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ESSE-RF study: epidemiology and public health promotion

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The largest population-based study in Russian modern history the Epidemiology of Cardiovascular Diseases and their Risk Factors in Regions of Russian Federation (ESSE-RF) for 8 years has become a platform for public health research and projects, relevant for the whole country. Results of the ESSE-RF study were used to identify Demography National Project parameters, to model mortality and morbidity risk at the population level, to estimate the economic burden of risk factors, to predict the economic effect of population prevention measures, to assess the feasibility of using novel biomarkers for risk stratification, as well as for external evaluation of health care system. Further, results can be used to develop a novel cardiovascular risk score, to analyze COVID-19-related risk factors, and to study health protection environment. Epidemiological studies ESSE-RF1 and ESSE-RF2 have already become a significant component of public health system in Russia, and taking into account the scope of the ESSE-RF3 study (30 regions), the role of epidemiology will increase.

Keywords: epidemiology, public health promotion, public health programs, population-based prevention.

Relationships and Activities: none.

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Epidemiological studies are an important and integral part of the public health promotion system. Data on the prevalence of risk factors (RFs), their contribution to development of diseases and death are necessary for the effective implementation of life cycle of any health promotion project [1], since they allow to quantify the severity of problem initially and over time using implemented measures (Figure 1).

Analysis of the current prevalence of RFs is the first step in planning health promotion measures. Identification of goals with subsequent resource assessment and analysis of data on RF contribution to morbidity and mortality allow for prioritization in conjunction with data on economic costs, which will be described below. Epidemiological data are used for developing a detailed plan of measures and actions. Epidemiological data are very important at the stage of monitoring the results of the implementation of measures and programs. They allow to assess RF changes over time against the background of implementing related measures (for example, legislative measures aimed at reducing smoking, or communication campaigns aimed at promoting healthy eating). Continuous epidemiological monitoring allows tracking medium- and long-term effects, including obtained by modeling morbidity and mortality over time on the basis of RF changes.

In 2012, the largest study in the modern Russian history the Epidemiology of Cardiovascular Diseases and their Risk Factors in Regions of Russian Federation (ESSE-RF) was started [2]. In the following 12 Russian constituent entities with different geographic location, demographic, climatic and ecological characteristics, representative samples of the population were formed and examined: Vladivostok (Far Eastern Federal District), Vologda (Northwestern Federal District), Voronezh (Central Federal District), Ivanovo (Central Federal District), Krasnoyarsk (Siberian Federal District), Orenburg (Volga Federal District), Samara (Volga Federal District), Volgograd (Southern Federal District), St. Petersburg (Northwestern Federal District), Republic of North Ossetia-Alania (North Caucasian Federal district), Tomsk (Siberian Federal District), Tyumen (Ural Federal District). Every two years, prospective observation is carried out with the analysis of following fatal and non-fatal cardiovascular events — myocardial infarction (MI), stroke, revascularization. The study included persons aged 25-64 years. The results of a cross-sectional study have been published in numerous publications [3, 4], which are widely cited. The ESSE-RF study results became the basis for public health promotion studies, the results of which are widely used today. The results of both cross-sectional and prospective stages of the ESSE-RF were used to create indicators of state programs, model the population-based risk of diseases, assess the economic damage of RFs, predict the economic effect of prevention measures, assess the feasibility of supplementing risk

scales with novel biomarkers, as well as for external assessment of health care system (Figure 2).

In 2017, the ESSE-RF2 study was implemented in 4 Russian regions, and currently data is being collected as part of the ESSE-RF3 study.

The aim was to describe the main directions of using the ESSE-RF study results for public health promotion now and in the future.

Epidemiological data for determining effectiveness of government programs

In 2019, the National Project "Demography" [5] was launched in Russia, the main aim of which is to improve the Russian demographic situation by reducing the death rate of population and increasing the birth rate by 2024. To reduce mortality at the population level, it is necessary to reduce the weight of RFs. Therefore, within the national project, some health promotion Federal projects are being implemented. In order to assess behavioral RFs over time, as an indicator of the effectiveness of National Project "Demography", the indicator "Share of people leading a healthy lifestyle" was defined. In 2018, there was no data that would make it possible to determine the baseline value of this indicator on a national scale. Therefore, the values of this parameter are not indicated in the project passport. Experts from the National Medical Research Center for Therapy and Preventive Medicine used data from the ESSE-RF study to develop this indicator and demonstrate its significance for the health of Russian population [6]. The indicator was developed based on ESSE-RF study results and includes the following components:

— no smoking;

— daily consumption of vegetables and fruits at least 400 g;

— adequate physical activity (at least 150 minutes of moderate or 75 minutes of intense physical activity per week);

— normal (no more than 5 g per day) salt intake;

— alcohol consumption no more than 168 g and 84 g of pure ethanol per week for men and women, respectively.

According to ESSE-RF, in 2012-2013 in 12 regions this parameter of complete adherence to a healthy lifestyle was 16,7%, while in women it was 2 times higher than in men — 20,6 and 10,7%, respectively ($p<0,001$). To study the significance of developed indicator, we analyzed its association with all-cause and cardiovascular mortality, as well as with fatal and non-fatal cardiovascular events [6]. In individuals adhering to a healthy lifestyle, all-cause mortality was 39% lower ($p=0,0003$) compared with non-adherent ones, which

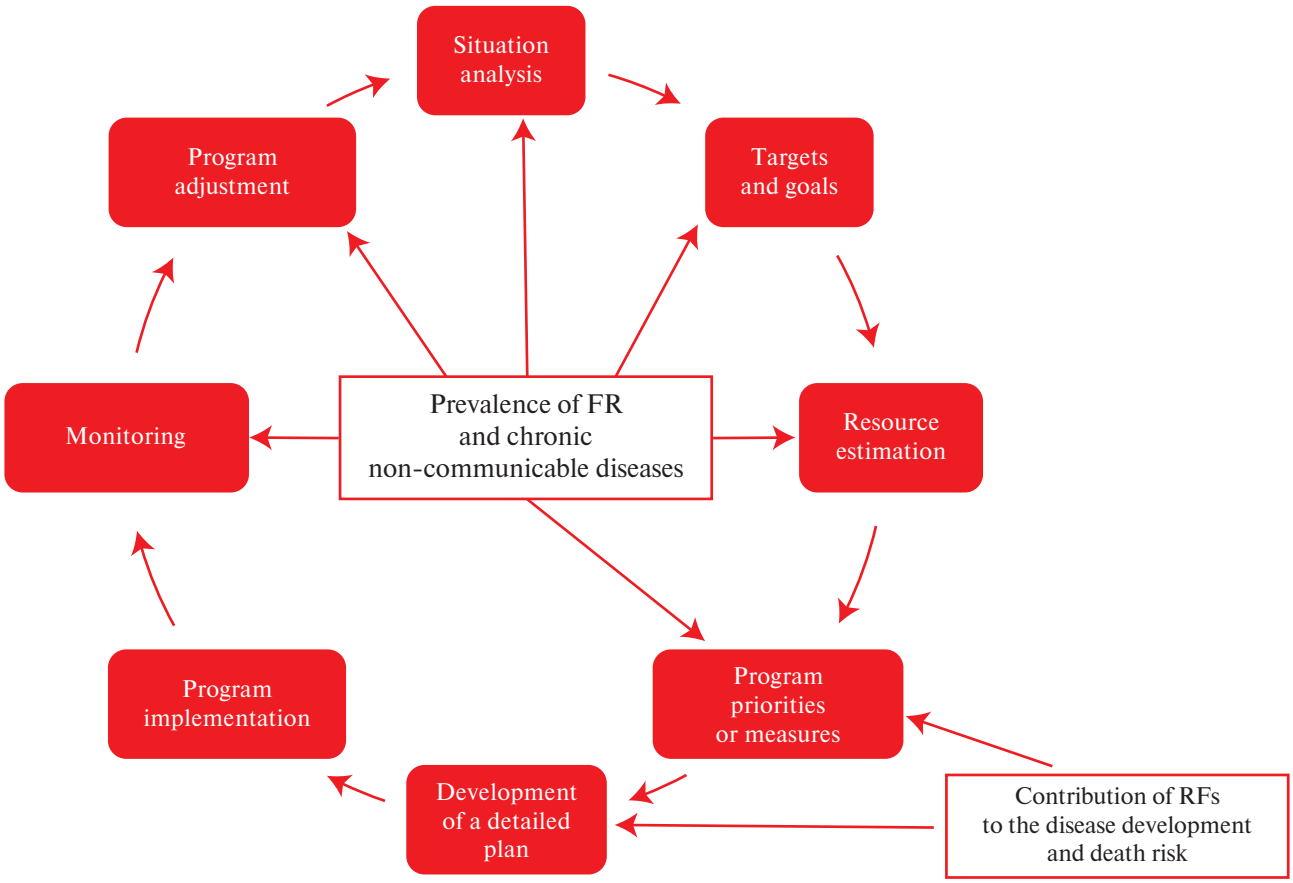

Figure 1 The role of epidemiological data on RF prevalence and contribution to the prognosis of morbidity and mortality in the development of public health promotion programs and measures.

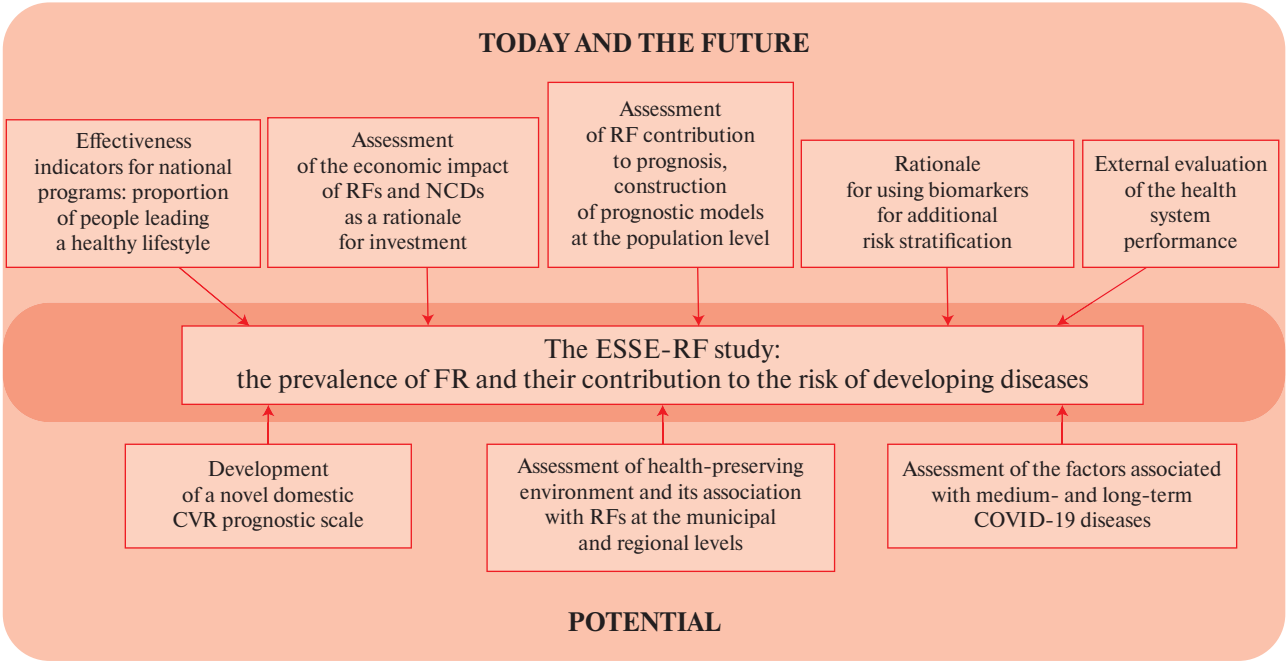

Figure 2 The ESSE-RF study: directions of results use for public health today and the future potential.

confirms the significance of developed indicator for prognosis.

The methods for calculating the proportion of people leading a healthy lifestyle, developed by experts from the National Medical Research Center for Therapy and Preventive Medicine, was approved by Federal State Statistics Service (Rosstat) order in March 2019 [7] and in the same year the first Rosstat study was conducted including 60 thousand people and an assessment of this parameter throughout the country and in certain regions [8]. The proportion of people leading a healthy lifestyle in 2019 across the country was 12%, while significant regional variability was established. In federal districts, its highest value was found in the Southern Federal District (17,2%), while the lowest — in the Far Eastern Federal District (6,5%) (Figure 3). The first assessment of this indicator throughout the country was widely covered in the media not related to medicine: publications were in RBC [9], Kommersant [10], RIA Novosti [11], etc.

In 2020, despite the Coronavirus disease 2019 (COVID-19) pandemic, Rosstat re-conducted a study to assess the proportion of people leading a healthy lifestyle. The expected negative changes of this indicator was revealed due to pandemic-related restrictions: the indicator decreased from 12 to 9,1% in the country as a whole, while in some federal districts the decrease was significant (Southern Federal District — from 17,2 to 12,1%, Volga Federal District — from 14,9 to 9,5%, the Central Federal District — from 11,1 to 7,6%). However, in some regions, there were practically no changes (North Caucasian Federal District, Northwestern Federal District). Thus, the data on proportion of people leading a healthy lifestyle allows to assess the impact of COVID-19 pandemic on the lifestyle of Russian population. These data will be important in the development of public health promotion measures aimed at leveling the negative effects of pandemic. No other country in the world has such data for 2019 and 2020 across the country and individual regions.

Epidemiological data for calculating economic damage and economic effect

Demonstration of economic parameters, including the assessment of loss from diseases and RFs, is important to justify the feasibility of investing in human health.

To assess the economic impact of RFs in Russia, data from the ESSE-RF study on RF prevalence and the results of foreign meta-analyzes on the contribution of RF to morbidity and mortality from non-communicable diseases (NCDs) was used [12]. At first, the contribution of various RFs to morbidity and mortality in the Russian population was shown. For example, mortality from CVDs is mostly due to hypertension (HTN) (35%), obesity (23%) and smoking (13%), while mortality from colorectal cancer is mostly due to insufficient consumption of vegetables and fruits (22%) and obesity (21%). The greatest economic loss was associated with the HTN (RUB 869,9 bn) — 1,01% of the gross domestic product (GDP). The next largest contribution to the economic damage from NCDs was the damage from obesity — RUB 605,8 bn (0,7% of GDP), smoking — RUB 421,4 bn (0,49% of GDP) and low physical activity — RUB 273,0 bn (0,32% of GDP). The contribution of malnutrition, which is represented by insufficient

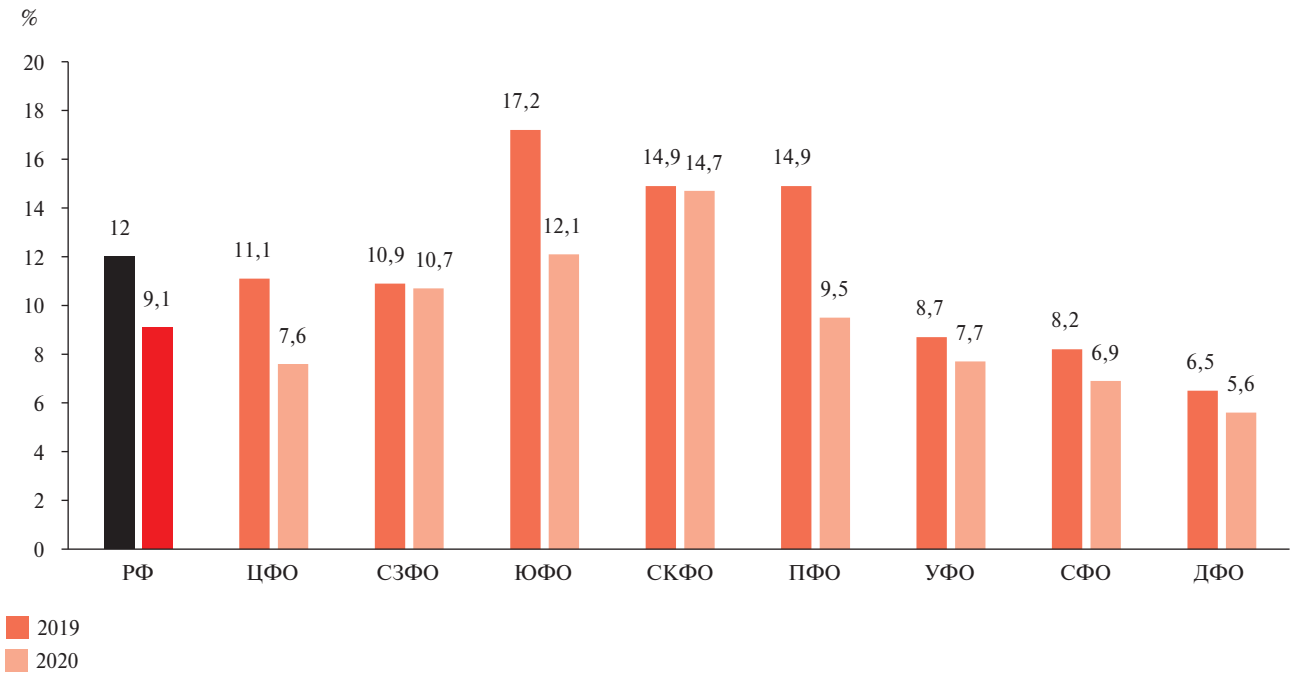

Figure 3 Proportion of people leading a healthy lifestyle according to the Rosstat research in 2019 and 2020.

consumption of fresh vegetables and fruits, excess consumption of salt and processed red meat, amounted to 0,46% of GDP. The obtained results of the study make it possible to provide an economic justification for introducing measures of population prevention aimed at reducing the NCD RFs, and, therefore, to highlight the priorities of public health programs and prevent diseases in Russian population.

Obviously, accumulation of data from the ESSE-RF study will make it be possible to estimate the relative risks based on domestic data, which will make it possible to correct the calculations and make them more accurate.

Epidemiological data for predicting risk and assessing the contribution of RFs to morbidity and mortality

In addition to individual risk assessment, it is important to develop population-based models for assessing the risk of NCDs (country, region, etc.). Such models represent a simulation of the risk of developing major events (fatal and non-fatal) over a certain period of time based on a set of data characterizing a certain population [13]. To create such a model, data are needed on the prevalence of RFs for chronic diseases included in the analysis, their impact on the prognosis (results of epidemiological studies), official statistics (morbidity, mortality, socio-demographic pattern), the actual practice of treating patients with certain diseases and outcomes (registry data), as well as a block of economic parameters. The modeling results are important for making decisions for public health promotion, including justification of investment priorities, forecasting the costs of health care system associated with an increase in life expectancy and, accordingly, an increase in the burden of NCDs, etc.

In Russia, there have been some attempts at population modeling. For example, the Archimedes model was used to assess the potential outcomes of measures aimed at improving adherence to treatment and monitoring of HTN in the population [14]. An attempt was made to construct a Markov model for predicting cardiovascular outcomes at the population level. HTN, smoking and hypercholesterolemia were included as RFs, while the following condition were considered outcomes: coronary artery disease, MI, unstable angina, heart failure (HF), HF after myocardial infarction, transient ischemic attack, stroke, atrial fibrillation [15]. Despite the fact that the model was mathematically fully constructed, there was a large deficit of domestic data necessary for creating such a population model. For example, there was no data on the likelihood of developing RF in those who do not have them. At this time, the prospective data of the ESSE-RF study were limited (2-year follow-up) and therefore there was little data on the relative risk of developing diseases and complications, which were replaced by data from foreign analyzes, which significantly limited the model applicability.

The next attempt at population prediction was a departure from the conventional mathematical model and the use of an ontological approach to model the effect of population prevention measures aimed at changing RFs [16]. At the same time, population prevention is considered as a complex system consisting of components that interact with each other. When

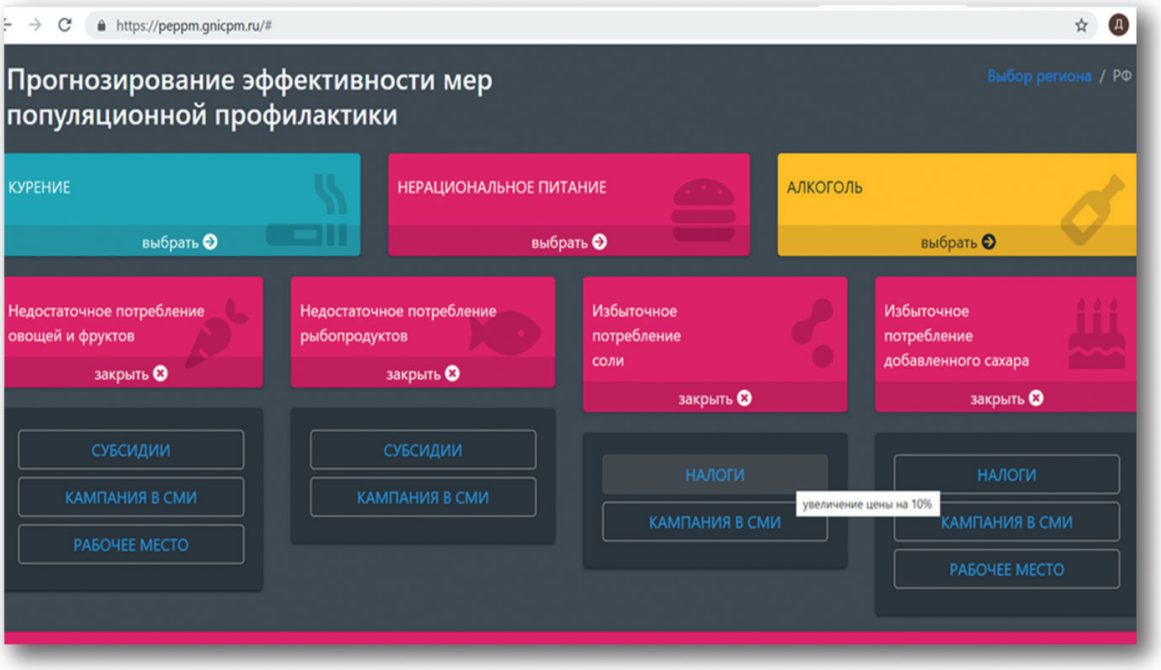

Figure 4 Tool for predicting the economic effect of population prevention measures.

constructing the ontological model, ESSE-RF data on the prevalence of RFs was also used. This model was used to predict the effectiveness of measures aimed at reducing salt consumption in the Russian population [17]. The effectiveness of the introduction of an excise tax on sodium used for the production of food at the industrial level (scenario 1) and an educational media campaign aimed at increasing the population literacy on salt consumption (scenario 2) were studied. It is shown that over 15 years due to the prevention of morbidity, disability and mortality, the total economic effect will amount to RUB 4,1 and 9,9 bn in the 1st and 2nd scenarios, respectively.

Based on the ontological model, an online tool has been created, which in a visual form allows to assess the potential effect of the introduction of population prevention measures aimed at reducing the consumption of tobacco, alcohol and changing dietary habits at the population level (reducing the consumption of salt, sugar, processed red meat and increasing the consumption of vegetables and fruits, fish products) (Figure 4).

However, the ontological approach is simplified. Therefore, the need to create a population mathematical model that is highly sensitive for relatively small changes in RFs remains.

Rationale of using biomarkers for cardiovascular risk (CVR) stratification

Risk stratification is an important component of the choice of management strategy for both patients and individuals with RFs. However, the existing risk scales have a number of limitations, including the phenomenon of so-called residual risk. The search for additional biochemical markers that would improve the accuracy of risk stratification is an important task. The features of the ESSE-RF study, including the collection of biological material and storage in the Biobank, on the one hand, and 8-year prospective observation of participants with fixation of endpoints, on the other hand, make it possible to assess the contribution of individual biomarkers to risk reclassification. Foreign studies have revealed a clear association of CVR with cardiac troponin I (cTnI) levels and developed algorithms for its cTnI for additional stratification of moderate-risk patients [18]. The results of the first Russian study were published, where the predictive value of cTnI and its ability to reclassify risk were assessed on a cohort of residents of one region participating in the ESSE-RF [19]. Promising results have been obtained that require verification on a large data set, which should be provided by ESSE-RF3. In addition, research is planned to study the predictive value of lipoprotein(a), C-reactive protein, aimed at finding an effective and economically justified strategy for CVR stratification.

External evaluation of the health system performance

Epidemiological data allow assessment of some aspects outside of the health system at population level. For example, epidemiological data can be used to study the coverage of the population with health care and monitoring of diseases and risk factors (for example, diabetes or hypertension).

The ESSE-RF2 study showed that in 2017 the proportion of people with high blood pressure (BP), but

not aware of it, was quite high (women, 23,2%; men, 30,6%), which was mostly due to inadequate interaction with the health care system [20]. Only half of people with HTN taking antihypertensive drugs are treated effectively.

Also, the ESSE-RF showed that not only diseases, but also RFs are associated with the spending of health care system resources [21]. Smoking and obesity were associated with more frequent medical visits (hospitalizations, emergency calls), which indicates the RF burden on the health care system and the need to reduce RFs not only due to the related risk in the future, but also due to the current burden on health care system.

Prospects for using epidemiological data to promote public health

The development of more modern risk assessment tools is an urgent task, since over time, the RF profile in the population changes, new factors appear, and a redistribution of RF contribution occurs. It is no coincidence that the Systematic Coronary Risk Evaluation (SCORE), developed on cohorts recruited before 1986, is replaced by the new SCORE2, which was published in June 2021 [22] and includes not only fatal cardiovascular events, but non-fatal complications and is presented in the form of 4 risk tables (previously there were two). As for the Russian data, the scale included only data from the Health, Alcohol and Psychosocial factors In Eastern Europe (HAPPIEE) study, where a prospective observation of residents from one Russian city (Novosibirsk) was carried out, which can hardly be considered representative for the entire country. Therefore, the relevance of developing a domestic scale for assessing the 10-year CVR remains. By 2023, the ESSE-RF study will have 10 years of prospective observation of cardiovascular outcomes, and its scope will allow building a scale based on a multicenter study that will have sufficient power.

In recent years in the world, population risk modeling has been developing in several directions. First, there are higher number of diseases included in the model as follows: if 10-20 years ago the vast majority of models included CVDs, such as coronary artery disease, then in recent years models have been created to predict dementia in the population [23], all-cause premature death [24] or first significant NCD [25]. Another promising direction is the use of IT technologies in population modeling, for example, machine learning, in order to improve the accuracy of predicting the all-cause death risk [26].

The data of the ESSE-RF prospective observation will make it possible to create accurate mathematical models for predicting population risk. In addition, it is planned to use the ESSE-RF results for adaptation of Preventable Risk Integrated Model (PRIMEtimeR) [27].

The human environment has a significant impact on human health and behavior. It has been proven that shops and salespoints of alcohol, tobacco, fast food have a negative impact on lifestyle, contributing to the growth of smoking and tobacco consumption (including among young people), fast food consumption and obesity, while markets selling vegetables and fruits and infrastructure for physical activity are associated with favorable changes in diet and physical activity [28-30]. The sample of the ESSE-RF3 study was created based on health localities and the addresses included in the sample represent residence place. The scope of the ESSE-RF3 study will allow assessing an infrastructure that promotes or inhibits a healthy lifestyle and evaluate the influence of a person's living environment on RF development.

Due to the COVID-19 pandemic, research is being conducted on factors associated with the risk of illness, hospitalization and death from COVID-19 [31], including behavioral RFs. The scope of the ESSE-RF study will allow assessing long-term predictors of morbidity and mortality from COVID-19, since it will be possible to collect information about COVID-19 survivors, as well as those who were hospitalized and died. This will make it possible to identify associations with socio-demographic characteristics, RFs and other parameters studied in the ESSE-RF, as well as to establish the categories of people vulnerable to infection, not only with current NCDs, but also with RFs.

Limitation of this review is the use of studies known to authors and publications from citation lists with the ESSE-RF data. It is possible that the ESSE-RF data were used in other directions, but there are no scientific publications about this.

Conclusion

The largest population-based study in Russian modern history the ESSE-RF for 8 years has become a platform for public health research and projects, relevant for the whole country. Results of the ESSE-RF study were used to identify Demography National Project parameters, to estimate the economic burden of NCD RFs, to create an ontological model for predicting the economic impact of population prevention measures, etc. Further, results can be used to develop a novel domestic CVR score, to analyze COVID-19-related risk factors, and to study health protection environment.

Currently, the large-scale (30 regions, 60 thousand subjects) ESSE-RF3 study is implemented. Collecting data in the context of a pandemic opens up potential for analyzing the infection in relation to NCDs and their RFs.

Relationships and Activities: none.

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