**Project topic name:** Development and introduction of the national register of patients with familial hypercholesterolemia in Kazakhstan.

**Relevance:** Familial hypercholesterolemia (FH) is a common genetic disorder affecting low-density lipoprotein cholesterol (LDL-C) metabolism, resulting in decreased catabolism of LDL particles and a marked increase in circulating LDL.1–3 Untreated, lifelong exposure to elevated LDL cholesterol leads to the development of atherosclerotic lesions early in life and a significantly increased risk of premature cardiovascular disease compared with the general population.1

Life expectancy of untreated patients with familial hypercholesterolemia is 20-30 years shorter compared to life expectancy in the general population.2 Today in the Republic of Kazakhstan there is no protocol for the diagnosis and treatment of FH diagnosis, patients are not under regular medical supervision and do not receive the necessary amount of medical care. The creation of a national register will make it possible to determine the amount of healthcare resources needed to provide adequate medical care to patients with FH.

On the contrary, early detection and effective treatment of FH can lead to significant improvements in clinical outcomes. Despite these compelling data, FH remains largely undiagnosed: less than 5% of people with FH are identified in most regions of the world. Its burden is exacerbated by the observation that FH is under-treated even among patients who are diagnosed. Moreover, more evidence-based recommendations for identifying and treating patients with FH are needed to reduce cardiovascular risk: while the grade of recommendations for FH in lipid guidelines is high, the level of evidence still often falls to C.4

Familial hypercholesterolemia is an inherited condition most commonly caused by heterozygous and homozygous mutations in the LDLR, APOB, and PCSK9 genes (autosomal dominant forms) and, much less frequently, by homozygous mutations in the LDLRAP1, ABCG5, ABCG8, and CYP7A1 genes (autosomal recessive forms). Autosomal dominant forms are commonly divided into heterozygous familial hypercholesterolemia, which is the most common type, and homozygous familial hypercholesterolemia, characterized by very severe hypercholesterolemia and low prevalence in the population (1 per 300 thousand to 1 million people).5

Globally, the average prevalence of FH in the general population is 0.32% (0.26 to 0.39). According to a population-based study by Berkinbaev S.F., Davletov K.K., et al, 0.92% of the population aged 18 to 69 years living in Almaty had a lipid spectrum health score reflecting a potential diagnosis of familial hypercholesterolemia. It has been estimated that more than 11,000 people in Almaty live with this diagnosis.6

The prevalence of FH varies from country to country because of local variations, the use of different diagnostic criteria, and screening strategies. However, little is known about the differences in the prevalence of FH according to ethnicity. Therefore, there is a need to investigate the ethnic distribution of FH in different populations in Kazakhstan and assess the prevalence of FH depending on ethnicity.

**The purpose of the project** is to develop and introduce the national register of patients with the diagnosis of familial hypercholesterolemia (FH) for the following monitoring, adequate treatment and prevention of cardiovascular complications (infarcts and strokes) and to establish the nature of the relationship between FH by age, sex, to identify genetic associations and their prevalence in the studied sample, with further extrapolation of the results to the national scale and implementation in the practical healthcare.

**Project objectives**

1. To analyze prevalence of FH (primary and general, point and period prevalence) and the frequency of macrovascular complications based on the data of opportunistic screening at the level of PHC organizations for the period 2022-2023.

2. To analyze medical, social, clinical and laboratory characteristics of patients with FH.

3. To develop and implement a registry for the management of patients with FH based on best practices.

4. Train GPs in the diagnosis and management of patients with FH. Create a FH school to organize clinical and laboratory self-management in patients with a probable diagnosis of FH.

5. To study the frequency of polymorphisms associated with FH in the candidate genes LDLR, APOB, PCSK9 (autosomal dominant forms) among a random sample of 960 patients with FH and 960 individuals without a diagnosis of FH as a control group.

6. Develop guidelines for monitoring patients with FH to prevent cardiovascular complications (heart attacks and strokes).

**Expected results of the study:**

1. It is planned to publish 3 articles in peer-reviewed scientific journals indexed by international databases Web of Science, included either in Q1-3 and (or) having Cite Score percentile in Scopus database not less than 35 in the scientific field; 1 article in Kazakhstani journals (CQAFSHE MSHE of RK);
2. It is planned to publish the monograph "Development of the register of patients with familial hypercholesterolemia" in 2025.
3. The results of the project will be presented at international and national conferences, reported at meetings and panels of government agencies, and master classes for potential consumers.

Composition of the research group for scientific research:

1) Davletov K.K., Vice-Rector for Science of KazNMU named after. S.D. Asfendiyarova, project manager;

2) Glushkova N., associate. Professor of the Department of Epidemiology, Biostatistics and Evidence-Based Medicine, KazNU named after. Al-Farabi, chief scientist of the project.

3) Saliev T.M., head of the Research Institute of Physics and Mathematics named after. B.A. Atchabarova, leading researcher;

4) Kachieva Z.S., head of the Scientific Literature Center for Shared Use, KazNMU named after. S.D. Asfendiyarova, senior researcher;

5) Kulimbet M., researcher at the Research Institute of Physics and Mathematics named after. B. Atchabarova, KazNMU named after. Asfendiyarova, project manager, researcher;

6) Fakhradiev I.R., head of LEM, KazNMU named after. S.D. Asfendiyarova, project researcher;

9) Tazhieva A.E., head of the department for management of scientific projects and programs, senior researcher;

8) Baibolsynova I.Zh., chief specialist of the department for management of scientific projects and programs, junior researcher;

9) Ongalova R.A., specialist in the department for management of scientific projects and programs, junior researcher, project;

10) Turarova D.B., junior researcher at the SL Center for Collective Use, KazNMU named after. S.D. Asfendiyarova;

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14) Baydildinova G., project researcher.