).

Materials and methods: We performed two-sample Mendelian randomization (MR) analysis. As instruments for shingles, we used summary statistics from 23andMe genome-wide association study (GWAS; PMID:28928442). As the outcome data, we used two RPL/RM datasets: (1)LUCAR (Lviv Ukrainian Cohort for Advancing Reproductive Health) study from the Western Ukraine, including 350 women with confirmed idiopathic RPL and 458 control women with at least one healthy child; (2)UK Biobank (UKBB) dataset, consisting of 15,338 women with RM and 136,274 control women with at least one (self-reported) healthy-born child. The LUCAR/UKBB genome-wide array datasets were QCed, imputed to TopMED/HRC reference panels density. *PRSice-2* was used for clumping of shingles GWAS summary statistics ($P\text{-}value \leq 5\times10^{-5}$). MR was done using *TwoSampleMR 0.5.2* package.

Results: The MR using only two established lead shingles SNPs as instruments (rs2523591, rs7047299) did not show causality ($P\text{-}value > 0.5$) between shingles and RPL/RM. We then expanded the sets of independent instruments to 73/183 for LUCAR/UKBB RPL/RM GWAS ($P\text{-}value \leq 5\times10^{-5}$), respectively. After performing MR analyses in each study, we meta-analysed them and detected a nominally significant (OR[95% CI]=0.998[0.996-1.0000], $P\text{-}value = 0.055$) protective causal effect of shingles on the risk of RPL/RM.

Conclusions: Our findings suggest that exposure to *herpes zoster* infections should be investigated further for its protective effect on susceptibility to idiopathic pregnancy loss.

KEY WORDS: polygenic risk scores, recurrent miscarriage, recurrent pregnancy loss, herpes zoster infection, Mendelian randomization.

RESEARCH OF THE PROFESSIONAL TRAINING OF MASTERS OF DENTISTRY DURING THE PANDEMIC AND MARTIAL STATE

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Introduction: The conditions, in which Ukraine was put after the large-scale russian invasion urged professionals to rethink, change, and reevaluate almost every aspect of the professional training of future masters of medicine, namely the format of conducting classes, the means and methods of using educational tools, assessment approach. The conducted research became the basis for substantiating the organizational model of blended technology teaching in orthodontics focused on training future dentists to work with digital equipment. Modern dentistry is one of the leading medical specialties as for the implementation of transformative innovations. Moreover, it widely involves leading scientists in the development and improvement of digital equipment and methods of its application in various dentistry areas and at various stages of medical interventions: in diagnosis, planning, treatment, prevention, processing of results, etc. It is obvious that the use of digital methods has become the paradigm of the dental industry in the 21st century.
The aim: To investigate the effectiveness of educational technologies that were used in the process of professional training of masters of dentistry in the conditions of quarantine restrictions and martial law.
Materials and methods: To accomplish the tasks set, the following theoretical and empirical methods of scientific research were used: system analysis; comparison and generalization for the theoretical substantiation of approaches to the organization of blended learning of masters of dentistry; bibliosemantic method; empirical methods (interviews with students, interns, and teachers); statistical analysis (Pearson's test).
Results: In 2019 and at the beginning of 2022, the educational process in Bogomolets NMU was implemented in three forms with using different techniques: auditorium; synchronous/hybrid (practical, laboratory, and seminar classes are held in classrooms and combined real-time with distance learning for the students who cannot attend classrooms due to their being not vaccinated); blended (auditorium-distance), which offered distance learning of individual academic groups with confirmed cases of COVID-19. Therefore, we conducted a study of the results of blended learning of dental masters at the department of orthodontics and propaedeutics of orthopedic dentistry was conducted. Three homogeneous samples of students were formed, whose education was realized differently. It is worth mentioning that a pairwise comparison of the entrance control results of student groups proved the statistical homogeneity of the samples at the beginning of the experiment. In order to test the null and alternative hypotheses was used the c^2 criterion. A comparison of the educational achievements results gives reasons for rejecting the null hypothesis H_0 and indicates the presence of statistically significant differences in the studied student groups.
Conclusions: The outbreak of the COVID-19 pandemic and the full-scale war unleashed by the russian federation in Ukraine forced to quickly find and implement mixed forms of teaching future masters of dentistry, which, in combination with digital technologies, enables implementing high-quality and effective training. The conducted analysis of students' success gave reasons for making an assumption that a didactically justified, balanced, and adapted to the requirements of the time combination of forms and methods of blended learning, classes in the digital laboratory and in the simulation, center is able to ensure the proper theoretical and practical preparation of dentistry students for mastering the professional basics of their future profession.

KEY WORDS: professional training, dental masters, blended learning, distance learning, simulation training.

TO THE HISTORY OF FORMATION OF MEDICAL POLICE AS A SCIENCE AND A SUBJECT OF TEACHING

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Introduction: The formation of Medical Police falls on the age of enlightenment, in the second half of the 18th century. The concept of Medical Police followed logically from the ideas of enlightened absolutism. Medical Police arose as an empirical science of the actions of the authorities aimed at protecting and restoring the health of their subjects. By the beginning of the 20th century, enriched by scientific methods, having undergone transformation, Medical Police became Social Hygiene, and now this science is known as Public Health.
The aim: To find out the role of Ukrainian scientists of the 18th century in spreading the concept of Medical Police.
Materials and methods: Published historical sources are materials; the method is historical.
Results: In 1764, the German physician W.T. Rau (1721-1772) introduced the term Medical Police (German: Medicinische Policey) to designate state health services. Johann Peter Frank (1745-1821) started using the phrase Medical Police. He is considered the founder of Medical Police as a science. In 1779, his German multi-volume work began to be published with the title, which has this phrase. In 1784 he became Professor at the University of Göttingen, where he began to teach several academic disciplines, including Medical Police. Just at that time, the Ukrainian Ivan Lukyanovich Danilevsky (1747-1807) was graduating from the Medical Faculty of the University of Göttingen. Danilevsky received his initial education at the Kiev-Mohyla Academy. In Göttingen, perhaps under the influence of Professor J.P. Frank he took the topic of the role of the state in the organization of the health care system for his doctoral dissertation. On September 11, 1784, he successfully defended his thesis (De magistratu, medico felicissimo) for the degree of Doctor of Medicine and Surgery. At the same time J.P. Frank placed this work of Danilevsky in «Delecta opuscula» (Bd. V. N 2. S.70-126). In accordance with the concept of Medical Police, the author argues that the authorities should take care of the health of their subjects. The administrative measures that this government takes make it possible to preserve public health more effectively than the activities of individual doctors. Therefore, the state is the best doctor. A certain contribution to the formation of the teaching of Medical Police was made by the Ukrainian Oleksandr Mikhailovich Shumlyansky (1748-1795). He received his initial education, like I. Danilevsky, at the Kiev-Mohyla Academy. He defended his doctoral thesis at the University of Strasbourg (1782). In 1787, O. Shumlyansky published a book dedicated to the improvement of teaching in higher medical school. The book proposes a coherent system of sciences, which should be the basis for teaching future doctors. He was the first in the Russian Empire to point out the need to include Medical Police among the disciplines taught. And another Ukrainian scientist pointed out the need to teach Medical Police at higher Medical school. It was Martyn Matviyovych Terekhovsky (1740-1796). Like Danilevsky and Shumlyansky, he studied at the Kiev-Mohyla Academy. He defended his doctoral thesis at the University of Strasbourg (1770). He took part in the development of the charter of the higher medical school in St. Petersburg in 1792. The charter of 1792 provided for the teaching of Medical Police as one of the academic disciplines. Then this provision was enshrined in the charter of 1806, which was written by the founder of Medical Police, I.P. Frank. (In 1805-1808, Frank lived and worked in St. Petersburg).
Conclusions: Ukrainians I.L. Danilevsky, O.M. Shumlyansky and M.M. Terekhovsky were among those scientists who contributed to the spread of the idea of the concept of Medical Police that arose in the German-speaking states. They received their initial education at home, at the Kiev-Mohyla Academy, and graduated in Western Europe, where they had the opportunity to get acquainted with the emerging new direction in medicine, i.e. Medical Police.

KEY WORDS: Medical Police (Public Health), Ukraine, 18th century.