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THE EU COHESION POLICY AND HEALTHY NATIONAL DEVELOPMENT: MANAGEMENT AND PROMOTION IN UKRAINE

Editors

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**THE EU COHESION POLICY AND
HEALTHY NATIONAL
DEVELOPMENT: MANAGEMENT AND
PROMOTION IN UKRAINE**

Monograph

Edited by Nataliia Letunovska, Liudmyla Saher, Anna Rosokhata

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The monograph focused on the specifics of the principles of the EU Cohesion Policy implementation. The authors conducted an analysis of the economic, ecological and social aspects of the integration of the EU experience into the state policy of Ukraine. The monograph summarizes approaches to the restoration of the country and healthy development. Particular attention is paid to the issues of health care system management, the trends and prospects of achieving the state of resilience of the medical and social provision system of the population in the context of the impact of COVID-19 on the national economy. The experience of using marketing and innovative technologies in the context of healthy national development is summarized.

The monograph is generally intended for government officials, entrepreneurs, researchers, graduate students, students of economic, medical, and other specialties.

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3.2. Impact of Russian full-scale invasion into Ukraine on international food security	378
3.3. Solidarity in wartime as a component of national policy	388
3.4. Assessment of the damage of the Russian-Ukrainian war	396
and the landscape of post-economic recovery	396
3.5. Provision of social protection for persons with disabilities affected by the War in Ukraine: a critical analysis	407
3.6. The role of CSR practices in forming the cohesion of territorial communities in the conditions of war: European integration aspect	417
3.6. The role of the teacher in forming a healthy lifestyle in future doctors in the conditions of war	428
References to Chapter 3	439
Chapter 4 MANAGEMENT OF THE HEALTH CARE SYSTEM IN UKRAINE AND EU COUNTRIES	454
4.1. European experience of public management of the health care system	454
4.2. The evolution of national development: from the concept of endogenous growth to a health-oriented economy in the context of the COVID-19 pandemic	464
4.3. Formation of competitiveness of medical institutions on the basis of partnership.....	473
4.4. Formation and implementation of the development strategy of Ukraine's health care institutions in the challenges and threats conditions of the XXI century: directions of increase in efficiency	487
4.5. Improvement of the quality management system of.....	512
medical services (on the example of the municipal non-profit enterprise "Consultative and diagnostic center" of Holiivskyi district of Kyiv).....	512
4.6. Chronic inflammatory processes of the maternal genitourinary system, its role in cardiovascular diseases development in their	

children: Ukrainian and European experience of prevention as the key to the health of future generations.....	521
4.7. Urogenital inflammatory diseases in women of reproductive age as a cause of an unhealthy start of children's life: Ukrainian and European research.....	528
4.8. The impact of COVID-19 on the national economy: trends and prospects for achieving the state of resilience of the medical and social welfare system of the population.....	534
4.9. Prospects for the implementation of investment projects in the field of health care in Ukraine.....	539
References to Chapter 4	562
Chapter 5 THE ROLE OF MARKETING AND TECHNOLOGY IN HEALTHY DEVELOPMENT: EUROPEAN AND UKRAINIAN EXPERIENCE	580
5.1. Formation of Ukraine's brand in the context of integration into the EU: current realities.....	580
5.2. The key role of future marketing professionals in environmental safety ensuring at the European region.....	592
5.3. Opportunities for applying neuromarketing research and artificial intelligence tools to promote a healthy lifestyle in Ukraine.....	609
5.4. The impact of artificial intelligence tools in the management of human resource behaviour on the outcome of decision-making by economic agents in the digital space.....	617
5.5. Ukrainian electronic commerce: current trends and development prospects in the conditions of Ukraine's integration into the EU digital single market.....	624
References to Chapter 5	635
Conclusions	644

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in which case the quality of care will be unacceptable (Levytska, 2012). Continuous development of medical staff is maintaining or increasing the level of professionalism and developing individual medical practice to meet the needs of patients and optimize the functioning of the healthcare sector.

Expanding laboratory diagnostic services can improve consultation and treatment for patients and accessibility to the public. Simplification of certain stages of the service delivery process allows patients to choose the time of their visit to the doctor and make an appointment either in the helpline electronic system or through the reception. And a separate time has been set aside for urgent patients. Improving the diagnostic base allows for better patient diagnosis and the introduction of new diagnostic methods and timely treatment, meaning that patients receive medical care in a short time and, if necessary, are referred to specialized institutions for consultation. Improvement of the latest methods and their practical application in practice is the key to the effective functioning of healthcare facilities, achievement of general medical goals and provision of timely care to sick people. The study has shown that the innovation process requires the use of a process-oriented approach in the management of healthcare organizations, which will not only help to overcome urgent problems but also open up new prospects for development.

Thus, summarizing the above, by implementing the advanced achievements of medical science in their practice, doctors create conditions for improving the quality of life of patients. By modernizing equipment, introducing modern methods of diagnosis, treatment and prevention of diseases, and continuously improving capabilities. The MCC of Holosiivskyi district of Kyiv will be able to achieve the highest results by constantly improving its quality to facilitate the provision of qualified, high-quality and comfortable medical services.

4.6. Chronic inflammatory processes of the maternal genitourinary system, its role in cardiovascular diseases development in their children: Ukrainian and European experience of prevention as the key to the health of future generations

Cardiovascular diseases (CVDs) remain the leading cause of morbidity in the world. The burden of CVDs continues to increase over the past decade in almost all countries of the world. The prevalence of CVDs in the world has almost doubled from 271 million in 1990 to 523 million in 2019. The number of deaths from CVDs over the same period has

increased by twofold from 12.1 million to 18.6 million. The indicators of years of life with disability and lost years also doubled in total from 17.7 million in 1990 to 34.4 million in 2019 (Roth et al., 2020).

In Ukraine, CVDs take the lead among the causes of population mortality. According to the Global Burden of Disease (GBD) Study, 449,376 people died from CVDs in 2019, accounting for 64.33% of the total number of deaths, while in 1990 this figure was 350,605 (56.55%). The prevalence of CVDs increased from 9,701.67 cases per 100,000 population in 1990 to 12,679.43 in 2019, and the incidence rate rose from 1,420.96 to 1,918.33 over the same period (Global Burden of Disease Study, 2019). The increase in morbidity, prevalence, and mortality from CVDs in Ukraine is not as dramatic as compared to the global dynamics, but it is still continuous, and CVDs continue to be the leading cause of death in Ukraine.

The economic losses from CVDs in the United States of America alone, according to the Centers for Disease Control and Prevention, amount to 219 billion dollars annually (Centers for Disease Control and Prevention, 2021). American Heart Association data increase this figure to approximately 351.3 billion dollars due to the inclusion of indirect costs associated with premature cardiovascular mortality (Virani et al., 2020).

Data from Ukrainian and European statistics testify to the need for timely active measures aimed at preventing the development of CVDs. Modern strategies for the prevention of CVDs are primarily aimed at correcting the known risk factors: quitting smoking, regular physical exercise, normalizing body mass index, "ideal lipids", "ideal glucose", normalizing blood pressure, etc. (Reamy et al., 2018). What is not taken into account in this strategy? The very first periods of a human life, which significantly "program" health, duration and quality of life, remain beyond attention.

David Barker was the first to recognize the extraordinary importance of the intrauterine period in the pathogenesis of future CVDs, who put forward the world-famous theory of "intrauterine programming". The key postulate of this theory is the appearance of irreversible metabolic, physiological and structural changes in the organism as a result of the action of several negative factors during the intrauterine and perinatal periods of development (Barker & Fall, 1993). Today, the theory of "intrauterine programming" is perceived by medical and social professionals as the key to the health of future generations (Nazarenko & Nestertsova, 2020).

The cardiovascular system begins to form at 2-3 week of pregnancy in the mesodermal layer of the trophoblast. The main development of the heart occurs approximately from the 21st to the 42nd day of intrauterine life. By the end of the 4th week in the cardiac tube already distinguish 3 parts that are separated by shallow furrows and dilations of the lumen. From the end of the 5th week, the primary system of embryonic circulation begins to function. By 8-10 weeks, the formation of all parts of the heart is completed, which coincides with the development of the placenta and the emergence of placental circulation, which determines gas exchange and all nutritive support of the embryo developing. Full separation of the flows of right and left heart blood is only completed in the postnatal period (Frolova et al., 2020). Thus, the development of the child as a whole and the cardiovascular system in particular is a complex multifactorial process, which can affect a number of factors that can lead to both congenital defects in the development of the child and lay the foundation for the development of CVDs in the future ontogenesis. There are many of these factors. Among the main ones are medicines and various chemical compounds, ionizing radiation, bad habits, genital and extragenital pathology, etc. (Kaleelullah & Garugula, 2021).

In the structure of genital and extragenital pathology of women of reproductive age, significant parts are inflammatory diseases of the genitourinary system, which are characterized by predominantly chronic course. Simultaneous development of inflammatory diseases of the urinary and reproductive systems is explained by the facts that these systems' organs develop from one primary germ layer (mesoderm), they have a close anatomical-physiological connection, a common blood supply and lymphatic system, and are also target organs of sex hormones activity (Rudenko et al., 2018).

The analysis of statistics in Ukraine from 2000 to 2017 revealed that the prevalence and incidence of salpingitis and oophoritis had a tendency to decrease, and in 2017 it was 15.8 and 8.6 per 1000 women of working age, respectively, compared to 19.67 and 11.42 in 2000. During the period under consideration, an increase in the prevalence and incidence of inflammatory diseases of the uterus from 6.85 and 5.03 in 2000 to 12.5 and 8.6 in 2017 per 1000 women of the corresponding cohort (an increase of 82.5% and 70.9%, respectively) was revealed (Zhilka et al., 2018; Antypkin et al., 2020).

Approximately one third of women under the age of 24 and half of women under 35 suffer from chronic inflammatory diseases of the

genitourinary system. Up to 70% of women suffer from this pathology throughout their lives, of which 30% have recurrent course (Abou Heidar et al., 2019).

Chronic inflammatory diseases of the genitourinary system in mothers may be one of the risk factors for the development of fetal intrauterine growth restriction (IUGR) syndrome, which, according to current European recommendations, is characterized by a decrease in anthropometric indicators of the fetus below the 10th percentile (Kehl et al., 2017; Mericq et al., 2017). In Ukraine, the frequency of IUGR syndrome ranges from 12% to 36%, and the number of newborns with IUGR is 67.4 per 1000 live births and 179.5 per 1000 preterm births (Hromova & Berezna, 2018). Our studies on autopsy material revealed changes in the morphological and functional state of the fetal and newborn hearts with IUGR, which increased in newborns compared to fetuses and were more significant in the asymmetric variant of IUGR compared to the symmetric one. Catamnestic studies show a partial development of arterial hypertension, coronary heart disease in people with prenatally IUGR (Yakovtsova et al., 2015).

Chronic inflammatory diseases of the genitourinary system in women can lead to the development of placentitis, which in turn can lead to premature rupture of the fetal membranes and preterm birth (Redelinguys et al., 2020; Romero et al., 2016). The frequency of premature birth varies depending on clinical and sociodemographic factors. Thus, in the USA 1 out of 10 newborns are born prematurely (Tesfalul et al., 2021), in Europe the frequency ranges from 5% to 10% (Delnord et al., 2015), in Ukraine it is also at the level of approximately 10% and has a tendency to increase (Ibadova et al., 2022). Preterm birth in women with chronic inflammatory diseases of the genitourinary system can lead to developmental disorders in the fetus and newborn in subsequent ontogenesis of key organs and systems, including the cardiovascular system (Nobile et al., 2022).

Preterm birth is a risk factor for the development of arterial hypertension in people at different stages of ontogenesis. Thus, in adults born at 32 weeks of gestation, higher systolic, mean and diastolic blood pressures, as well as pulse pressure, were determined compared to adults born at 37-40 weeks of gestation (Tauzin et al. 2014). It's important to keep in mind that even minor fluctuations in blood pressure can have a significant impact on the risk of cardiovascular disease. Research has shown that a relatively small decrease of 4.7 mmHg in average blood

pressure can lead to a 32% lower risk of stroke and a 20% lower risk of ischemic heart disease (Cook et al., 1995).

Babies born prematurely are at a greater risk of developing heart failure later in life. The incidence of heart failure in individuals born extremely prematurely (less than 28 weeks' gestation) was 17.0 times higher compared to those born at term (37 weeks or more), after taking into account other factors. Similarly, those born very prematurely (28 to 31 weeks' gestation) had an incidence of heart failure 3.58 times higher compared to term births (Carr et al. 2017).

Another study used echocardiography to compare the cardiac function of healthy preterm infants born at less than 30 weeks of gestational age with that of term-born infants. The infants were all examined 28 days after birth, and a subset of preterm infants were examined at a term-equivalent age. The study found that preterm infants had left ventricular dysfunction during both systole and diastole, but there were no differences in fractional shortening, ejection fraction, or strain rates compared to term infants. However, at term-equivalent age, the preterm infants showed normal systolic left ventricular function but abnormal left ventricular diastolic function (Hirose et al., 2015).

Two clinical studies compared cardiac growth and function between young adults born preterm and term using magnetic resonance imaging (MRI). One study (Lewandowski et al., 2013a, January) found that the left ventricular mass of individuals born preterm was higher than that of term-born individuals (66.5 ± 10.9 versus 55.4 ± 11.4 g/m²; $P < 0.001$), and the degree of prematurity was positively associated with the mass ($r = -0.22$, $P = 0.03$). Preterm-born individuals had a short left ventricle with a small internal diameter and a displaced apex. Although the ejection fraction was preserved ($P > 0.99$), both systolic (peak strain, strain rate, and velocity, $P < 0.001$) and diastolic (peak strain rate and velocity, $P < 0.001$) longitudinal function and rotational movement (apical and basal peak systolic rotation rate, $P = 0.05$ and $P = 0.006$; net twist angle, $P = 0.02$) were significantly decreased. Offspring of mothers who were diagnosed with preeclampsia during pregnancy had further reductions in longitudinal peak systolic strain ($P = 0.02$, $n = 29$). Second study (Lewandowski et al., 2013b, August) found that preterm birth was associated with a small right ventricle (end diastolic volume, 79.8 ± 13.2 versus 88.5 ± 11.8 mL/m²; $P < 0.001$), but a greater right ventricular mass (24.5 ± 3.5 versus 20.4 ± 3.4 g/m²; $P < 0.001$) compared to term-born controls. The severity of differences was proportional to gestational age. Young adults born preterm had significantly lower right

ventricular ejection fraction, with 21% having values below the lower limit observed in term-born adults and 6% exhibiting mild systolic dysfunction. The changes are greater in the right ventricle than previously observed in the left ventricle, with potentially clinically significant impairment in right ventricular systolic function.

Asymptomatic course of the inflammatory process of the reproductive system caused by chlamydia in women may be a teratogenic factor causing the development of congenital heart defects in their children (Appiah et al., 2023). Maternal hyperthermia caused by the presence of chronic inflammatory diseases of the genitourinary system during pregnancy leads to the development of cardiovascular malformations in the offspring (Tikkanen & Heinonen, 1991).

Maternal genitourinary system infection during pregnancy is known to alter the development and function of offspring's immune system, leading to inappropriate immune responses to common childhood infections and immunizations (Gibbs & Fairfax, 2022).

Fetal stressor such as maternal chronic inflammatory diseases of the genitourinary system may directly or indirectly impact cardiovascular programming, by inducing a sustained inflammation and activation of hypothalamic-pituitary-adrenal axis, alterations to cellular and molecular levels of cardiovascular system, with the result of programming the endothelium and the susceptibility to onset of diverse pathologies, such as atherosclerosis (Balistreri, 2020).

Through experimental studies on nonhuman primates, it has been determined that multiple sets of genes, biological pathways, and transcription factors associated with morphogenesis and vasculogenesis are disrupted in the context of intrauterine infection and inflammation. This occurs as a result of inflammatory cytokines produced by the placenta in response to bacteria and/or components of the bacterial wall. These cytokines diffuse into the amniotic fluid and fetal blood, leading to a placental and fetal inflammatory response (Mitchell et al., 2018).

In another experimental study on the effects of intrauterine inflammation on sheep hearts, by introducing lipopolysaccharide (a component of the bacterial wall) intra-amniotic, it was found that intrauterine inflammation alters heart growth, suppresses contractile function, and increases stress response. The hearts of fetuses exposed to lipopolysaccharide (LPS) showed a 40% reduction in contractility in both the left and right ventricles and a 25% decrease in the number of cardiomyocytes. Immature mono-nucleated cardiomyocytes had smaller

volumes (about 18%), while mature bi-nucleated cardiomyocytes had volumes about 77% larger. Although the basal coronary flow was increased by $21\pm 7\%$ in LPS-exposed hearts, there was a significant increase in end-diastolic pressure (2.4 ± 0.3 -fold) and infarct area (3.2 ± 0.6 -fold) following experimental ischemia/reperfusion (IR) compared to the control group (Tare et al., 2014).

The analysis of the research results of Ukrainian and European scientists has shown that chronic inflammatory processes of the genitourinary system of the mother are a significant damaging factor that can change the morphological and functional state of the fetal and newborn cardiovascular system and cause the development of CVDs at various stages of ontogenesis.

Considering the prevalence of chronic inflammatory processes of the genitourinary system in women of reproductive age, the significance of the mentioned pathology of the mother in the development of CVDs in their children, the current issue is a change in the classical approaches to the prevention of CVDs. In the concept of CVDs prevention throughout life, emphasis should be made on preconceptional and prenatal stages, i.e. from the moment parents make a decision to have children. It is also necessary to start with the prevention of infectious and inflammatory diseases in future mothers. This will fully correspond to the principles of the World Health Organization "Action Plan for Sexual and Reproductive Health: towards achieving the 2030 Agenda for Sustainable Development in Europe" – leaving no one behind, such as the realization of the potential of sexual and reproductive health, minimizing maternal and perinatal mortality and morbidity that can be avoided, integration of sexual and reproductive health into national health strategies and programs (World Health Organization, 2016).

Educational initiatives are needed to increase women's awareness about their own reproductive health and potential risk factors for mother and child. On the part of the health system, measures should be taken to diagnose and treat infectious and inflammatory diseases of the genitourinary system in a timely manner.

Thus, chronic inflammatory processes of the mother's genitourinary system are one of the factors that can cause the development of CVDs in children at different stages of ontogenesis. The classic concept of CVDs prevention should be supplemented taking into account the "programming" effect of harmful factors that act on the preconception and prenatal stages and reliably increase the risk of CDVs development. Among the

reproductive age, it is extremely necessary to carry out measures aimed at prevention, timely diagnostics and treatment of infectious and inflammatory diseases of the genitourinary system. Ensuring reproductive health at the proper level is one of the priorities and values of European civilization, so the promotion of a healthy approach to life is one of the ways of European integration of Ukraine.

4.7. Urogenital inflammatory diseases in women of reproductive age as a cause of an unhealthy start of children's life: Ukrainian and European research

Maternal and child health is the most important medical and social problem in the world. Modern scientific research of the world's leading specialists has shown (Sekikubo et al., 2020; Sureshababu et al., 2021) that fetus and newborn adaptive reserves depend to a greater extent on case of maternal diseases during pregnancy, especially infectious diseases, which can definitely lead to pathology of various organs and systems in fetus, defects in immune response, metabolic problems and affect life expectancy. Recently interest to the problems of perinatal nephropathy has increased, as many kidney diseases in elder children have their origins in the antenatal and intranatal periods. No pathological condition in pregnant woman affecting the fetus leaves the kidneys intact (Gomi et al., 2015; Kazemier et al., 2016).

Epidemiological studies demonstrate that in the first year of life, nephropathology is more often diagnosed in boys, and from the second year of life and throughout childhood, girls suffer from this pathology more often (Budnik, 2019).

The non-specificity of clinical symptoms of perinatal nephropathies, the hidden onset and torpid course of pathological process, the low informativeness, technical complexity, invasiveness of many existing methods in studying newborn's kidney functions complicate in-time diagnosis of perinatal renal pathology and contribute to chronic pathology, development of chronic kidney disease and formation of chronic renal deficiencies just in childhood (Govindarajan et al., 2022; Henderson et al., 2023).

The increase in the incidence of newborn's kidney pathology is associated with an increase in the frequency of chronic urogenital

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