https://doi.org/10.22416/1382-4376-2025-35-1-94-152
UDC 616.36-003.826-07/-08

Clinical Guidelines of the Russian Society for the Study of the Liver, Russian Gastroenterological Association, Russian Society for the Prevention of Non-Communicable Diseases, Russian Association of Endocrinologists, Russian Scientific Medical Society of Therapists, National Society of Preventive Cardiology, Russian Association of Gerontologists and Geriatricians on Non-Alcoholic Fatty Liver Disease

Vladimir T. Ivashkin[1], Oksana M. Drapkina[2], Marina V. Maevskaya[1], Karina L. Raikhelson[3,4], Sergey V. Okovityi[5], Maria S. Zharkova[1], Vasilisa R. Grechishnikova[1]*, Diana I. Abdulganieva[6], Sergei A. Alekseenko[7], Maria D. Ardatskaya[8], Igor G. Bakulin[9], Natalia V. Bakulina[9], Pavel O. Bogomolov[10,11], Valeriy V. Breder[12], Elena V. Vinnitskaya[13], Natalia I. Geyvandova[14], Elena V. Golovanova[10], Vladimir B. Grinevich[15], Vladimir L. Doshchitsin[16], Ekaterina N. Dudinskaya[16], Ekaterina V. Ershova[17], Khava B. Kodzoeva[18], Irina V. Kozlova[19], Kseniya A. Komshilova[17], Yuri V. Konev[10], Natalia V. Korochanskaya[20], Yulia V. Kotovskaya[16], Yuri A. Kravchuk[15], Irina D. Loranskaya[21], Igor V. Maev[10], Anatoly I. Martynov[10], Sabir N. Mekhtiev[4], Ekaterina E. Mishina[17], Maria Yu. Nadinskaia[1], Igor G. Nikitin[16,22], Marina F. Osipenko[23], Olga D. Ostroumova[21], Chavdar S. Pavlov[1,24], Nana V. Pogosova[25], Valery G. Radchenko[15], Grigory E. Roytberg[16], Rafik G. Saifutdinov[26], Aleksey A. Samsonov[10], Pavel V. Seliverstov[15], Stanislav I. Sitkin[9,27], Larisa V. Tarasova[28], Aida I. Tarzimanova[1], Olga N. Tkacheva[16], Evgeny I. Tkachenko[15], Ekaterina A. Troshina[17], Svetlana V. Turkina[29], Yury P. Uspenskiy[4,30], Yulia A. Fominykh[27,30], Olga V. Khlynova[31], Yulia V. Tsyganova[28], Minara Sh. Shamkhalova[17], Olga O. Sharkhun[16], Marina V. Shestakova[17]

[1] *I.M. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation*
[2] *National Medical Research Center for Therapy and Preventive Medicine, Moscow, Russian Federation*
[3] *Saint Petersburg State University, Saint Petersburg, Russian Federation*
[4] *Academician I.P. Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation*
[5] *Saint Petersburg State Chemical-Pharmaceutical University, Saint Petersburg, Russian Federation*
[6] *Kazan State Medical University, Kazan, Russian Federation*
[7] *Far Eastern State Medical University, Khabarovsk, Russian Federation*
[8] *Central State Medical Academy of the Department of Presidential Affairs, Moscow, Russian Federation*
[9] *North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russian Federation*
[10] *Russian University of Medicine, Moscow, Russian Federation*
[11] *Moscow Regional Research Clinical Institute, Moscow, Russian Federation*
[12] *National Medical Research Center of Oncology named after N.N. Blokhin, Moscow, Russian Federation*
[13] *Loginov Moscow Clinical Scientific Center, Moscow, Russian Federation*
[14] *Stavropol State Medical University, Stavropol, Russian Federation*
[15] *Kirov Military Medical Academy, Saint Petersburg, Russian Federation*
[16] *N.I. Pirogov Russian National Research Medical University, Moscow, Russian Federation*
[17] *Endocrinology Research Center, Moscow, Russian Federation*
[18] *National Medical Research Center for Transplantology and Artificial Organs named after Academician V.I. Shumakov, Moscow, Russian Federation*

[19] Saratov State Medical University named after V.I. Razumovsky, Saratov, Russian Federation
[20] Kuban State Medical University, Krasnodar, Russian Federation
[21] Russian Medical Academy of Continuous Professional Education, Moscow, Russian Federation
[22] National Medical Research Center "Treatment and Rehabilitation Center", Moscow, Russian Federation
[23] Novosibirsk State Medical University, Novosibirsk, Russian Federation
[24] Moscow Multidisciplinary Scientific and Clinical Center named after S.P. Botkin, Moscow, Russian Federation
[25] National Medical Research Center of Cardiology named after Academician E.I. Chazov, Moscow, Russian Federation
[26] Kazan State Medical Academy — Branch Campus of the Russian Medical Academy of Continuous Professional Education, Kazan, Russian Federation
[27] V.A. Almazov National Medical Research Center, Saint Petersburg, Russian Federation
[28] Chuvash State University named after I.N. Ulyanov, Cheboksary, Russian Federation
[29] Volgograd State Medical University, Volgograd, Russian Federation
[30] Saint Petersburg State Pediatric Medical University, Saint Petersburg, Russian Federation
[31] Perm State Medical University named after Academician E.A. Wagner, Perm, Russian Federation

Aim. The clinical guidelines are intended to provide information support for making decisions by gastroenterologists, general practitioners and internists that will improve the quality of medical care for patients with non-alcoholic fatty liver disease, taking into account the latest clinical data and principles of evidence-based medicine.
Key points. Clinical guidelines contain information about current views on etiology, risk factors and pathogenesis of nonalcoholic fatty liver disease, peculiarities of its clinical course. Also given recommendations provide information on current methods of laboratory and instrumental diagnostics, invasive and non-invasive tools for nonalcoholic fatty liver disease and its clinical phenotypes assessment approaches to its treatment, considering the presence of comorbidities, features of dispensary monitoring and prophylaxis. The information is illustrated with algorithms of differential diagnosis and physician's actions. In addition, there is information for the patient and criteria for assessing the quality of medical care.
Conclusion. Awareness of specialists in the issues of diagnosis, treatment and follow-up of patients with nonalcoholic fatty liver disease contributes to the timely diagnosis and initiation of treatment, which in the long term will significantly affect their prognosis and quality of life.
Keywords: dyslipidemia, fatty liver disease, cardiometabolic risk factors, nonalcoholic steatohepatitis, liver steatosis, steatohepatitis
Conflict of interest: the authors declare no conflict of interest.

For citation: Ivashkin V.T., Drapkina O.M., Maevskaya M.V., Raikhelson K.L., Okovityi S.V., Zharkova M.S., Grechishnikova V.R., Abdulganieva D.I., Alekseenko S.A., Ardatskaya M.D., Bakulin I.G., Bakulina N.V., Bogomolov P.O., Breder V.V., Vinnitskaya E.V., Geyvandova N.I., Golovanova E.V., Grinevich V.B., Doshchitsin V.L., Dudinskaya E.N., Ershova E.V., Kodzoeva K.B., Kozlova I.V., Komshilova K.A., Konev Yu.V., Korochanskaya N.V., Kotovskaya Yu.V., Kravchuk Yu.A., Loranskaya I.D., Maev I.V., Martynov A.I., Mekhtiev S.N., Mishina E.E., Nadinskaia M.Yu., Nikitin I.G., Osipenko M.F., Ostroumova O.D., Pavlov Ch.S., Pogosova N.V., Radchenko V.G., Roytberg G.E., Saifutdinov R.G., Samsonov A.A., Seliverstov P.V., Sitkin S.I., Tarasova L.V., Tarzimanova A.I., Tkacheva O.N., Tkachenko E.I., Troshina E.A., Turkina S.V., Uspenskiy Yu.P., Fominykh Yu.A., Khlynova O.V., Tsyganova Yu.V., Shamkhalova M.Sh., Sharkhun O.O., Shestakova M.V. Clinical Guidelines of the Russian Society for the Study of the Liver, Russian Gastroenterological Association, Russian Society for the Prevention of Non-Communicable Diseases, Russian Association of Endocrinologists, Russian Scientific Medical Society of Therapists, National Society of Preventive Cardiology, Russian Association of Gerontologists and Geriatricians on Non-Alcoholic Fatty Liver Disease. Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2025;35(1):94–152. https://doi.org/10.22416/1382-4376-2025-35-1-94–152

Клинические рекомендации Российского общества по изучению печени, Российской гастроэнтерологической ассоциации, Российского общества профилактики неинфекционных заболеваний, Российской ассоциации эндокринологов, Российского научного медицинского общества терапевтов, Национального общества профилактической кардиологии, Российской ассоциации геронтологов и гериатров по неалкогольной жировой болезни печени

В.Т. Ивашкин[1], О.М. Драпкина[2], М.В. Маевская[1], К.Л. Райхельсон[3,4], С.В. Оковитый[5], М.С. Жаркова[1], В.Р. Гречишникова[1], Д.И. Абдулганиева[6], С.А. Алексеенко[7], М.Д. Ардатская[8], И.Г. Бакулин[9], Н.В. Бакулина[9], П.О. Богомолов[10,11], В.В. Бредер[12], Е.В. Винницкая[13], Н.И. Гейвандова[14], Е.В. Голованова[10], В.Б. Гриневич[15], В.Л. Дощицин[16], Е.Н. Дудинская[16], Е.В. Ершова[17], Х.Б. Кодзоева[18], И.В. Козлова[19], К.А. Комшилова[17], Ю.В. Конев[10], Н.В. Корочанская[20], Ю.В. Котовская[16], Ю.А. Кравчук[15], И.Д. Лоранская[21], И.В. Маев[10], А.И. Мартынов[10], С.Н. Мехтиев[4], Е.Е. Мишина[17], М.Ю. Надинская[1], И.Г. Никитин[16,22], М.Ф. Осипенко[23], О.Д. Остроумова[21], Ч.С. Павлов[1,24], Н.В. Погосова[25], В.Г. Радченко[15], Г.Е. Ройтберг[16], Р.Г. Сайфутдинов[26], А.А. Самсонов[10], П.В. Селиверстов[15], С.И. Ситкин[9,27], Л.В. Тарасова[28], А.И. Тарзиманова[1], О.Н. Ткачева[16], Е.И. Ткаченко[15], Е.А. Трошина[17], С.В. Туркина[29], Ю.П. Успенский[4,30], Ю.А. Фоминых[27,30], О.В. Хлынова[31], Ю.В. Цыганова[28], М.Ш. Шамхалова[17], О.О. Шархун[16], М.В. Шестакова[17]*

[1] ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет), Москва, Российская Федерация

[2] *ФГБУ «Национальный медицинский исследовательский центр терапии и профилактической медицины» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[3] *ФГБОУ ВО «Санкт-Петербургский государственный университет», Санкт-Петербург, Российская Федерация*

[4] *ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. академика И.П. Павлова» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*

[5] *ФГБОУ ВО «Санкт-Петербургский государственный химико-фармацевтический университет» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*

[6] *ФГБОУ ВО «Казанский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Казань, Российская Федерация*

[7] *ФГБОУ ВО «Дальневосточный государственный медицинский университет» Министерства здравоохранения Российской Федерации, Хабаровск, Российская Федерация*

[8] *ФГБУ ДПО «Центральная государственная медицинская академия» Управления делами Президента Российской Федерации, Москва, Российская Федерация*

[9] *ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*

[10] *ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[11] *ГБУЗ МО «Московский областной научно-исследовательский клинический институт им. М.Ф. Владимирского» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[12] *ФГБУ «Национальный медицинский исследовательский центр онкологии им. Н.Н. Блохина» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[13] *ГБУЗ «Московский клинический научно-практический центр им. А.С. Логинова» Департамента здравоохранения города Москвы, Москва, Российская Федерация*

[14] *ФГБОУ ВО «Ставропольский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Ставрополь, Российская Федерация*

[15] *ФГБВОУ ВО «Военно-медицинская академия им. С.М. Кирова» Министерства обороны Российской Федерации, Санкт-Петербург, Российская Федерация*

[16] *ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[17] *ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[18] *ФГБУ «Национальный медицинский исследовательский центр трансплантологии и искусственных органов им. академика В.И. Шумакова» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[19] *ФГБОУ ВО «Саратовский государственный медицинский университет им. В.И. Разумовского» Министерства здравоохранения Российской Федерации, Саратов, Российская Федерация*

[20] *ФГБОУ ВО «Кубанский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Краснодар, Российская Федерация*

[21] *ФГБОУ ДПО «Российская медицинская академия непрерывного профессионального образования» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[22] *ФГАУ «Национальный медицинский исследовательский центр «Лечебно-реабилитационный центр» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[23] *ФГБОУ ВО «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Новосибирск, Российская Федерация*

[24] *ГБУЗ «Московский многопрофильный научно-клинический центр им. С.П. Боткина» Департамента здравоохранения города Москвы, Москва, Российская Федерация*

[25] *ФГБУ «Национальный медицинский исследовательский центр кардиологии им. академика Е.И. Чазова» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*

[26] *Казанская государственная медицинская академия — филиал ФГБОУ ДПО «Российская медицинская академия непрерывного профессионального образования» Министерства здравоохранения Российской Федерации, Казань, Российская Федерация*

[27] *ФГБУ «Национальный медицинский исследовательский центр им. В.А. Алмазова» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*

[28] *ФГБОУ ВО «Чувашский государственный университет им. И.Н. Ульянова» Министерства науки и высшего образования Российской Федерации, Чебоксары, Российская Федерация*

[29] *ФГБОУ ВО «Волгоградский государственный медицинский университет» Министерства здравоохранения Российской Федерации, Волгоград, Российская Федерация*

[30] *ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Министерства здравоохранения Российской Федерации, Санкт-Петербург, Российская Федерация*

[31] *ФГБОУ ВО «Пермский государственный медицинский университет им. академика Е.А. Вагнера» Министерства здравоохранения Российской Федерации, Пермь, Российская Федерация*

Цель: представления клинических рекомендаций заключается в обеспечении информационной поддержки для принятия врачами-гастроэнтерологами, врачами общей практики и врачами-терапевтами решений, способствующих повышению качества оказания медицинской помощи пациенту с неалкогольной жировой болезнью печени с учетом новейших клинических данных и принципов доказательной медицины.
Основное содержание. Клинические рекомендации содержат информацию о современных представлениях об этиологии, факторах риска и патогенезе неалкогольной жировой болезни печени, особенностях ее клинического течения. Также в рекомендациях представлена информация об актуальных методах лабораторной и инструментальной, инвазивной и неинвазивной диагностики неалкогольной жировой болезни печени и ее клинических фенотипов, подходах к ее лечению с учетом наличия коморбидностей, особенностей диспансерного наблюдения и профилактики. Приведенная информация проиллюстрирована алгоритмами дифференциального диагноза, действий врача. Помимо этого, присутствует информация для пациента и критерии оценки качества оказания медицинской помощи.
Заключение. Осведомленность специалистов в вопросах диагностики, лечения и наблюдения пациентов с неалкогольной жировой болезнью печени способствует своевременной постановке диагноза и инициации лечения, что в перспективе будет существенно влиять на их прогноз и качество жизни.
Ключевые слова: дислипидемии, жировая болезнь печени, кардиометаболические факторы риска, неалкогольный стеатогепатит, стеатоз печени, стеатогепатит
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Ивашкин В.Т., Драпкина О.М., Маевская М.В., Райхельсон К.Л., Оковитый С.В., Жаркова М.С., Гречишникова В.Р., Абдулганиева Д.И., Алексеенко С.А., Ардатская М.Д., Бакулин И.Г., Бакулина Н.В., Богомолов П.О., Бредер В.В., Винницкая Е.В., Гейвандова Н.И., Голованова Е.В., Гриневич В.Б., Дощицин В.Л., Дудинская Е.Н., Ершова Е.В., Кодзоева Х.Б., Козлова И.В., Комшилова К.А., Конев Ю.В., Корочанская Н.В., Котовская Ю.В., Кравчук Ю.А., Лоранская И.Д., Маев И.В., Мартынов А.И., Мехтиев С.Н., Мишина Е.Е., Надинская М.Ю., Никитин И.Г., Осипенко М.Ф., Остроумова О.Д., Павлов Ч.С., Погосова Н.В., Радченко В.Г., Ройтберг Г.Е., Сайфутдинов Р.Г., Самсонов А.А., Селиверстов П.В., Ситкин С.И., Тарасова Л.В., Тарзиманова А.И., Ткачева О.Н., Ткаченко Е.И., Трошина Е.А., Туркина С.В., Успенский Ю.П., Фоминых Ю.А., Хлынова О.В., Цыганова Ю.В., Шамхалова М.Ш., Шархун О.О., Шестакова М.В. Клинические рекомендации Российского общества по изучению печени, Российской гастроэнтерологической ассоциации, Российского общества профилактики неинфекционных заболеваний, Российской ассоциации эндокринологов, Российского научного медицинского общества терапевтов, Национального общества профилактической кардиологии, Российской ассоциации геронтологов и гериатров по неалкогольной жировой болезни печени. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2025;35(1):94–152. https://doi.org/10.22416/1382-4376-2025-35-1-94–152

Terms and definitions

Arterial hypertension (AH) — a syndrome of increased clinical blood pressure (BP) in a hypertensive disease and symptomatic AH above threshold values diagnosed as a result of epidemiological and randomized controlled studies (systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg), demonstrating an association with an increased cardiovascular risk, as well as feasibility and benefit of the treatment aimed at lowering BP below these levels.

Body mass index — an indicator used for diagnosing overweight and obesity, as well as assessing its degree (body weight in kilograms divided by the square of height in meters, kg/m^2).

Cardiometabolic risk factors — risk factors for developing cardiovascular diseases, type II diabetes mellitus, and non-alcoholic fatty liver disease.

Chronic kidney disease — a supranosologic concept grouping all patients with the signs of kidney injury and/or reduced function, assessed by the glomerular filtration rate, which persist for 3 months and more.

Clinical Practice Guidelines Development/Update Working Group — a professional team working together and in coordination to develop/update clinical practice guidelines and bearing shared responsibility for the results of this work.

Clinical study — any study carried out with the participation of a human as a subject to identify or confirm clinical and/or pharmacological effects of investigational products and/or to identify adverse reactions to investigational products and/or to study their absorption, distribution, metabolism and elimination in order to assess their safety and/or efficacy.

Condition — changes in the body occurring in connection with the influence of pathogenic and/or physiological factors and requiring medical aid.

Conflict of interest — a situation in which a medical or pharmaceutical employee, in the course of their professional activities, has a personal interest in receiving, personally or through a company's representative, a material benefit or other advantage that affects or may affect the proper execution of their professional duties due to a contradiction between the personal interest of the medical or pharmaceutical employee and a patient's interests.

Disease — a state that occurs in relation to the influence of pathogenic factors, a dysfunction

in the body activity, performance, adaptability to changing conditions of the external and internal environment with a simultaneous change in the protective-compensatory and protective-adaptive reactions and mechanisms of the body.

Dyslipidemias — conditions characterized by the concentrations of blood lipids and lipoproteins going beyond reference values.

Evidence-based medicine — the appropriate, consistent and judicious use of the best present-day evidence (clinical research results) combined with individual clinical experience and considering a patient's values and preferences in making decisions on the patient's health and treatment.

Fatty liver disease of specific etiology — a supranosologic concept comprising monogenic diseases, individual phenotypes of the drug-induced liver injury, and other diseases in which the development of steatosis/steatohepatitis has a proven cause not associated with metabolic dysfunction and alcohol intake.

Fatty liver disease — a supranosologic concept grouping liver diseases characterized by steatosis and steatohepatitis.

Grades of recommendation — degrees of confidence in the intervention effect accuracy and in medical advice compliance producing more benefit than harm in a particular situation.

Hepatic steatosis — an accumulation of fat in the liver, in which lipid accumulation occurs in more than 5 % of hepatocytes.

Level of evidence — a degree of confidence in true nature of the effect obtained from the use of medical intervention.

Lifestyle changes — measures aimed at normalizing body weight, diet and physical activity with the purpose of disease prevention and treatment.

Medical intervention — a type of medical examinations and/or medical manipulations, performed by a medical or another employee entitled to carry out medical activities in relation to a patient, affecting the physical or mental state of a person and having a preventive, diagnostic, therapeutic, rehabilitation or research focus; this also includes artificial termination of pregnancy.

Medicines — medicinal products in dosage forms used for the prevention, diagnosis, and treatment of a disease, rehabilitation, preservation, prevention or termination of pregnancy.

Metabolic dysfunction-associated fatty liver disease in combination with excessive alcohol consumption (MetALD) — a chronic liver disease in which non-alcoholic (metabolic dysfunction-associated) fatty liver disease is combined with an average alcohol consumption of 20 to 50 g/day for women and 30 to 60 g/day for men.

Non-alcoholic (metabolic dysfunction-associated) fatty liver disease (NAFLD) — a chronic liver disease associated with a metabolic dysfunction, in which macrovesicular steatosis is detected in more than 5 % of hepatocytes.

Non-alcoholic steatohepatitis (NASH) — a progressive form (phenotype) of NAFLD, which is characterized by the steatosis, intralobular inflammation, ballooning degeneration of hepatocytes and can occur with the development of pericentral and perisinusoidal (less often — portal) fibrosis.

Obesity — a chronic disease characterized by excess accumulation of adipose tissue in the body posing a health hazard and being a major risk factor for a number of other chronic diseases.

Outcome — any possible result arising from the influence of a causative factor, preventive or therapeutic intervention, all established changes in the health status emerging as a consequence of the intervention.

Patient — an individual who is administered medical care or who has applied for medical care, regardless of having a disease or their condition.

Prediabetes — a carbohydrate metabolism disorder in which diabetes mellitus criteria are not met, however, normal blood glucose values are exceeded (includes any of the following disorders: impaired fasting glycemia and impaired glucose tolerance).

Steatohepatitis — an accumulation of fat in the liver, accompanied by intralobular inflammation, ballooning degeneration of hepatocytes and possible fibrosis development.

Syndrome: a stable set of symptoms with a single pathogenesis.

Type 2 diabetes mellitus — a carbohydrate metabolism disorder caused by predominant insulin resistance and relative insulin deficiency or predominant impairment of insulin secretion with or without insulin resistance.

Waist circumference — an indicator used for diagnosing visceral fat accumulation, abdominal (visceral) obesity.

1. Summary review on a disease or condition (a group of diseases or conditions)

1.1. Definition of a disease or condition (group of diseases or conditions)

Non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease associated with a metabolic dysfunction, in which macrovesicular steatosis

is detected in more than 5 % of hepatocytes [1, 2]. NAFLD covers the pathological spectrum from simple steatosis to steatohepatitis and liver cirrhosis (LC). According to the concepts of recent years, steatosis (simple steatosis) and non-alcoholic steatohepatitis (NASH) represent two separate pathological conditions (phenotypes or forms) with a different prognosis [3]:

a) simple steatosis is a condition in which there is no inflammation or fibrosis, while steatosis is an independent risk factor for developing cardiovascular diseases (CVD) and their complications [3]. Simple steatosis may have a progressive course with fibrosis development, but its progression rate is significantly slower than in the original NASH [4];

b) NASH is characterized by steatosis, intralobular inflammation, ballooning degeneration of hepatocytes and can occur with the development of pericentral and perisinusoidal (less often, portal) fibrosis. NASH is a clinically progressive form of NAFLD with the risk of developing LC, hepatocellular carcinoma (HCC), as well as CVD and their complications [3].

In 2023, a new fatty liver disease nomenclature [2] developed by a large team of international experts was published. The very concept of "fatty liver disease" has become a unifying term or an umbrella term with various nosological forms identified within, including NAFLD. International experts suggested a new name for NAFLD: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) and optimized its diagnostic criteria. Russian experts discussed all aspects of the new nomenclature and possibilities of its use in the Russian Federation arriving at the following conclusions and recommendations: to use optimized diagnostic criteria for NAFLD in the clinical practice of Russian doctors and include them in these recommendations; to use the already familiar terms "NAFLD" and "NASH" for working with official medical documentation, due to the need to apply ICD-10; for scientific purposes, new terms with an agreed and approved translation into Russian may be used [5]. For example, MASLD — for NAFLD, metabolic-dysfunction associated steatohepatitis (MASH) — for NASH.

1.2. Etiology and pathogenesis

The initial concept of NAFLD pathogenesis as a two-hit theory [6] has been replaced by the concept of multifactorial pathogenesis, including parallel processes such as insulin resistance (IR), impaired autophagy, lipotoxicity, inflammation, cytokine and adipokine imbalance, activation of innate immunity and microbiota, and the impact of environmental and genetic factors [7, 8]. One of the key moments in the development of NAFLD is the systemic energy imbalance, characterized by an excess of substrates, mainly carbohydrates and fatty acids. The main sources of free (non-esterified) fatty acids (FFA) entering the liver include their increased release from adipocytes (approx. 60 %), conversion of carbohydrates in the liver (*de novo* lipogenesis, 26 %), and excessive fat intake in the diet (14 %) [9, 10].

Insulin resistance. IR is characterized by a decreased insulin sensitivity of peripheral tissues (muscles, adipose tissue, liver). Epidemiological studies show a correlation between a high-carbohydrate diet and NAFLD. Excessive carbohydrate consumption and elevated blood glucose levels have a detrimental effect on cells (glucotoxicity). The formation of IR in the liver is accompanied by an increased gluconeogenesis and a decreased glycogenesis with the development of hyperglycemia [11–13]. IR leads to decreased glucose uptake by adipocytes and muscles, while hepatocytes can secrete dipeptidyl peptidase type 4, which promotes inflammation of adipose tissue and IR development [12, 13]. Metabolic dysregulation of adipocytes creates conditions for excessive lipolysis of triglycerides (TG), FFA release into the bloodstream and their entry into the liver [14]. In NAFLD, excess glucose and fructose promote de novo lipogenesis in hepatocytes [15]. However, unlike glucose, the involvement of fructose in this process is not regulated by glycolysis [16].

Adipose tissue is not only the main source of FFA, but also an endocrine organ secreting adipokines with systemic regulatory effects. Leptin and adiponectin produced by visceral adipocytes influence NAFLD by regulating appetite, influencing fat composition, insulin sensitivity, and inflammation. In NAFLD, there is a decrease in adiponectin production and an increase in leptin synthesis, while in NASH, serum leptin levels are elevated compared to healthy controls [17, 18]. Hyperleptinemia and low levels of soluble leptin receptor (leptin binding protein) suggest leptin resistance in peripheral tissues and are found in NAFLD patients to a greater extent than in obese individuals without hepatic steatosis [19].

Excessive production of proinflammatory cytokines by visceral adipose tissue macrophages is critical in the development of systemic inflammation in obesity. Activated macrophages secrete cytokines and chemokines (tumor necrosis factor-alpha (TNF-α), interleukin (IL) 1β, IL-6 and

CCL2 (C-C Motif Ligand — a cytokine belonging to the group of C-C chemokines)), contribute to the development of local IR, leading to impaired lipid metabolism regulation, and can form systemic IR [20, 21]. Proinflammatory mediators activate key transcription factors such as JNK (Jun N-terminal kinase) and NF-κB (nuclear factor kappa-bi), leading to hepatocyte injury, inflammation, and stimulation of fibrogenesis [22].

Autophagy impairment and lipotoxicity. Autophagy is a universal intracellular catabolic process (including lipophagy, mitophagy, reticulophagy, and pexophagy) in which dysfunctional or redundant organelles (e.g., mitochondria, peroxisomes and endoplasmic reticulum, lipid droplets) are identified, labelled, delivered to lysosomes, and internalised for degradation into building blocks for subsequent use by the cell. The specificity of selective autophagy makes it a critical process in reducing hepatocyte damage caused by abnormal accumulation of dysfunctional organelles in NAFLD pathogenesis and no other system can replace it [23].

The direct connection between autophagy and apoptosis makes it an important player in the regulation of cellular life and death. One of the key roles in these processes is assigned to the beclin-1 protein, which initiates the formation and maturation of the phagophore. In a complex with the Bcl-2 protein (B-Cell Leukemia/Lymphoma 2 — an intracellular protein factor, apoptosis regulator), it inhibits autophagy, and disruption of this interaction due to the competitive formation of the Bcl-2/Bax (BCL2 Associated X Protein — bcl-2-like protein 4) bond leads to its activation. Thus, beclin-1 in complex with Bcl-2 functions as a molecular switch between autophagy and apoptosis [24]. Cellular stress, in particular, excessive entry of free fatty acids into the hepatocyte and accumulation of triglycerides, initially stimulates adaptive capacities of the hepatocyte and then leads to their depletion [25]. As a result, a deficiency of adenosine triphosphate (ATP) develops in the cell, adenosine monophosphate (AMP) accumulates, activating the work of adenosine monophosphate-activated protein kinase (AMPK). This enzyme initiates a complex process of autophagy, which in NAFLD is aimed at eliminating lipid droplets (lipophagy), damaged mitochondria (mitophagy), intermediate products of triglyceride synthesis (diacylglycerol, etc.).

Moreover, AMPK modulates hepatic lipogenesis through several mechanisms: phosphorylation (and inactivation) of transcription factors SREBP-1c (sterol regulatory element-binding transcription factor 1, induces expression of a gene family involved in glucose disposal and fatty acid synthesis; plays a role in liver steatosis development), SREBP-2 (transcription factor 2, a key regulator of cholesterol (CH) metabolism, activation of its gene leads to increased cholesterol uptake and synthesis), and ChREBP (Carbohydrate-Responsive Element-Binding Protein, it induces *de novo* lipogenesis from glucose in adipose tissue, while in the liver its induction by glucose promotes glycolysis and lipogenesis; plays a role in the development of type 2 diabetes mellitus (DM), dyslipidemia, and liver steatosis). AMPK activity is reduced in NAFLD patients, and its agonists may be effective in treating this disease [26–30].

A major influence on AMPK-dependent autophagy is exerted by hyperactivation of the serine/threonine kinase mTOR (mechanistic Target of Rapamycin), which inhibits lysosomal biogenesis and autophagy processes. This occurs under the influence of cytosolic Ca^{2+} overload, oxidative stress induced by the lipotoxicity of FFA, diacylglycerols, ceramides, lysophosphatidylcholine, and CH. As a result, an endoplasmic reticulum stress and a lysosomal dysfunction develop, lipid peroxidation (LPO) processes are aggravated, and damage or death of hepatocytes occurs [31, 32].

Oxidative stress and mitochondrial dysfunction. Increased intake of FFA into the liver results in increased peroxisomal α- and β-oxidation, as well as microsomal ω-oxidation with the participation of cytochrome P-450, leading to LPO initiation. Moreover, increased FFA disposal in mitochondria is accompanied by the production of highly active oxygen forms and compounds that damage these organelles, causing mitochondrial dysfunction and progressive energy deficiency [33]. This results in suppression of the main energy-dependent processes in hepatocytes, disorder in the work of enzymatic and non-enzymatic components of antioxidant protection, and further formation of new free radicals and lipid hydroperoxides, which, under the influence of the catalytic activity of iron ions, form secondary free radical products. This oxidative cascade is characterized by hepatocyte damage and leads to the development of inflammation, stimulation of stellate cells (SC) and fibrogenesis [34].

Immune mechanisms of inflammation and fibrogenesis. With an excess flow of FFA or other pathogens (such as endotoxins) from the intestine to the liver, Kupffer cells phagocytize pathogenic factors and present them through pattern recognition receptors (PRRs) [35]. These receptors include toll-like receptors (TLR) and nucleotide-binding

oligomerization domain-like receptors (NLRs) [36]. Inflammasomes, via the NLR protein, activate a cascade of events resulting in the activation of the transcription factor NF-κB [37, 38]. Kupffer cells differentiate into M1 or M2 phenotypes depending on the external inducer. The M1 phenotype produces proinflammatory cytokines TNF-α, IL-1 and IL-12, while M2 (the second type of macrophages) is able to stimulate the secretion of IL-4, IL-10 and transforming growth factor beta (TGF-β) having an anti-inflammatory effect [39]. IL-6 and TNF-α produced by activated macrophages are responsible for NASH progression [40, 41].

Helper T lymphocytes are also involved in the liver inflammation process. Following the immune activation, T cells differentiate into Th1, Th2, and Th17 effector cells. NASH is characterized by an excess of Th1-derived cytokines, such as interferon (IFN) γ and a deficiency of Th2-derived cytokines IL-4, IL-5, and IL-13 [42]. Th17 cells producing IL-17 infiltrate the liver in NASH and enhance inflammation and fibrosis influencing macrophages and SC [9]. Cytotoxic $CD8^+$ T cells in the NAFLD liver produce IFN-γ and TNF-α, leading to increased steatosis, IR, inflammation, and SC activation [43]. In turn, SC are transformed into an activated phenotype (myofibroblasts), strongly proliferate and produce collagen, fibronectin, laminin, hyaluronic acid, matrix metalloproteinases and their tissue inhibitors [44]. Accumulation of fibril-forming collagens (types I and III) in the Disse space causes sinusoidal capillarization, distortion of liver architecture, local hypoxia, and fibrogenesis progression.

Gut-liver axis. Four main types dominating among the commensal organisms which inhabit the human intestine are Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. Microbiota plays a vital role in maintaining intestinal barrier integrity and intestinal permeability. Intestinal microbiota also actively participates in the biokinetics of bile acids with the formation of their metabolites, thus indirectly influencing NAFLD development via bile acid receptors, such as the farnesoid X receptor (FXR), the bile acid membrane receptor (TGR5, GPBAR1) and the vitamin D receptor (VDR), which modulate nutrient metabolism and insulin sensitivity [45]. Disruption of the microbiota composition can result in damaged intestinal epithelium and disrupted tight junction proteins, leading to the release of intestinal bacteria, bacteria-produced ethanol, and endotoxins into the portal circulation [46, 47]. This induces inflammation and fibrogenesis in the liver, contributing to liver damage [48, 49].

Genetic aspects. Large-scale genetic studies (genome-wide association studies) conducted in various countries, mainly among Caucasians, identified dozens of genes with polymorphisms that may be associated with NAFLD and NASH development [50, 51].

The most convincing data in the majority of populations were obtained on the association with an unfavourable course of NAFLD (development of NASH, fibrosis and HCC) with polymorphisms rs738409 in the *PNPLA3* gene (patatin-like phospholipase domain-containing 3 gene (adiponutrin)) and rs58542926 in the *TM6SF2* gene (transmembrane 6 superfamily member 2). These mutations are assumed to be significant for the Russian population, however, studies have only been conducted in certain regions of the Russian Federation [52–55].

Thyroid hormones and NAFLD. Thyroid hormones modulate hepatic glucose and lipid metabolism. The role of hypothyroidism in the development and progression of NAFLD is being discussed [56, 57], since decreased activation of thyroid hormone receptors (THR-β) contributes to increased steatosis via a number of mechanisms, including mitochondrial dysfunction [58].

Thus, the NAFLD pathogenesis includes a broad range of pathological processes occurring in parallel. This diversity of pathological mechanisms characterizes NAFLD as a disease requiring a multidisciplinary approach, while the therapeutic strategy should be aimed at correcting different aspects of pathological changes in the patient.

1.3. Epidemiology

Currently, NAFLD is the most common chronic non-infectious liver disease affecting 25 to 30 % of adults in most countries [59, 60]. In Russia, the epidemiology of NAFLD has been explored in several studies. According to the multicenter studies DIREG (2007) and DIREG-2 (2015), the prevalence of NAFLD among outpatients in the Russian Federation is growing: 27 and 37.3 % respectively [61, 62].

According to the epidemiological study ESSE-RF-2 (2022), the prevalence of NAFLD in Russia was 38.5 % for men and 26.6 % for women [63]. Similar data on the prevalence of NAFLD in the Russian Federation and its upward trend were demonstrated in a recent meta-analysis of 5 studies with an overall population of 96,680 patients [64].

The prevalence of NASH is difficult to assess accurately, since a correct diagnosis requires a liver biopsy, being an expensive and invasive procedure that is not always available. Literature

data show that NASH occurs in 3–5 % of the world's population, most of whom have several comorbidities [65]. At the same time, the results of a prospective study of a large middle-aged cohort suggest that NASH occurs in 14 % of cases and is also significantly associated with the presence of type 2 DM and obesity in patients [66]. The development of fibrosis in NASH determines its clinical outcomes: approximately 20 % of patients develop LC and/or HCC, being the main cause of their death. The use of a Markov mathematical model, taking into account the prevalence of type 2 DM and obesity, showed that NASH global prevalence will increase to 15–56 % by 2030 [67]. Accordingly, the efforts of healthcare professionals, including in the Russian Federation, can and should influence this negative scenario.

NAFLD is closely associated with various comorbidities: obesity occurs in 51.34 % (95% confidence interval (95% CI): 41.38–61.20) and 81.83 % (95% CI: 55.16–94.28) of patients with NAFLD and NASH, respectively; type 2 DM occurs in 22.51 % (95% CI: 17.92–27.89) and 43.63 % (95% CI: 30.28–57.98) of patients with NAFLD and NASH, respectively; the prevalence of hyperlipidemia/dyslipidemia was 69.16 % (95% CI: 49.91–83.46) and 72.13 % (95% CI: 54.59–84.78) among patients with NAFLD and NASH, respectively, and arterial hypertension (AH) 39.34 % (95% CI: 33.15–45.88) and 67.97 % (95% CI: 56.31–77.74) among patients with NAFLD and NASH, respectively. Metabolic syndrome (MetS) is detected in 42.54 % (95% CI: 30.06–56.05) and 70.65 % (95% CI: 54.64–82.79) of patients with NAFLD and NASH, respectively [67].

In recent decades, there has been a global trend towards an increase of the NAFLD proportion in the structure of etiologic factors of LC [68], as well as HCC, including that developing without the cirrhosis stage [69].

1.4. Special aspects of coding a disease or condition (group of diseases or conditions) according to the International Statistical Classification of Diseases and Related Health Problems

K75.8 — other specified inflammatory liver diseases.

K76.0 — Fatty (change of) liver, not elsewhere classified.

1.5. Classification of a disease or condition (group of diseases or conditions)

There are two main phenotypes (forms) of NAFLD:

- steatosis;
- NASH.

Since the NASH diagnosis requires histological verification, hereinafter the term NAFLD is predominantly used when formulating indications for diagnostic and therapeutic measures.

The issues of managing patients with LC in NASH are discussed in clinical practice guidelines (CPG) related to LC [70], do not have significant distinctions in NASH, and therefore are not discussed in the present CPG.

1.6. Clinical presentation of a disease or condition (group of diseases or conditions)

NAFLD is characterized by a low-symptom and asymptomatic course. The most common complaints include hepatogenic weakness/fatigue, which occurs in more than 70 % of patients, a feeling of heaviness or discomfort in the right hypochondrium [71, 72]. Quite often, complaints of NAFLD patients are determined by comorbid conditions (obesity, etc.). A manifest clinical presentation is observed with the development of NASH and LC with its complications (see CPG "Liver Cirrhosis and Fibrosis", ID 715 [70]).

2. Diagnosis of a disease or condition (group of diseases or conditions), medical indications and contraindications for the use of diagnostic methods

NAFLD is diagnosed:

1) if liver steatosis is confirmed (based on imaging studies or histological examination of liver tissue);

2) in the presence of one or more cardiometabolic risk factors:

— body mass index (BMI) > 25 kg/m^2 or waist circumference > 94 cm for men, > 80 cm for women (or above the ULN for patients belonging to an ethnic group for which other standards for BMI and/or waist circumference are accepted);

— fasting glucose > 5.6 mmol/L or postprandial glucose > 7.8 mmol/L or glycated hemoglobin (HbA1c) > 5.7 % or previously diagnosed type 2 DM or being treated for type 2 DM;

— blood pressure ≥ 130/85 mmHg or pharmacotherapy for previously diagnosed AH;

— plasma TG ≥ 1.70 mmol/L or lipid-lowering therapy;

— plasma high-density lipoprotein (HDL) cholesterol < 1.0 mmol/L in men and < 1.3 mmol/L in women or lipid-lowering therapy;

3) exclusion of other leading causes of fatty liver disease (Table 1) [2, 73].

2.1. Complaints and past medical history

Taking complaints and past medical history should be aimed at identifying cardiometabolic

risk factors necessary for the diagnosis of NAFLD, associated diseases and their complications (overweight/obesity, AH, type 2 DM, dyslipidemia, atherosclerotic CVD (ASCVD), chronic kidney disease (CKD); study of lifestyle, nutrition, alcohol consumption.

2.2. Physical examination

• When taking past medical history and doing physical examination of a patient with NAFLD, it is recommended to measure waist circumference, body weight, BMI and to assess cardiometabolic risk factors in order to select treatment strategy [74].

Grade of recommendation — C;
level of evidence — 5.

Comments. Generally, a physical examination reveals signs of overweight or obesity, fat distribution according to the male (abdominal) type. It is necessary to assess such indicators as BMI, waist and hip circumference. Palpation and percussion of the abdomen in NAFLD patients without signs of severe fibrosis may reveal a moderate enlargement of the liver, the liver edge is rounded, its consistency is doughy. In severe fibrosis, the liver becomes dense; at the cirrhosis stage liver signs, splenomegaly, and ascites may be observed [74].

2.3. Laboratory diagnostic testing

• For NAFLD patients, it is recommended to conduct a general (clinical) blood test for assessing levels of hemoglobin, platelets, and leukocytes [74, 75].

Grade of recommendation — C;
level of evidence — 5.

Comments. Most often, deviations in the complete blood count in NAFLD patients are observed at the stage of severe fibrosis/LC and are manifested by cytopenia (to a greater extent, thrombocytopenia of varying severity levels). The presence of two- and three-lineage cytopenia is possible, being indicative of the hypersplenism syndrome [74, 75]. *Also, complete blood count results are used for calculation of non-invasive fibrosis scoring.*

• It is recommended to perform a general therapeutic blood chemistry test, including such indicators as alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), γ-glutamyl transferase (GGT), total bilirubin, direct bilirubin, total protein,

Table 1. Causes of fatty liver disease

Type of fatty liver disease	Group of causes	Causes
NAFLD (MASLD)	Metabolic dysfunction	
Alcoholic liver disease	Excessive alcohol consumption	
Fatty liver disease of specific etiology	Single-gene disorders	Wilson's disease, abetalipoproteinemia, hypobetalipoproteinemia, congenital lipodystrophy, familial hyperlipidemia, lysosomal acid lipase deficiency, type II citrullinemia, etc.
	Drug-induced liver injuries	Methotrexate**, Tamoxifen**, Amiodarone**, Irinotecan**, etc.
	Environmental toxins	Metals (lead, arsenic, mercury, cadmium); herbicides, pesticides; polychlorinated biphenyls, chloroalkenes (perchloroethylene, trichloroethylene, vinyl chloride)
	Infection	Hepatitis C virus (genotype 3), HIV infection
	Dietary/gut-related causes	Acute weight loss (bariatric surgery, starvation), malnutrition, total parenteral nutrition, short bowel syndrome, small intestinal bacterial overgrowth and microbiome changes, celiac disease, inflammatory bowel diseases, pancreatectomy
	Pregnancy-related diseases	Acute fatty liver of pregnancy
	Endocrine disorders	Hypothyroidism, polycystic ovary syndrome, hypothalamic/pituitary dysfunction, growth hormone deficiency

albumin in NAFLD patients to assess their liver condition (to detect signs of inflammation, cholestasis, decreased function) [74–76].

Grade of recommendation — C;
level of evidence — 5.

Comments. A blood chemistry test may show increased activity of serum transaminases (ALT and AST), GGT (an increase in the activity of this enzyme may be isolated), ALP and bilirubin levels. A number of major clinical studies have shown that the correlation between increased ALT activity and severity of the inflammatory response and liver fibrosis is not always evident [77]. *In NAFLD, serum transaminase activity usually does not exceed the upper limit of normal values (ULN) by more than 4–5 times. Both ALT and AST may predominate, but the AST/ALT ratio does not exceed 1.3* [78]. *Taking this ratio into account may be useful in making a differential diagnosis with the alcoholic liver disease (the AST/ALT ratio in the latter is usually higher than 2). GGT activity in patients may be elevated, but usually by no more than 2–3 times, and in some of them this may be the only deviation in the blood chemistry test. ALP activity increases less frequently and usually does not exceed normal values by more than 2 times* [75].

• It is recommended to determine the level of blood glucose and/or glycosylated hemoglobin (HbA1c) and/or perform a glucose tolerance test (GTT) in NAFLD patients to assess cardiometabolic risk factors [2].

Grade of recommendation — C;
level of evidence — 5.

• It is recommended to study the fasting plasma insulin level for calculation of the IR index (HOMA-IR), which serves as a clarifying study method in patients with suspected NAFLD in the absence of major cardiometabolic risk factors [2].

Grade of recommendation — C;
level of evidence — 5.

Comments. According to NAFLD diagnosing rules, cardiometabolic risk factors include fasting blood (plasma) glucose ≥ 5.6 mmol/L (100 mg/dL) or glycemia ≥ 7.8 mmol/L (≥ 140 mg/dL) in a glucose tolerance test or HbA1c ≥ 5.7 % (39 mmol/L) [2]. *It is reasonable to screen NAFLD patients for type 2 DM and other carbohydrate metabolism disorders by determining fasting blood (plasma) glucose or glycated hemoglobin or by performing an OGTT with 75 g of glucose pursuant to the values and rules given in the CPG "Type 2 Diabetes Mellitus in Adults"* [79]. *To assess IR, the HOMA-IR index is used, calculated using the formula: HOMA-IR = fasting plasma insulin (mcD/mL) × fasting plasma glucose (mmol/L) / 22.5. A HOMA-IR value ≥ 2.5 indicates the presence of IR. It should be kept in mind that the diagnostic value of the index in patients with overt diabetes is reduced* [2, 80].

• A recommended blood test for assessment of lipid metabolism disorders includes biochemical total cholesterol, low-density lipoprotein cholesterol (LDL), HDL cholesterol, TG) in NAFLD patients for assessing cardiometabolic risk factors and stratifying the risk of cardiovascular complications [2, 81, 82].

Grade of recommendation — C;
level of evidence — 4.

Comments. According to the NAFLD diagnosing rules, cardiometabolic risk factors include increase in TG content ≥ 1.70 mmol/L or ≥ 150 mg/dL, a decrease in HDL cholesterol level ≤ 1.0 mmol/L (≤ 40 mg/dL) in men and ≤ 1.3 mmol/L (50 mg/dL) in women [2]. *For NAFLD patients it is necessary to analyze total cholesterol, LDL cholesterol, and HDL cholesterol to stratify the risk of cardiovascular complications according to the CPG "Lipid Metabolism Disorders"* [83].

• It is recommended to make a coagulogram study (an indicative study of the hemostasis system) (international normalized ratio, prothrombin index, prothrombin time, activated partial thromboplastin time, fibrinogen) for assessing the coagulation status and liver function in NAFLD patients at the cirrhotic stage [84–89].

Grade of recommendation — C;
level of evidence — 4.

• For NAFLD patients at any stage of the disease it is recommended to make a general (clinical) urine analysis with a semi-quantitative determination of albumin/protein in the urine for CKD screening for assessing the presence of urinary sediment so as to exclude urinary infection [90, 91].

Grade of recommendation — B;
level of evidence — 2.

• For NAFLD patients at any stage of the disease it is recommended to test the blood creatinine level for CKD screening [90, 91].

Grade of recommendation — B;
level of evidence — 2.

Comments. The CKD prevalence is estimated to be 20–55 % in patients with NAFLD compared with 5–30 % in patients without NAFLD. There is increasing evidence indicating an association between NAFLD and CKD due to common risk factors for their

development, although there is evidence of an independent association between these conditions. If CKD signs are detected according to screening tests, further examination of patients is made in accordance with the CPG "Chronic Kidney Disease in Adults" [92]. *Patients with NAFLD and type 2 DM are prone to developing urinary infections* [92, 93].

• For NAFLD patients at any stage of the disease it is recommended to test serum uric acid for excluding/assessing the severity of hyperuricemia [94, 95].

Grade of recommendation — B;
level of evidence — 2.

Comments. Uric acid plays a certain role as a predictor of NAFLD development. Its level has an independent correlation with NAFLD. Also, elevated uric acid levels are associated with obesity, IR, liver damage severity and the risk of more severe NAFLD. As a marker of hyperuricemia, it is advisable to consider the level of uric acid above 360 umol/L [93].

• It is recommended to study markers of hepatitis B and C viruses: detection of Hepatitis B virus antigen (HBsAg) in the blood, qualitative testing; detection of antibodies to the Hepatitis C virus in the blood (anti-HCV IgG and anti-HCV IgM), testing of the immunoglobulin G level in the blood (IgG), blood serum transferrin, ceruloplasmin in the blood, as screening indicators for patients with suspected NAFLD to exclude other etiologic factors of liver disease [1, 75].

Grade of recommendation — C;
level of evidence — 5.

Comments. In clinical practice, other liver diseases that are more common in the adult population should be always ruled out. These include chronic Hepatitis B and C, HBsAg and total antibodies to the Hepatitis C virus (anti-HCV IgG and anti-HCV IgM) serving respectively as the screening tests; autoimmune hepatitis (screening tests: an assay of the class G immunoglobulins or gamma globulins in the blood serum, an increase in their values being significant); hereditary hemochromatosis (screening test: an increased proportion of transferrin saturation with iron > 45 %); Wilson's disease (screening test: a decrease in serum ceruloplasmin < 20 mg/dL) [96–98].

2.4. Instrumental diagnostic testing

• For NAFLD patients it is recommended to conduct an ultrasound examination (US) of the abdominal organs (comprehensive) for determining the liver size and ultrasound characteristics, in particular, its echogenicity for the diagnosis of steatosis, identifying signs of portal hypertension (detection of ascites, measurement of the portal and splenic vein diameter, spleen size), ruling out focal liver lesions, and assessing the patency of liver vessels [99, 100].

Grade of recommendation — C;
level of evidence — 5.

Diagnosis of steatosis

• For patients with suspected NAFLD, in clinical practice it is recommended to perform ultrasound examination of abdominal organs (comprehensive) as a first-line tool for detecting steatosis [99–101].

Grade of recommendation — B;
level of evidence — 2.

Comments. The following signs may be considered as ultrasound signs of NAFLD:

· diffuse hyperechogenicity of the liver parenchyma and heterogeneity of its structure;

· blurring and/or accentuation of the vascular pattern;

· distal echo signal attenuation [99, 100].

Most often, conventional transabdominal ultrasound is used in the diagnosis of hepatic steatosis, being widely available, harmless, inexpensive and having a good reputation. In a meta-analysis of 34 studies (2,815 patients with suspected liver disease), the pooled sensitivity and specificity of ultrasound in detecting steatosis were 85 % (95 % CI: 80–89 %) and 94 % (95 % CI: 87–97 %), respectively (compared with liver biopsy results). The main limitations of ultrasound are that it can only detect steatosis with fat accumulation greater than 12.5–20 %, its accuracy is reduced in obese patients and to some degree depends on the operator's experience [101]. *Nevertheless, ultrasound remains the most widely used and accepted method for detecting steatosis* [102].

• As a second-line tool for confirming liver steatosis, as well as for its quantitative assessment in patients with suspected NAFLD, it is recommended to evaluate the ultrasound Controlled Attenuation Parameter (CAP) in specialized health care facilities (HCF), if this method is available [103, 104].

Grade of recommendation — A;
level of evidence — 2.

Comments. A quantitative assessment of steatosis by measuring the attenuation of an ultrasound echo wave was made on the FibroScan device and is called the "controlled attenuation parameter" (CAP). This method has high sensitivity and specificity, particularly in detecting

minimal and moderate steatosis. In severe steatosis, the results were more heterogeneous affected by age, increased BMI, and differences in determining the cutoff value [104]. *A meta-analysis of 16 studies with individual data from 2,346 patients compared the results of quantitative steatosis assessment using the CAP method with histological data. For patients with obesity and excess subcutaneous fat, it is important to use an appropriate probe for the examination. An M or XL probe was selected according to the developed rules. An XL probe was recommended for 1,050 patients, 930 (89 %) of whom had NAFLD; the result turned out to be good for distinguishing any grade of steatosis from no steatosis (AUROC 0.819; 95 % CI: 0.769–0.869), however, it was suboptimal for distinguishing between mild and higher grade steatosis (S0–S1 vs. S2–S3; AUROC 0.754; 95 % CI: 0.720–0.787). According to this meta-analysis, the optimal cut-off value (according to the Youden index) for detecting steatosis per se in NAFLD patients is 294 dB/m (sensitivity 0.790, specificity 0.740)* [103]. *CAP is a high-potential method for rapid and standardized detection of steatosis using the XL probe. However, for its quantitative assessment it is inferior to magnetic resonance imaging (MRI-PDFF).*

• Magnetic resonance imaging of the abdominal organs (with assessment of liver fat fraction — MRI-PDFF) is recommended as a second-line tool to confirm liver steatosis, and for its quantitative assessment in patients with suspected NAFLD in specialized healthcare facilities, if this method is available [105].

Grade of recommendation — A;
level of evidence — 1.

Comments. The quantitative MRI-PDFF method allows to estimate the amount of fat in the liver. The most accurate result is obtained with the value of the proton density fat fraction (PDFF). It is the PDFF value that corresponds with high accuracy to the quantitative and volumetric content of fat in the liver. In a recent meta-analysis (6 studies involving 635 patients with histologically confirmed NAFLD), for MRI-PDFF, the pooled AUROC values for steatosis > 5 %, > 33 %, > 66 % were 0.98, 0.91, and 0.90, respectively. The overall sensitivity and specificity were 93 and 94 %, 74 and 90 %, 74 and 87 %, respectively. [105]. *Despite the high accuracy of MRI-PDFF in quantitative assessment of steatosis, the high cost and restricted availability of this method limit its use in widespread clinical practice.*

Diagnosis of steatohepatitis

• A liver biopsy (percutaneous puncture or laparoscopic) is recommended in patients with NAFLD and suspected NASH, as well as in diagnostically unclear cases, followed by a pathological examination of the biopsy (surgical) material to determine signs of inflammation (steatosis, ballooning degeneration, lobular inflammation). Morphological examination of liver tissue also assesses the degree of steatosis and fibrosis [75, 106].

Grade of recommendation — C;
level of evidence — 5.

Comments. Currently, there are no non-invasive methods for diagnosing steatohepatitis (inflammation), liver biopsy being the gold standard. To establish the NASH diagnosis, a histological examination of liver tissue, as well as simultaneous detection of steatosis, ballooning degeneration and lobular inflammation are necessary [107–110]. *Other histological changes are possible; however, they are not considered essential for diagnosis (portal inflammation, polymorphonuclear infiltrates, Mallory-Denk bodies, apoptotic bodies, clear vacuolated nuclei, microvesicular steatosis, and megamitochondria). Perisinusoidal and pericentral fibroses are also common but are not part of the diagnostic criteria; as for the term "borderline NASH", it is not quite clear and should not be used. The term "burned-out NASH" describes regression of a severe disease form (steatosis, inflammation, or ballooning) in patients with MetS risk factors. All other methods, such as CK-18 (cytokeratin 18), combinations of clinical variables, combination of clinical variables with the PNPLA3 I148M variant, etc., as well as imaging methods proposed for non-invasive diagnosis of NASH, do not reflect inflammation and are not recommended for use in clinical practice for this purpose, since they have either conflicting results, or an insufficient number of confirmatory studies, or the difficulty in obtaining some variables for wide and easy reproduction* [106].

Therefore, liver biopsy currently remains the reference standard for diagnosing NASH in patients with NAFLD. In addition to determining such NAFLD characteristics as the presence of steatosis, fibrosis stage, severity of lobular inflammation, liver biopsy in some cases allows to identify/rule out other causes of liver damage. In 2005, the NAFLD activity score (NAS) was proposed for assessing NAFLD based on the consensus of expert morphologists (CRN). It is

a modification of the previously used Brunt and Matteoni scales of 1999 and assesses the degree of morphological changes in scores (from 0 to 8): severity of liver steatosis, intralobular (lobular) inflammation, ballooning degeneration of hepatocytes and fibrosis stage [110] (Appendix D1). This scale can also be used to assess the effectiveness of NAFLD treatment, since it determines the reliability of the dynamics of morphological changes on treatment over a relatively short period of time [77, 111].

In 2012, the SAF (Steatosis, Activity, and Fibrosis) system was proposed and later validated (2014) for histological assessment of the liver condition in morbid obesity. It includes such characteristics as the steatosis severity (S — steatosis), ballooning dystrophy and lobular inflammation (A — activity) and liver fibrosis stage (F — fibrosis), see Appendix D2 (the assessment result is recorded in the form of the index S1A2F3, S2A1F1, etc.) [109]. *The SAF assessment system has been further developed and allows the use of the FLIP (Fatty liver inhibition of progression) algorithm, aimed at standardizing and improving the quality of morphological diagnostics* [109].

In the absence of a histological examination of liver tissue, but with convincing non-invasive data on the progressive course of the disease (for example, increased surrogate markers of inflammation — transaminases, data from non-invasive methods indicating fibrosis, etc.), it is acceptable, according to experts, to establish a diagnosis of "probable NASH".

Diagnosis of fibrosis

• In widespread clinical practice, the use of non-invasive, non-proprietary tests NFS (NAFLD Fibrosis Score) and FIB-4 (Fibrosis-4 index) is recommended for NAFLD patients to rule out severe fibrosis and cirrhosis [112].

Grade of recommendation — B;
level of evidence — 2.

Comments. The most proven and reliable among the non-proprietary (freely available) tests are NFS and FIB-4. In clinical practice, the following cutoff values (points) are used to decide whether a patient with NAFLD has severe fibrosis or not: 1.3 for FIB-4 and –1.455 for NFS (high sensitivity), 3.25 for FIB-4 and 0.676 for NFS (high specificity).

NFS and FIB-4 have the following advantages: 1) both tests are based on simple variables which are widely available in clinical practice; 2) their results can be easily obtained at the bedside using free online calculators; 3) they have good overall diagnostic accuracy for severe fibrosis, as demonstrated by a meta-analysis (36 studies involving 9,074 patients) — AUROC 0.80 for FIB-4 and 0.78 for NFS, respectively, NPV is ≥ 90 % [112]. *The disadvantages of NFS and FIB-4 include: 1) risk of obtaining false positive criteria for severe fibrosis: PPV < 70 %; 2) an inconclusive result in 1/3 of cases (between the upper and lower threshold values); 3) presumable effect of old age on diagnostic accuracy. This problem was solved by adopting a higher threshold for people aged 65 years and older: 2.0 for FIB-4 and 0.12 for NFS* [113]. *The informative value of calculation indices in older individuals and those with DM is probably lower* [114].

• The use of noninvasive proprietary tests such as FibroTest® is recommended for NAFLD patients to exclude severe fibrosis, when available [112, 115, 116].

Grade of recommendation — B;
level of evidence — 2.

Comments. Among the proprietary serum markers of fibrosis, the most common are FibroMeterTM, FibroTest® and ELFTM. Of all those listed, only FibroTest® is currently available in the Russian Federation. Generally, the diagnostic accuracy of proprietary noninvasive serum tests (FibroMeterTM, FibroTest® and ELFTM) for the diagnosis of fibrosis is satisfactory, but their widespread use in clinical practice is limited by high cost and limited availability [102, 112, 115, 116].

• Transient liver elastography is recommended for NAFLD patients to assess the fibrosis stage and exclude severe fibrosis/cirrhosis in specialized healthcare facilities, when available [112].

Grade of recommendation — B;
level of evidence — 2.

Comments. Transient elastography is the most widely used test to determine liver tissue stiffness with the largest data volume for NAFLD patients. A large meta-analysis (17 studies using an M-sensor and including 2,642 patients; 3 studies using an XL-sensor and including 318 patients) reported good diagnostic accuracy of this method for detecting severe fibrosis, i.e. stage 3 fibrosis (AUC 0.87 for the M-sensor and 0.86 for the XL-sensor) and cirrhosis (AUC 0.92 for the M-sensor and 0.94 for the XL-sensor) [112]. *In clinical practice, there is a lack of complete agreement regarding threshold values of liver tissue stiffness for the diagnosis of severe fibrosis in NAFLD. According to the latest data, the value ≥ 8 kPa is proposed, the*

sensitivity is 93 % [117]. *The result of transient elastography may be influenced by a number of factors, such as the activity of inflammation (the result is unreliable with high ALT levels).*

• For NAFLD patients it is recommended to use shear wave ultrasound elastography of the liver as part of an ultrasound examination for the assessment of liver tissue stiffness, when transient elastography is unavailable [102, 112].

Grade of recommendation — B; level of evidence — 2.

Comments. Measurement of liver tissue stiffness using shear wave techniques, which are available on modern ultrasound machines, is comparable in accuracy to transient elastography, but data for NAFLD patients are limited. The most accurate results for determining tissue stiffness are obtained using magnetic resonance elastography, but this method is expensive, has limited availability, and is used primarily in clinical trials.

• Esophagogastroduodenoscopy (EGDS) is recommended for NAFLD patients with severe fibrosis/LC to determine signs of portal hypertension (gastric and esophageal varices, signs of portal gastropathy) [118].

Grade of recommendation — C; level of evidence — 5.

3. Treatment, including pharmacological and non-pharmacological therapy, diet therapy, pain relief, medical indications and contraindications for the use of treatment modes

Treatment of NAFLD should pursue two goals:

1) prevention of liver disease progression, regression of steatosis, steatohepatitis and fibrosis;

2) reduction of cardiometabolic risk factors.

Essentially, treatment of NAFLD is divided into non-pharmacological measures (diet and physical activity) and pharmacotherapy.

3.1. Non-pharmacological therapy for NAFLD

3.1.1. Physical activity

• NAFLD patients are recommended to have regular physical activity for reducing liver fat [119, 120].

Grade of recommendation — B; level of evidence — 2.

Comments. The World Health Organization (WHO) has developed physical activity recommendations for adults to prevent a number of diseases, including those associated with NAFLD [119]. *To reduce liver fat, NAFLD patients are advised to engage in at least 150–300 minutes of moderate-intensity aerobic physical activity per week, or at least 75–150 minutes of vigorous-intensity aerobic physical activity per week, or a combination of moderate- and vigorous-intensity physical activity during the week. At least twice a week, it is recommended to supplement aerobic exercise with physical activity of medium or vigorous intensity (strength exercises) aimed at all muscle groups* [119, 120]. *Intensity is the pace at which physical activity is performed or the amount of effort required to perform an activity or exercise per unit of time (e.g. walking speed of 5 km/h). It can be described as follows: how hard a person works to perform a certain activity.*

Moderate-intensity physical activity increases the heart rate, but a person can comfortably engage in conversation while doing it. Examples: brisk walking, dancing, gardening, housework, active games and sports with children, walking with pets, etc.

Vigorous-intensity physical activity (such as running, aerobic exercise, distance swimming, fast cycling, climbing hills, etc.) significantly increases the heart rate, breathing rate, and causes sweating [119].

• Recommendations for physical activity should take into account a patient's specifics in terms of physical fitness and comorbidities. Since 95 % of NAFLD patients are overweight or obese, it is useful to consider the provisions of the CPG "Obesity" [121].

Systematic reviews and meta-analyses have found that physical exercise reduces liver fat even in the absence of significant weight loss [120, 122–125]. A study involving 115 patients with NAFLD and prediabetes reported that intense aerobic exercise 2–3 times a week for 30–60 min for 6 months or more resulted in a 24.4 % reduction in liver fat content [126]. A systematic review shows effectiveness of aerobic and muscle-strengthening exercises 3 times per week for 12 weeks in reducing liver fat in NAFLD patients [122]. A study of NAFLD patients with liver fat content assessment using MRI and spectroscopy, reported that vigorous-intensity aerobic exercise (a bicycle ergometer for 30–40 minutes 3 times a week) significantly reduced liver fat content compared to controls (individuals with a sedentary lifestyle) [127, 128].

• For patients who have difficulty performing aerobic activity (e.g., individuals with poor cardiorespiratory performance), muscle-strengthening exercises (resistance exercises) may be

recommended, which may also improve lipid metabolism and result in a more favourable course of NAFLD [122]. In general, patients should be encouraged to engage in as much physical activity as possible. Optimal physical activity in terms of duration and intensity should be chosen on an individual basis [129].

3.1.2. Diet

Dietary changes remain the most effective non-drug intervention for both NAFLD treatment and weight loss.

• NAFLD patients are recommended to follow a balanced diet with adherence to the principles of the Mediterranean type diet for reducing liver fat content [130–132].

Grade of recommendation — B;
level of evidence — 2.

Comments. The Mediterranean diet is a scientific concept that primarily involves the composition of macronutrients (carbohydrates 50–60 %, fats 30 %, proteins 20 %) and a balanced approach. This type of diet contains a large amount of natural antioxidants, biological components with anti-inflammatory activity and has a low glycemic index. The Mediterranean diet uses olive oil as the main source of fat and is characterized by intake of large amounts of vegetables, fruits and nuts, legumes, whole grains, fish and seafood, while having a low intake of dairy products, meat and meat products. Molecular mechanisms of beneficial effects on human health have been demonstrated for such components of the Mediterranean diet as polyphenols, carotenoids, oleic acid, polyunsaturated fatty acids (PUFA), dietary fiber, quercetin [130, 133]. *Two cross-sectional studies have reported that adherence to the Mediterranean diet is inversely associated with the risk of developing NAFLD and NASH* [134, 135].

A randomized crossover study showed that 6 weeks of the Mediterranean diet compared with a standard low-fat, high-carbohydrate diet reduced liver fat by 39 % versus 7 %, respectively, with HOMA-IR also decreased, regardless of changes in body weight [136]. *Adherence to the Mediterranean diet is one of the independent prognostic factors that positively influence the severity of NAFLD* [137]. *The advantage of this diet type is the ability to follow it without harm to health for an unlimited period of time and adapt it to any geographic region and the patient's personal food preferences* [129].

• NAFLD patients are advised to avoid foods containing added fructose to reduce fat accumulation in the liver [138, 139].

Grade of recommendation — B;
level of evidence — 2.

Comments. Consuming added fructose (found primarily in sweetened beverages) contributes to the development of NAFLD. Meta-analyses of controlled trials report that added fructose intake results in significant increases in liver fat and ALT. The negative effect of added fructose may be partly associated with the increased caloric content of the diet. No negative impact on NAFLD of natural sources of fructose (honey, fruits, dried fruits) has been established, provided that adequate energy value of the diet is observed [138, 139].

• According to WHO guidelines regular physical activity is recommended for NAFLD patients without overweight/obesity [119], as well as balanced diet following the principles of the Mediterranean type of nutrition to reduce IR, prevent CVD and sarcopenia, and reduce visceral fat [130, 140].

Grade of recommendation — B;
level of evidence — 3.

Comments. Managing NAFLD patients with normal body weight presents a clinical challenge. In these cases, a thorough differential diagnosis should be performed to rule out rare causes of fatty liver disease (monogenic diseases, drug effects, etc.). The general recommendation to reduce body weight is for the most part unacceptable for such cases, although a randomized controlled trial (RCT) reported that lifestyle changes ensured NAFLD remission in patients with normal body weight with a reduction in body weight of 3–5 % [1, 141, 142]. *Dietary changes and exercise in this group of patients may be beneficial for reducing IR, increasing muscle mass, and preventing CVD and its complications. These patients are advised to reduce their intake of alcohol, added fructose, saturated fats, simple carbohydrates, and ultra-processed foods* [143].

• NAFLD patients are recommended to abstain from any amount of alcohol to prevent fat accumulation and progression of liver fibrosis [144].

Grade of recommendation — B;
level of evidence — 3.

Comments. Currently, it is a generally known fact that alcohol consumption in doses exceeding 20 and 30 g of ethanol per day for women and men, respectively, results in steatosis,

steatohepatitis and liver fibrosis in addition to cardiometabolic risk factors. Moreover, alcohol consumption can act as a major factor causing the development of alcoholic fatty liver disease and also can be an additional link potentiating the disease progression [145, 146]. *This was clearly demonstrated in a systematic review, the authors of which also came to the conclusion that any doses of alcohol, even conditionally safe ones, affect the disease progression* [144].

Weight loss recommendations for obese patients are presented in section 3.3.2 "Treatment of NAFLD in combination with obesity".

3.2. Pharmacological therapy for NAFLD

Currently, despite the progress made in understanding the pathogenesis, clinical course and prognosis of NAFLD, issues of pharmacological therapy of this disease are still being discussed and studies are being conducted on drugs targeting different metabolic pathways: regulation of carbohydrate and lipid metabolism, the thyroid pathway, autophagy and apoptosis, etc. The main targets in NAFLD treatment are steatosis (serving as an independent factor of cardiometabolic risk), inflammation and fibrosis [147, 148]. All NAFLD phenotypes are associated with an increased risk of developing CVD, endocrine pathology and other metabolic disorders [149]. A characteristic feature of NAFLD is its multisystemic nature and comorbidity, which affects therapeutic approaches. Based on this, two main goals of NAFLD therapy can be formulated:

1) reduction of lipid content in hepatocytes, reduction of inflammatory activity, prevention of development/slowing down of fibrosis progression;

2) reduction of cardiometabolic risks associated with excess lipids in hepatocytes and/or inflammation and/or fibrosis.

Accordingly, the optimal drug should contribute to simultaneous achievement of these goals, ensure cost optimization and have a high safety profile.

Various medications used for NAFLD treatment can be conditionally classified into two groups:

1) drugs with a hepatotropic effect, including those with a registered indication for NAFLD; some of them have a pluripotential effect and simultaneously influence the cardiovascular system, lipid and carbohydrate metabolism;

2) drugs registered for the treatment of comorbid conditions typical for NAFLD with an additional hepatotropic effect. For example, statins — HMG-CoA reductase inhibitors — for the treatment of hypercholesterolemia and dyslipidemia; glucagon-like peptide-1 (GLP-1) analogues (liraglutide, semaglutide**) and sodium-glucose cotransporter-2 inhibitors (dapagliflozin**, empagliflozin**, ipragliflozin**) — for the treatment of type 2 diabetes.

This section discusses hepatotropic drugs (group 1 drugs). The use of group 2 drugs is described in the section on the treatment of comorbid conditions. The effectiveness of hepatotropic drugs is assessed primarily by the dynamics of the ALT level (a surrogate marker of inflammation), as well as using non-invasive methods that semi-quantitatively or quantitatively assess liver fat content — CAP or MRI-PDFF (if available), with the use of non-invasive methods for assessing fibrosis (calculated indices, elastography) (*see Section 2 "Diagnosis of a disease or condition"*).

Serum transaminases (ALT and AST) serve as a simple and reliable laboratory indicator of hepatocellular damage (inflammation); their reduction is used as a benchmark when assessing the effectiveness of treatment for patients with any liver damage etiology. ALT is more specific for hepatocyte damage as compared to AST [150]. A positive correlation has been proven between the level of serum transaminases and mortality from diseases of the digestive system (89 % of which are liver diseases), cancer and CVD [151, 152]. An increase in ALT > 30 U/L in men and > 19 U/L in women correlate with increased mortality from liver diseases and diabetes [150, 153]. According to the Framingham risk score, NAFLD patients with elevated serum ALT have an increased estimated risk of coronary heart disease (CHD), this particularly applies to women [154].

Currently, there are only a few studies on NAFLD treatment that include analysis of histological data before and after treatment (paired biopsies) and almost no studies assessing the long-term course of the disease based on "hard" endpoints (life expectancy, mortality, etc.). At the same time, a large number of randomized and observational studies, as well as their meta-analyses, have been conducted in which the effectiveness of pharmacotherapy for NAFLD was assessed using surrogate markers of inflammation (serum transaminase levels, GGT) and fibrosis. This may be explained by the fact that liver biopsy is an invasive, expensive and not widely available procedure. In clinical practice, the effectiveness of liver disease therapy is assessed by the dynamics of ALT levels (a surrogate marker

of inflammation), and modern non-invasive techniques make it possible to assess the dynamics of steatosis and fibrosis [1]. The choice of drug for NAFLD treatment depends on clinical manifestations of the disease, its phenotype and course characteristics, and is determined by the attending physician for each patient individually.

• Pharmacological therapy of NAFLD is recommended in combination with lifestyle changes (physical activity and proper diet), especially in the case of their insufficient effectiveness, obstacles to implementation and/or progressive course of the disease [155, 156].

Grade of recommendation — B; level of evidence — 1.

Comments. Lifestyle changes (physical activity and proper diet) form the basis for NAFLD treatment. Research shows that < 10 % of patients achieve weight loss within a year with a structured approach to physical activity, and less than half of them maintain weight loss within 5 years [157]. *In addition, meta-analyses in recent years indicate uncertainty about the impact of lifestyle interventions in NAFLD patients on long-term prognosis and disease outcomes due to the relatively short (max. 2 years) duration of the studies and their heterogeneity* [155, 156, 158].

• Ursodeoxycholic acid (UDCA)** at a dose of 13–15 mg/kg/day is recommended for NAFLD patients to reduce the lipid content in hepatocytes, reduce inflammation and prevent the progression of fibrosis [159, 160].

Grade of recommendation — B; level of evidence — 1.

*Comments. A clinical study reports that the use of UDCA** at a daily dose of 13–15 mg/kg of body weight for 12 months in patients with histologically proven NASH and paired liver biopsies resulted in a statistically significant reduction in liver steatosis severity and a decrease in the levels of ALT, AST, GGT and ALP as compared to the control group* [161]. *Similar data were demonstrated in another study with a 6-month use of UDCA**** [162].

*In one of the studies, high-dose UDCA** (#28–35 mg/kg/day, a dose higher than the labelled dose) for 12 months in patients with biopsy-proven NASH resulted in a significant reduction in ALT levels: by the end of the study, normalization of this indicator was observed in every fifth patient and only in about every twentieth patient in the placebo group. The results did not depend on the dynamics of the patients' body weight. Also, in the UDCA** group, a significant decrease in FibroTest® values was observed compared to placebo (potential antifibrotic effect). No serious adverse events were observed* [163].

*According to a domestic meta-analysis conducted in 2018 based on 4 studies with a total sample size of 510 people, UDCA** in NAFLD had a high safety profile, while the effect on the histological and biochemical parameters of the disease was not proven* [164]. *However, a systematic review and two later meta-analyses reported that UDCA** resulted in a decrease in serum transaminases (ALT, AST) and GGT and also reduced liver steatosis* [159, 165, 166]. *Prospective observational multicenter non-comparative study "SUCCESS" carried out in real clinical practice showed that treatment with UDCA** at a dose of 15 mg/kg of body weight for 6 months in NAFLD patients led to a statistically significant ($p < 0.001$) decrease in the activity of ALT, AST, GGT, concentration of total cholesterol, TG, LDL in the blood, and liver steatosis index FLI (Fatty Liver Index). No progression of fibrosis, as assessed by the NFS index, was observed* [167].

*Molecular studies have shown that UDCA** exerts its effect on reducing liver steatosis and inflammation through modulation of the autophagy effect, being a stimulator of one of the main intracellular sensors of homeostasis — AMPK* [168], *the activity of which is reduced in liver steatosis* [25]. *In NAFLD patients, stimulation of lipophagy and mitophagy by UDCA** results in a reduction of liver fat, lipotoxicity and, consequently, inflammation. Autophagy is closely linked to apoptosis via Bcl-2/beclin-1 proteins, and the antiapoptotic effect of UDCA** is well known* [169]. *Reducing steatosis and inflammation prevents the development and progression of fibrosis. In preclinical studies, UDCA** has been shown to reduce the severity of liver steatosis also as a TGR5 ligand* [170]. *An experimental study on a NAFLD model proved that UDCA** was capable of preventing the development of both steatosis and fibrosis without having a significant effect on ballooning degeneration of hepatocytes. UDCA** helps to reduce lipogenesis in the liver, increases tissue sensitivity to insulin, restores the synthesis of bile acids and is involved in the positive modulation of the activity of the bile acid receptor GPBAR1* [171].

*The recommended duration of UDCA administration** is at least 6 months; the optimal dose used in most clinical studies is 13–15 mg/kg/day.*

• It is recommended to prescribe #Alpha-tocopherol acetate (vitamin E) at a dose of 800 international units (IU) per day to NAFLD patients with a proven progressive course of the disease (fibrosis F2 and higher) to reduce the severity of steatosis and inflammation, and to slow down the disease progression [172–176].

Grade of recommendation – A; level of evidence – 1.

Comments. #Vitamin E is used for NAFLD treatment in patients with histologically confirmed progressive NASH and is included in a number of CPG for the management of NAFLD patients, which are based on the results of the randomized PIVENS trial [1, 177–180]. *#Vitamin E at a dose of 800 IU/day was administered for 22 months and was superior to placebo in NASH patients in terms of its effect on steatosis, inflammation and ballooning degeneration, but had no significant effect on fibrosis* [172]. *In cases where NASH was combined with type 2 DM, only the combination of #vitamin E (800 IU/day) with #pioglitazone (45 mg/day) for 18 months had an effect on histological activity; no effect on fibrosis was noted either* [173]. *A large controlled study demonstrated a reduced risk of death or need for liver transplantation, and disease decompensation with administration of #vitamin E at a dose of 800 IU/day for more than 2 years in patients with histologically proven NASH and advanced stages of the disease (bridging fibrosis, cirrhosis). The average duration of patients' follow-up was 5.6 years* [176]. *According to meta-analyses, #vitamin E improves laboratory parameters and reduces histological manifestations of steatosis and inflammation* [174, 175].

A potential safety concern with administering high doses of vitamin E – an increase in all-cause mortality and hemorrhagic stroke – was identified in meta-analyses published in 2005 and 2013 [181, 182], *however, these findings were not confirmed in a later meta-analysis of 2014* [183]. *The relationship between #vitamin E intake and an increased risk of developing prostate cancer in men is also being discussed* [184]. *However, all of these studies have not evaluated vitamin E safety specifically in patients with NAFLD.*

*In addition, the possible interaction of high doses of #vitamin E (> 300 mg/day) with concomitantly administered acetylsalicylic acid**, warfarin**, tamoxifen**, and cyclosporine** with changes in their activity should be taken into account* [185]. *Accordingly, high doses of vitamin E should be administered with caution, taking into account the patient's drug history. Potential benefits of #vitamin E administration in patients with NAFLD and DM are being discussed* [56, 173]. *The recommended duration of treatment is at least 12 months.*

• Oral administration of ademetionine** at a dose of 10–25 mg/kg/day (but not more than 1600 mg/day) is recommended for patients with NAFLD and complaints of weakness/fatigue for its correction [186, 187].

Grade of recommendation – B; level of evidence – 2.

*Comments. Hepatogenic weakness/fatigue is a symptom affecting patients' quality of life and limiting their compliance with recommendations to increase physical activity. The effect of ademetionine** on hepatogenic weakness/fatigue in various liver diseases, including NAFLD, has been shown in systematic reviews and meta-analyses* [186, 187]. *A reduced proportion of patients with hepatogenic weakness/fatigue with the use of the drug was observed in a single-center comparative study in NASH patients and in a multicenter prospective non-comparative observational study in NAFLD patients in routine practice* [188, 189]. *A diminished weakness/fatigue is observed with a short-term (2–4 weeks) use of ademetionine**, while an extended duration of the course increases the proportion of patients with a reduction in this symptom* [186, 187]. *The recommended duration of treatment is at least 4 weeks.*

• Administration of bicyclol is recommended at a dose of 75–150 mg/day for 24 weeks to patients with NAFLD (NASH) with moderate and severe increase in ALT levels (> 3 and > 5 ULN, respectively) to reduce disease activity [190, 191].

Grade of recommendation – B; level of evidence – 1.

Comments. In preclinical studies, bicyclol prevented the increase in transaminase levels, accumulation of lipids in liver tissue and fibrogenesis by inhibiting inflammatory and oxidative stress signaling pathways in a high-fat diet [192–194].

According to a meta-analysis comprising 12 NAFLD studies with a total sample size of 1,008 people, bicyclol as monotherapy and in combination with other drugs had a positive effect on laboratory parameters of inflammatory activity and lipid metabolism, stimulating decreases levels of ALT, AST, TG and cholesterol [190].

Similar results were obtained in a cohort study involving 93 people, where, according to fibroelastometry data, a decrease in fibrosis and steatosis signs was noted after 24 weeks of taking bicyclol, in addition to improving

laboratory parameters [195]. *An open, non-comparative observational study of 51 patients with chronic diffuse liver diseases of any etiology and elevated serum transaminase levels (including 29 NAFLD patients) demonstrated that the use of bicyclol led to a decrease/normalization of ALT levels, which statistically significantly decreased from baseline after just two weeks of treatment* [191]. *According to experts, a moderate increase in ALT is understood to be a range from 3- to 5-fold increase above the ULN, and a pronounced increase is more than 5-fold increase above the ULN. The recommended duration of treatment is no more than 24 weeks.*

• It is recommended to administer a fixed combination of "inosine + meglumine + methionine + nicotinamide + succinic acid**" at a dose of 400 mL/day to NAFLD patients at the hospital stage of treatment, including in the day hospital mode, for improving clinical symptoms and laboratory parameters [196, 197].

Grade of recommendation — C;
level of evidence — 3.

*Comments. The fixed combination of "inosine + meglumine + methionine + nicotinamide + succinic acid**" in the form of an infusion solution has a hepatotropic effect due to the ability of succinic acid to correct the phenomena of mitochondrial dysfunction developing in NAFLD, maintaining the activity of succinate dehydrogenase and increasing the production of macroergs. Methionine is an essential amino acid that plays a key role as a regulator of a number of cellular functions. Inosine is able to interact with adenosine A2a and A3 receptors with their subsequent activation, which leads to a decrease in hepatocyte damage by hypoxia and FFA, and also has a systemic anti-inflammatory effect by modulating the activity of NF-κB. Nicotinamide plays the role of a coenzyme of NAD-dependent enzyme systems, an acceptor and carrier of protons in the electron transport chain, thus indirectly stimulating the processes of cellular respiration, energy production, cellular regeneration, biosynthesis and metabolism of proteins, carbohydrates and lipids. In addition, nicotinamide is involved in ensuring sirtuin-mediated processes (DNA repair, mitochondrial biogenesis, apoptosis, inflammation). Meglumine, as a part of the drug, ensures better penetration of succinic acid through biomembranes* [196].

In small RCT, this combination drug (400 mL once a day for 10–11 days) in NASH patients resulted in improved laboratory parameters of cytolysis and cholestasis [198, 199]. *In a comparative study, the inclusion of such a fixed combination in the treatment regimen of patients with NAFLD in the form of steatohepatitis led to a more rapid relief of asthenovegetative and dyspeptic syndrome and a decreased severity of biochemical manifestations of cytolytic and cholestatic syndromes* [197].

*The fixed combination of "inosine + meglumine + methionine + nicotinamide + succinic acid**" is administered at 400 mL intravenously by drop infusion once a day for 10 days at the hospital stage of treatment. Indications for hospital treatment are set out in Section 6 "Organization of medical care".*

• Oral administration of ademetionine** at a dose of 10–25 mg/kg/day (max. 1600 mg/day) is recommended for patients with NAFLD in combination with secondary cholestasis for its correction [188].

Grade of recommendation — B;
level of evidence — 3.

Comments. According to studies evaluating the morphological features of NAFLD, histological signs of cholestasis in this disease occur in 27.0–30.1 % of cases, although they are much less often reflected in the laboratory cholestatic profile [200, 201]. *Secondary cholestasis in NAFLD indicates a more active course of the disease, development of its late stages and a worsening prognosis* [201, 202].

A reduced endogenous ademetionine synthesis in chronic liver disease and NAFLD contributes to the development of intrahepatic cholestasis by reducing the activity of the bile salt export pump (BSEP) and disrupting the integrity of hepatocyte membranes [203]. *Ademetionine** treatment for progressive NAFLD should be administered for at least 4 months, maximum duration of the course not being limited* [188]. *A two-stage treatment regimen is possible: parenteral administration at a dose of 5–12 mg/kg/day with a transition to oral administration at a dose of 10–25 mg/kg/day, but not more than 1600 mg/day.*

• Ornithine peroral administration at a dose of 9 g/day is recommended for NAFLD patients to correct hyperammonemia [204–207].

Grade of recommendation — C;
level of evidence — 5.

Comments. A study of liver biopsies from NAFLD patients demonstrated a significant decrease in the activity of urea and glutamine synthesis versus control [208], *and dysregulation of genes and expression of ornithine cycle proteins was established in experimental NASH models* [209]. *A significant proportion of patients*

at precirrhotic stages of NAFLD showed the development of hyperammonemia [206, 207, 210].

Of the ornithine preparations, the greatest evidence base is for ornithine (L-ornithine-L-aspartate (LOLA)) in oral form, which dissociates into its constituent amino acids and stimulates urea synthesis in periportal hepatocytes and glutamine formation in perivenous hepatocytes, skeletal muscles, and brain. *It is suggested that LOLA, in addition to its hypoammonemic effect in NAFLD, may exert beneficial effects via mechanisms of metabolic transformation into L-glutamine, L-arginine and glutathione, reducing lipid peroxidation, exerting an anti-inflammatory effect and improving portal hemodynamics* [204, 205].

In a parallel controlled clinical trial, 12 weeks of oral LOLA treatment resulted in dose-dependent improvements in liver laboratory parameters and imaging features in patients with NASH [211]. *Experimental results also suggest a direct beneficial effect of LOLA on skeletal muscles in NASH modelling: it prevents the development of myosteatosis and qualitative changes in muscles* [212] *and also allows for increased adaptation to physical activity in this pathology* [213]. *The recommended duration of treatment is at least 12 weeks.*

Combined use of hepatotropic drugs

There is a pathogenetic rationale for the joint use of a number of hepatotropic drugs in the form of both non-fixed and fixed combinations, which either expand the spectrum of their hepatotropic action or promote a unidirectional increase (additivity, summation, potentiation) of a particular pharmacological effect. Although the evidence level of most clinical studies is not very high, it may nevertheless serve as a rationale for choosing the combined use of a number of drugs in routine clinical practice [214]. In this case, only combinations studied in NAFLD or NASH should be used, taking into account additional indications and contraindications.

• It is recommended to add #Alpha-tocopherol acetate (vitamin E) to UDCA** therapy in NAFLD patients in case of insufficient effectiveness of UDCA** in order to reduce the inflammatory activity of the disease and steatosis severity [215, 216].

Grade of recommendation — B; level of evidence — 2.

*Comments. A comparative study demonstrated that the addition of vitamin E (800 IU/day) to UDCA treatment ** (12–15 mg/kg/day) in NASH patients for 2 years resulted in a statistically significant increase in blood adiponectin levels correlating with a decrease in the severity of liver steatosis* [217]. *The repeated biopsy analysis in another study showed that a decrease in the histological activity index with regression of liver steatosis occurred only with combination therapy with UDCA** and #vitamin E* [215]. *A long-term use (4 years, 1–12 year range) of a combination of UDCA** (average of 16.6 mg/kg/day) and #vitamin E (average of 555 IU/day) in NASH patients allowed to reduce ALT, AST and GGT in 65–80 % of patients and to achieve improvement in the histological liver pattern in the majority of patients with a low (5 %) number of side effects requiring drug discontinuation [216]. The recommended dose of the combination of #vitamin E and UDCA** drugs should not exceed maximum doses of the drugs prescribed separately: for #vitamin E — max. 800 IU/day, UDCA** — max. 10–15 mg/kg/day.*

3.3. Treatment of NAFLD and associated conditions

3.3.1. Treatment of NAFLD in combination with type 2 diabetes mellitus

• Normalization of body weight through lifestyle changes (dietary changes and increased physical activity) is recommended for patients with NAFLD and type 2 diabetes mellitus for improving tissue sensitivity to insulin and reducing liver fat content [79, 218].

Grade of recommendation — A; level of evidence — 2.

Comments. Lifestyle changes for the combination of type 2 DM and NAFLD should comply with the CPG "Type 2 Diabetes Mellitus in Adults" [79]. *Nutrition principles for NAFLD and type 2 DM are close and do not contradict each other. The degree of weight loss is associated with the degree of improvement in histological parameters of NAFLD and NASH. The 12-month prospective study demonstrated that all patients with the loss of more than 10 % of the body weight had an improvement in their histological NAS scores, with 90 % of patients showing resolution of NASH and 45 % showing regression of fibrosis* [219].

In addition to mere weight loss, adherence to a diet (with limited carbohydrate content and increased protein content) for 6 weeks allows for better glycemic control, leads to a decrease in serum TG levels, and reduces the severity of liver steatosis (assessed by MR spectroscopy) in patients with type 2 diabetes [218].

Given the fact that type 2 DM and NAFLD have common pathogenetic features, it is not surprising that some methods used for treating type 2 DM are also actively used in NAFLD treatment. Currently, numerous studies have been conducted aimed at finding a hypoglycemic drug that could affect pathological changes in NAFLD and NASH. Such a drug should lower body weight, reduce cardiovascular events, prevent the development of late NAFLD stages, and improve quality of life, while having a low cost and long-term safety.

• The use of glucagon-like peptide-1 (GLP-1) analogues (liraglutide (1.8–3.0 mg/day), semaglutide** (2.4 mg/week) is recommended for patients with NAFLD and type 2 DM in order to reduce body weight, decrease IR, and reduce laboratory parameters of inflammation [220–223].

Grade of recommendation — A;
level of evidence — 2.

Comments. Incretin mimetics, including glucagon-like peptide-1 analogues, are used for treatment of type 2 DM and obesity. They stimulate glucose-dependent insulin secretion, reduce de novo lipogenesis, and lead to a decrease in body weight, IR, and serum transaminase levels. The use of glucagon-like peptide-1 analogues is a very attractive and promising method for NAFLD treatment, but it is still unknown whether this group of drugs has a direct effect on hepatocytes, directly reducing hepatic steatosis and inflammation, or the effect is achieved through weight loss.

*#Liraglutide is one of the most studied drugs in this group for the treatment of patients with type 2 DM and NAFLD. According to the meta-analysis of 8 studies, this drug led to a decrease in both BMI and waist circumference, as well as liver fat content, which was assessed by non-invasive methods, and was superior in terms of the effects to other hypoglycemic drugs (#metformin**, insulins and their analogues, dipeptidyl peptidase-4 (DPP-4) inhibitors)* [220]. *Similar results were obtained in the systematic review with meta-analysis* [221]. *In addition, administering liraglutide contributed to a decreased level of serum transaminases and bilirubin, as well as an improvement in the non-invasive fibrosis index APRI (Aspartate Aminotransferase to Platelet Ratio Index)* [220].

*Studies have also been initiated on #semaglutide**, another drug from the group of glucagon-like peptide-1 analogues. Currently, phase II of the clinical trial of #semaglutide drug** in patients with NASH and fibrosis has been completed. #Semaglutide** has provided statistically significant regression of NASH, however, no statistically significant difference between the drug and placebo in terms of fibrosis reduction has been observed* [222]. *Although there is no convincing evidence of a reduction in liver fibrosis based on histological examination, some meta-analyses report a reduction in liver tissue stiffness with administration of semaglutide**** [223–225].

*In studies of the efficacy of #liraglutide and #semaglutide** in patients with type 2 DM, a reduction in cardiovascular and cerebrovascular events was noted* [226, 227], *which was associated, among other reasons, with a decrease in body weight* [228]. *The recommended duration of use of #liraglutide (1.8–3.0 mg/day) is at least 48 weeks; for #semaglutide** (2.4 mg/week) it ranges from 48 to 72 weeks according to research data.*

• It is recommended to consider administering #pioglitazone at a dose of 30–45 mg/day to patients with NAFLD and type 2 DM for reducing steatosis and inflammation in the liver with ALT levels < 2.5 ULN [179, 229–231].

Grade of recommendation — A;
level of evidence — 1.

Comments. Thiazolidinediones are a class of antidiabetic drugs that increase insulin sensitivity of tissues involved in the lipid metabolism regulation. One of the representatives of this class, #pioglitazone at a dose of 30–45 mg/day, compared with placebo, has demonstrated efficacy in the treatment of NASH in several studies and meta-analyses in terms of improving liver panel laboratory tests and histological findings (severity of steatosis and inflammatory activity) in NASH patients with and without type 2 DM [179, 230, 232]. *The systematic review of studies analysing the effects of pioglitazone therapy reported a reduction in signs of liver steatosis in patients with NAFLD and type 2 DM, which was also confirmed histologically* [232]. *Despite the absence of an obvious effect on fibrosis, a number of studies reported reduction of liver stiffness, assessed by transient and MR elastometry; nevertheless, there was no decrease in the content of type IV 7S collagen in the blood serum, which suggests that the reduction in stiffness occurs mainly due to the fat fraction. This work also noted a significant positive effect on laboratory parameters of inflammation (decreased activity of ALT, AST, GGT) and dyslipidemia (decreased LDL levels and increased HDL levels) in patients with*

NAFLD and type 2 DM with administration of #pioglitazone [175].

*The negative aspects of treatment with #pioglitazone include weight gain, an increased risk of developing bladder cancer in the long term and osteoporosis. The drug is also not recommended for patients with congestive heart failure (CHF) and those receiving high doses of insulin and their analogues or amlodipine*** [233]. *Both the European and American Associations for the Study of the Liver consider the use of pioglitazone for NASH therapy only for certain groups of patients, given the risks of developing the above conditions. The recommended dose of the drug is 30–45 mg per day, the duration of administration is at least 24 weeks. A contraindication to the administration of #pioglitazone is the ALT level exceeding the ULN by 2.5 times* [234].

• The use of sodium-glucose cotransporter type 2 inhibitors is recommended in patients with NAFLD and type 2 DM to control glycemia and reduce liver fat content [235, 236].

Grade of recommendation – A; level of evidence – 1.

Comments. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors are a relatively new class of antidiabetic drugs inhibiting glucose reabsorption in the proximal renal tubules via an insulin-independent mechanism. In addition to their main function, these drugs have been shown to have a number of pleiotropic effects, including cardio- and nephroprotection. Recently, the ability of SGLT-2 inhibitors to exert a positive effect on the course of NAFLD has attracted attention [237]. *The meta-analysis of 10 RCT, including 573 patients with NAFLD and type 2 DM, reported that taking SGLT-2 inhibitors (mainly dapagliflozin**, ipragliflozin**) for 12 weeks led to a more significant decrease in ALT, AST levels, and a decrease in the FIB-4 index compared to other oral hypoglycemic drugs. A positive effect on body weight loss, reduction of visceral fat and liver fat content, as assessed by MRI-PDFF, was also noted* [236]. *The large meta-analysis reported similar results, however, when fibrosis was assessed using type IV collagen 7S rather than FIB-4, there was no statistically significant difference between the SGLT-2 inhibitor group and the control group, which included other hypoglycemic drugs. The study also noted a significant positive effect on LDL-C levels with SGLT-2 inhibitor intake over 24 weeks compared to the control group. Another important conclusion of the study is confirming the high safety of SGLT-2 inhibitors. Despite the known adverse drug reactions in the form of an increased risk of urogenital infections, the authors report the presence of an insignificant statistical difference between the study groups* [238].

*According to two meta-analyses including 16 RCT (699 patients) and 18 RCT (1,330 patients), the use of SGLT-2 inhibitors (#dapagliflozin**, #empagliflozin**, #ipragliflozin**) for 12–24 weeks resulted in a statistically significant reduction in non-invasive indices of steatosis (according to MRI data) and fibrosis (FIB-4 index, liver stiffness, CAP parameter, type IV collagen 7S serum content)* [239, 240]. *The recommended dose of #dapagliflozin** is 5–10 mg per day; for #empagliflozin** it is 10–25 mg/day. The use of drugs is intended for a long period of time, both as monotherapy and as part of combination treatment.*

• It is recommended to add UDCA** at a dose of 13–15 mg/kg/day to hypoglycemic therapy regimens for patients with NAFLD and type 2 DM for improving glycemic control [241, 242].

Grade of recommendation – A; level of evidence – 1.

*Comments. A large systematic review with meta-analysis of clinical trials demonstrated the effect of UDCA** administered at different doses on glycemic parameters for durations ranging from 6 weeks to 2 years* [241]. *Thus, the meta-analysis of 7 studies using 8 UDCA treatment groups** demonstrated a statistically significant reduction in fasting glucose levels after such therapy (weighted mean difference: 3.30 mmol/L). The meta-analysis of 2 treatment groups showed a statistically significant reduction in glycated hemoglobin concentrations (weighted mean difference: –0.41 %). In addition, the meta-analysis of 4 treatment groups also revealed a statistically significant reduction in plasma insulin levels without a significant effect on HOMA-IR. The results of this meta-analysis showed that UDCA** significantly reduced fasting plasma glucose, glycated hemoglobin and insulin concentrations, indicating its positive effect on glucose homeostasis.*

*In 2021, an RCT with 240 participants was published assessing the effects of #empagliflozin** at a dose of 25 mg and UDCA** at a dose of 250 mg/day for 6 months. Thus, in the #empagliflozin** group, a more significant reduction in steatosis was observed according to MRI-PDFF data, as well as a more pronounced decrease in the level of TG*

*and glucose compared to the UDCA** group. However, UDCA** was superior to #empagliflozin** in terms of reducing liver fibrosis indices and IR. The effects on BMI and serum transaminase levels were comparable in both groups. The obtained results allowed the authors to conclude that both drugs have sufficient safety and efficacy and may be used to treat NAFLD in patients with type 2 DM* [242]. *The recommended dose of UDCA** is 13–15 mg/kg/day. The duration of treatment is at least 6 weeks.*

3.3.2. Treatment of NAFLD in combination with obesity

Non-pharmacological therapy

• Patients with NAFLD and obesity are recommended to change their lifestyle (diet correction, increased physical activity) as mandatory measures to reduce body weight, steatosis, inflammation and liver fibrosis [243].

Grade of recommendation – B; level of evidence – 1.

Comments. Lifestyle changes (diet and physical activity) are the basis of treatment for both NAFLD and obesity and are most effective when done under medical supervision. In the management of patients with NAFLD and obesity, CPG "Obesity" should also be followed [121]. *Weight loss in obesity has a beneficial effect on the severity of steatosis and the activity of steatohepatitis in both short-term studies and meta-analyses* [243, 244], *although the results of high-quality long-term observations are not yet available* [158, 243, 244].

Aerobic exercise and strength training are effective in reducing liver fat. Exercises are selected individually based on the patient's preferences to increase compliance [177]. *Resistance exercises may be more appropriate than aerobic ones for NAFLD patients with poor cardiorespiratory training or for those who are unable to tolerate or participate in aerobic exercises. Both aerobic and resistance exercises reduce hepatic steatosis in NAFLD with similar exercise frequency and duration (40–45 min/session 3 times per week for 12 weeks)* [122].

An important condition for the effective treatment of patients with NAFLD and obesity is the simultaneous adherence to dietary recommendations and increased physical activity. Thus, the RCT involving 80 people showed that a combination of a calorie-restricted diet and moderate physical activity led to a more significant reduction in liver steatosis according to MRI-PDFF data, a decrease in body weight, fat content, waist circumference, and lipid metabolism parameters than physical activity and diet alone [245]. *At the same time, drastic calorie restriction and rapid weight loss may lead to the progression of fibrosis and an increase in the level of serum transaminases. A slow weight loss of 0.5–1 kg per week is recommended* [178, 246, 247].

For achieving the target weight loss, maintaining adherence to weight loss and controlling the achieved weight, it is desirable to use a number of measures at the physician's discretion, such as faster weight loss at the beginning of treatment, personalized feedback, a positive attitude from the medical staff, support from other people (friends and family members), participation in structured weight loss programs [248, 249].

Pharmacological therapy

• For patients with NAFLD and obesity who have not responded to lifestyle changes, it is recommended to prescribe drugs registered as obesity treatment drugs in order to reduce body weight and improve the course of NAFLD [177, 178, 250, 251].

Grade of recommendation – A; level of evidence – 1.

Comments. Drug therapy may be used in the absence of clinically significant weight loss with non-pharmacological methods, and also for increasing the obesity treatment effectiveness: liraglutide (glucagon-like peptide-1 (GLP-1) analogue) 0.6–1.8 mg/day or orlistat (peripherally acting antiobesity drug) 120 mg/day or sibutramine (centrally acting antiobesity drug) 10–15 mg/day. This allows for more effective weight loss, makes it easier to follow dietary recommendations, helps develop new eating habits and maintain reduced body weight over the long term [177, 178, 250, 251]. *These drugs are recommended for the treatment of obesity according to the CR "Obesity"* [121].

• UDCA** is recommended at a dose of 10–15 mg/kg/day for NAFLD patients during the period of weight loss against the background of diet therapy or bariatric surgery to prevent the formation of bladder stones until body weight stabilization is achieved [252–255].

Grade of recommendation – A; level of evidence – 1.

Comments. In obese patients, the incidence of cholelithiasis is higher than in the general population, and rapid weight loss, especially when following a diet with a sharp restriction of fat, increases the risk of stone formation, development of symptomatic cholelithiasis, and need for cholecystectomy [256, 257]. *Meta-analyses have demonstrated that UDCA** use during a weight loss diet prevents the risk of gallstone formation*

[252], *and UDCA** therapy after bariatric surgery reduces the risk of symptomatic cholelithiasis* [253, 254, 258]. *It should be noted that in the study on the prevention of cholelithiasis against the background of weight loss through the use of UDCA, 84 % of patients had NAFLD* [255].

Surgical treatment

In patients with obesity (BMI > 35 kg/m^2) and NAFLD who have not achieved a positive result with lifestyle changes and/or pharmacotherapy, bariatric surgery may be considered (see Section 3.4 "Surgical treatment").

3.3.3. Treatment of NAFLD in combination with dyslipidemia and ASCVD

NAFLD, already at the steatosis stage, is an independent risk factor for the development of cardiovascular diseases, independent of type 2 DM, dyslipidemia or obesity. In patients with NAFLD and dyslipidemia, target levels of lipid metabolism parameters are determined by cardiovascular risk. When prescribing lipid-lowering therapy to NAFLD patients, target lipid levels should be selected in accordance with the CPG "Lipid Metabolism Disorders" [83].

• It is recommended to administer HMG-CoA reductase inhibitors (statins) in doses necessary to achieve the target LDL-C level in patients with NAFLD and dyslipidemia/ASCVD to prevent the risk of complications and improve the course of NAFLD [83, 259, 260].

Grade of recommendation — A;
level of evidence — 1.

Comments. HMG-CoA reductase inhibitors (statins) suppress the synthesis of cholesterol in the liver and are widely used in the treatment of dyslipidemia, ASCVD, for primary and secondary prevention of CVD and their complications. NAFLD is often combined with dyslipidemia and other cardiometabolic disorders, such as arterial hypertension, coronary heart disease, chronic heart failure, rhythm and conduction disorders [93, 261]. *For this reason, such patients are often prescribed statins. Statin doses are calculated according to the CR "Lipid Metabolism Disorders"* [83, 262].

According to systematic reviews and meta-analyses, HMG-CoA reductase inhibitors have a good safety profile in NAFLD and help reduce ALT, AST and GGT levels [260, 263, 264]. *This is especially relevant for patients with elevated liver enzymes before starting HMG-CoA reductase inhibitors. Several studies have shown that HMG-CoA reductase inhibitors in patients with NASH and dyslipidemia lead to a reduction in steatosis, inflammation and fibrosis* [260, 263–266].

When administering hypolipidemic therapy, transaminases are monitored in 8–12 weeks after its start. If ALT exceeds 3 ULN, the drug is discontinued. In patients with NASH and baseline elevated ALT levels, baseline ALT should be used instead of ULN [267].

• For patients with NAFLD and dyslipidemia/ASCVD, it is recommended to combine therapy with HMG-CoA reductase inhibitors** at a dose of 10–15 mg/kg to enhance their hypolipidemic effect in case of insufficient effectiveness of standard tactics or intolerance to high doses of HMG-CoA reductase inhibitors [268, 269].

Grade of recommendation — C;
level of evidence — 4.

*Comments. A randomized prospective clinical study of patients with hypercholesterolemia demonstrated that in case of ineffective therapy with simvastatin** (20 mg/day) or atorvastatin** (20 mg/day), their combination with UDCA** was statistically significantly more effective compared to doubling the dose of HMG-CoA reductase inhibitors in terms of the effect on total cholesterol and LDL cholesterol levels* [270].

*The multicenter observational study RAKURS assessed the efficacy and safety of the combined use of statins and UDCA** in patients with chronic liver diseases and CVD who required statins. According to the study results, the addition of UDCA** to statin therapy resulted in a statistically significantly better effect compared to monotherapy with HMG-CoA reductase inhibitors: target LDL-C levels among patients taking HMG-CoA reductase inhibitors and UDCA** were achieved by the end of the 6-month therapy period in 37 % of patients, and among those taking HMG-CoA reductase inhibitors — only in 20 % of patients. It was also noted that the combination of UDCA** with HMG-CoA reductase inhibitors prevented statin-induced increase in serum transaminases* [268].

*In a secondary analysis of the RAKURS study, patients with NAFLD were selected from the overall group of participants (89 %). During the first month of treatment, statin monotherapy in these patients was characterized by positive dynamics of lipid metabolism parameters in the absence of adverse effects on liver function tests. In turn, combination therapy with HMG-CoA reductase inhibitors and UDCA** for 6 months led to a significant decrease in total cholesterol and LDL cholesterol levels compared to monotherapy with HMG-CoA reductase inhibitors* [269].

*In an experimental NAFLD model, it was demonstrated that the combination of UDCA**,

#rosuvastatin and #ezetimibe led to a statistically significant decrease in ALT levels, had an anti-apoptotic and anti-fibrotic effect compared to the effect of the combination of "#rosuvastatin + #ezetimibe" [271].

*The results of the studies showed that UDCA** is capable of potentiating the action of HMG-CoA reductase inhibitors, which is especially important for patients with ineffectiveness of low doses of HMG-CoA reductase inhibitors and intolerance to their high doses. The recommended dose of UDCA** is 10–15 mg/kg/day.*

• It is recommended to administer #ezetimibe at a dose of 10 mg/day to patients with NAFLD and dyslipidemia/ASCVD in mono- or combination therapy in case of intolerance or insufficient efficacy of HMG-CoA reductase inhibitors in order to reduce the risk of cardiovascular complications and improve the course of NAFLD [83, 272].

Grade of recommendation – B;
level of evidence – 2.

Comments. #Ezetimibe blocks the sterol transporter NPC1L1 (Niemann-Pick C1-Like 1) on the apical membrane of enterocytes, which reduces the absorption of dietary cholesterol and can lead to certain positive dynamics of histological signs of NAFLD. In NAFLD patients, the beneficial cardiovascular effects of HMG-CoA reductase inhibitors are maintained in monotherapy and in combination with #ezetimibe [272]. *According to the meta-analysis of 6 clinical trials, #ezetimibe reduced transaminase and GGT levels, reduced liver steatosis and hepatocyte ballooning, but did not affect inflammation and fibrosis* [272]. *By contrast, in another meta-analysis #ezetimibe reduced the activity of steatohepatitis, but did not affect the severity of steatosis* [273]. *Such differences in the conclusions of the two meta-analyses may be due to the small number of studies that assessed liver histology. In the open-label RCT "ESSENTIAL", the combination of #ezetimibe with an HMG-CoA reductase inhibitor reduced liver fat content assessed by the MRI-PDFF method* [274].

When using a combination of #ezetimibe with #HMG-CoA reductase inhibitors, monitoring of laboratory parameters (ALT, AST) is also required. In case of an increase in transaminases, a further decision on discontinuing the therapy (the entire combination or HMG-CoA reductase inhibitors only) and/or adjusting drug doses should be made in accordance with the instructions applicable to statins. In the development of LC, the use of #ezetimibe should be avoided if signs of liver function decompensation appear (Child – Pugh class B–C).

• For patients with NAFLD and hypertriglyceridemia/ASCVD, it is recommended to administer #omega-3-acid ethyl esters at a dose of 4 g/day to reduce TG levels and liver steatosis [275].

Grade of recommendation – B;
level of evidence – 1.

Comments: #Omega-3 triglycerides, including other esters and acids (omega-3 PUFAs) are drugs used for reducing TG levels. Preclinical studies have demonstrated the ability of omega-3 triglycerides, including other esters and acids, to reduce hepatic lipogenesis and increase insulin sensitivity [276]. *The REDUCE-IT study, involving 8,179 patients, demonstrated a positive effect of eicosapentaenoic acid (#omega-3 triglycerides, including other esters and acids) in combination with a statin on the "hard" endpoints of cardiovascular events* [277]. *CT, administration of eicosapentaenoic acid (#omega-3 triglycerides, including other esters and acids) at a dose of 2.4 g/day in NAFLD patients reduced the TG level compared with placebo without increasing serious side effects, although it did not affect the histological parameters of NASH* [278]. *At the same time, another study, in which liver fat content was determined using magnetic resonance spectroscopy allowing for a more accurate assessment of overall liver fat content, showed that a course of a combination of #omega-3-acid ethyl esters – docosahexaenoic and eicosapentaenoic acid at a dose of 4 g/day reduced liver fat content* [270]. *According to meta-analyses, #omega-3 triglycerides, including other esters and acids, may reduce liver fat, indices of liver enzymes, and blood lipids* [279–281].

Only the medicinal product #omega-3 acids ethyl esters can be recommended, since biologically active supplements containing #omega-3 PUFAs do not have approved clinical indications, proven therapeutic efficacy, pharmaceutical and biological equivalence and may not be used to replace prescription drugs [282]. *The dose and duration of use is regulated by the CR "Lipid Metabolism Disorders"* [83].

• For patients with NAFLD and hypertriglyceridemia/ASCVD, it is recommended to administer #fenofibrate** at a dose of 145–200 mg/day for reducing cardiovascular risk and transaminase levels [83, 283].

Grade of recommendation – C;
level of evidence – 5.

*Comments. Fibrates are used in the treatment of dyslipidemia, while only #fenofibrate** may be used in combination with*

*statins. There are theoretical assumptions and experimental data indicating that #fenofibrate** may have a positive effect on NAFLD* [284]. *No large studies examining the effects of fibrates on NAFLD have been conducted. A small RCT with paired biopsies showed that a 48-week therapy with fenofibrate** resulted in a decrease in the proportion of patients with elevated levels of aminotransferases, glucose, ALP and GGT and a reduction in ballooning degeneration without affecting the degree of steatosis, lobular inflammation, and fibrosis* [283]. *Studies examining the efficacy of fibrates in dyslipidemia in combination with NAFLD have not shown an increase in side effects, and some studies, on the contrary, reported a decrease in transaminases* [283–285].

*When administering fenofibrate** in the first year of therapy, it is necessary to monitor the level of transaminases and creatinine every 3 months; when used in combination with statins, the risk of rhabdomyolysis increases.*

• For patients with NAFLD and comorbidities (dyslipidemia, obesity, type 2 DM), it is recommended to consider additional administration of phospholipids (essential phospholipids (EPL)) at a dose of 1800 mg/day as part of combined therapy to increase the effectiveness of pharmacotherapy [286, 287].

Grade of recommendation – C; level of evidence – 4.

*Comments. Currently, a large number of studies have been accumulated devoted to the use of EPL in the treatment of NAFLD. Most of them are small in size but nevertheless form the scientific basis for the use of this class of drugs. In research, EPL is mainly used as part of combined therapy: in combination with hypoglycemic, lipid-lowering therapy, together with UDCA** or probiotics. This is explained by the fact that EPL not only have their own pharmacological activity but also act as bioenhancers (biopotentiators). When used in a complex or co-administered with other medicinal substances, they can potentially provide them with higher bioavailability (pharmacokinetic enhancement), and therefore, an increase in the biological effect (pharmacodynamic enhancement)* [288, 289]. *The adjuvant effect of EPL was demonstrated in an observational study including 2,843 patients with liver steatosis and cardiometabolic comorbidity (type 2 DM, hypercholesterolemia, AH, obesity or overweight). In 69.6 % of patients after three months of EPL use and in 81.4 % of patients after 6 months of therapy, there was an improvement in the ultrasound characteristics of the liver condition against the background of basic pharmacotherapy with the addition of the drug (1800 mg/day)* [286]. *According to the results of a systematic review with meta-analysis, the use of EPL in combination with hypoglycemic therapy led to a more significant decrease in the levels of ALT, cholesterol and TG, as well as an improvement in the ultrasound image of the liver in NAFLD patients with obesity and type 2 DM, but this meta-analysis has methodological errors* [287].

*Other lipid-lowering agents (#proprotein convertase subtilisin/kexin type 9 (PCSK) inhibitors) appear to be promising drugs in NAFLD. They may have a beneficial effect on the course of NAFLD, but high-quality studies have not yet been performed. A small RCT in 40 patients with heterozygous familial hyperlipidemia showed resolution of previously diagnosed NAFLD and NASH after 1 year of treatment with other lipid-lowering agents (#proprotein convertase subtilisin/kexin type 9 (PCSK) inhibitors) – #evolocumab** or #alirocumab**. No signs of steatosis, inflammation or fibrosis were detected* [290]. *Other lipid-lowering agents (#proprotein convertase subtilisin/kexin type 9 (PCSK) inhibitors) are considered safe drugs in NAFLD* [291], *however, further studies are needed on the efficacy and safety of drugs of this class in NAFLD patients.*

3.3.4. Treatment of NAFLD in combination with chronic kidney disease

There is increasing evidence indicating an association between NAFLD and CKD due to common risk factors for their development, although there is evidence of an independent association between these conditions. The presence of NAFLD is associated with an increased incidence of proteinuria, a greater reduction in estimated glomerular filtration rate (eGFR), and the development and progression of CKD [292, 293]. In patients with type 2 DM, the presence of NAFLD is associated with an increased incidence of CKD, regardless of the age, gender, and AH [294].

CKD risk factors not related to liver function in NAFLD patients include older age, DM, AH, initially decreased eGFR, smoking, thyroid dysfunction (hypothyroidism due to fat accumulation, hyperthyroidism due to the formation of reactive oxygen species), and alcohol consumption. Involved in the development of CKD in NAFLD patients are a number of factors, the key one being systemic low-grade inflammation,

which is triggered by several inflammatory cascades [295–299].

• The use of renin-angiotensin-aldosterone system (RAAS) blockers (angiotensin-converting enzyme inhibitors (ACE inhibitors)) and angiotensin II receptor blockers (ARB II)) is recommended in patients with NAFLD and CKD to slow the progression of renal dysfunction and prevent the progression of NASH [300, 301].

Grade of recommendation – C;
level of evidence – 4.

*Comments. Preliminary studies have shown a positive effect of #losartan**, #telmisartan and #valsartan on histological indices of necroinflammation and laboratory markers in NASH, with #telmisartan being more effective than #valsartan* [302–304]. *The effect of RAAS blockade using ACE inhibitors and ARB II on the course of NAFLD has also been assessed in small RCT. In particular, in a small, open-label, comparative study involving patients with NAFLD, diabetes, and hypertension, the ARB II therapy with #telmisartan, which also has agonism for PPARs (Peroxisome Proliferator-Activated Receptors), led to a decrease in liver fat content assessed by CT data and a reduction in serum FFA levels compared with #losartan**.* [301]. *In another study, a long-term (> 1 year) use of ACE inhibitors or ARB II in patients with stage C3 CKD, end-stage CKD, and after kidney transplantation was associated with a lower incidence of NAFLD and lower liver stiffness compared with patients not taking these drugs* [298]. T*he ability of ACE inhibitors and ARB II to inhibit liver fibrogenesis has been demonstrated in experimental models* [305]. *In a cohort study of 12,327 patients with NAFLD treated with ACE inhibitors or ARB II and followed for at least 5 years, the use of ACE inhibitors but not ARBs was associated with a reduction in liver-related events (liver cancer and complications of cirrhosis), with a greater reduction in those with CKD than those without it* [300].

• The use of sodium-dependent glucose cotransporter type 2 (SGLT2) inhibitors (#dapagliflozin**, #empagliflozin**) is recommended for patients with NAFLD and CKD, regardless of the presence of type 2 DM, to slow the progression of renal dysfunction, reduce the risk of cardiovascular complications and reduce liver fat content [306].

Grade of recommendation – C;
level of evidence – 5.

Comments. Sodium glucose cotransporter type 2 inhibitors reduce afferent arteriolar vasoconstriction and may provide nephroprotection by reducing glomerular hyperfiltration, preventing oxidative stress and inflammation in proximal tubular cells, and other mechanisms [307–309]. *Evaluation of the nephroprotective potential demonstrated that in patients with CKD, #dapagliflozin**, compared with placebo, was able to reduce the combined risk of persistent decrease in eGFR by at least 50 %, development of end-stage renal disease, or death from renal or cardiovascular causes, regardless of the state of carbohydrate metabolism and renal function. In addition, treatment with #dapagliflozin** was associated with a reduction in cardiovascular mortality and hospitalizations for CHF, as well as all-cause mortality* [310].

*Administering #empagliflozin** to patients with CKD, in turn, led to an improvement in the combined outcome – the risk of kidney disease progression or death from cardiovascular causes in patients with and without DM* [311].

CKD treatment guidelines comprise the inclusion of sodium-glucose cotransporter-2 inhibitors for patients with CKD and type 2 DM to reduce the risk of CKD progression and cardiovascular events [92]. *The effect of sodium-glucose cotransporter type 2 inhibitors on the course of NAFLD is described in detail in section 3.3.1 "NAFLD in combination with type 2 DM".*

• The use of glucagon-like peptide-1 (GLP-1) analogues (#liraglutide, #dulaglutide, #semaglutide**) is recommended for patients with NAFLD and CKD against the background of type 2 DM in order to slow the progression of renal dysfunction, reduce the risk of cardiovascular events and laboratory indicators of liver inflammation [92, 312].

Grade of recommendation – A;
level of evidence – 1.

*Comments. The nephroprotective effect of glucagon-like peptide-1 (GLP-1) analogues (#liraglutide, #dulaglutide, #semaglutide**) is realized through numerous direct and indirect mechanisms, including stimulation of natriuresis in the proximal tubules, activation of cyclic adenosine monophosphate-dependent protein kinase A (cAMP/PKA), reconstitution of endothelium-dependent relaxation of renal vessels, normalization of tubuloglomerular feedback (via a decrease in the activity of the sodium-hydrogen transporter (NHE3)), a reduction in the severity of renal hypoxia, etc.* [313]. *These drugs are primarily able to prevent the occurrence of macroalbuminuria and, to a lesser extent, reduce the decrease in eGFR in patients with type 2 DM.*

*In placebo-controlled studies of liraglutide (LEADER) after 3.8 years of treatment and use of #semaglutide** (SUSTAIN-6) after 2.1 years of treatment, it was possible to achieve a significant reduction in the combined renal endpoint (development of macroalbuminuria, doubling of creatinine, initiation of renal replacement therapy, or renal death) in patients with type 2 DM, predominantly suffering from ASCVD* [314, 315]. *A similar effect in reducing the risk of developing a combined renal endpoint (renal outcomes as part of microvascular outcomes) was demonstrated by #dulaglutide (REWIND study with a median follow-up of 5.4 years), primarily due to a reduction in the development of macroalbuminuria* [316]. *However, in terms of their ability to prevent the development of renal complications and reduce the risk of hospitalization in CHF, these drugs are apparently inferior to sodium-glucose cotransporter type 2 inhibitors* [317].

The CKD treatment guidelines propose the inclusion of glucagon-like peptide-1 (GLP-1) analogues in patients with CKD and type 2 DM in the treatment regimen to reduce the risk of CKD progression and cardiovascular events [92]. *The effect of glucagon-like peptide-1 (GLP-1) analogues on the course of NAFLD is described in detail in section 3.3.1 "NAFLD in combination with type 2 DM".*

3.3.5. NAFLD in combination with excessive alcohol consumption

The terms NAFLD, NASH and their criteria proposed in the 1980s implied strict exclusion of the alcohol factor [318, 319]. It later became clear that a combined genesis of fatty liver disease is possible, and excessive alcohol consumption by a patient with cardiometabolic risk factors (metabolic dysfunction) potentiates the progression of steatohepatitis. In this regard, in 2023, it was proposed to identify a new form — MASLD in combination with excessive alcohol consumption (MetALD) [2, 5].

• It is recommended that NAFLD patients consuming excessive amounts of alcohol completely stop drinking it to prevent the progression of fibrosis and development of HCC [144, 320, 321].

Grade of recommendation — B; level of evidence — 3.

Comments. Alcohol consumption negatively affects the course and prognosis of steatohepatitis in individuals with a metabolic background, and alcohol abuse clearly has an adverse effect on the course of NAFLD. In a large cohort study with a long-term follow-up, overall mortality was significantly higher among individuals with NAFLD and excessive alcohol intake compared with moderate alcohol intake [322]. *In a prospective clinical study, episodic alcohol abuse at least once per month was associated with significant fibrosis progression in NASH* [323].

Although individual meta-analyses have previously suggested a protective effect of moderate and low doses of alcohol on NAFLD [324, 325], *many of the studies included in them were methodologically flawed. Both moderate and low alcohol consumption have been shown to have adverse effects on the development of fibrosis in NASH* [326, 327]. *In addition, individuals who consumed alcohol in moderate doses had a smaller reduction in the degree of steatosis and a lower chance of NASH resolution compared with those who did not drink alcohol at all* [320]. *Even moderate alcohol consumption increases the risk of HCC in patients with NASH* [321]. *A systematic review of* 6 *longitudinal observational cohort studies found that any level of alcohol consumption was associated with worse liver state in NAFLD* [144].

• It is recommended to consider the use of ademetionine** in patients with NAFLD in combination with alcohol-related liver damage to improve the prognosis of the disease [328].

Grade of recommendation — C; level of evidence — 5.

*Comments. Ademetionine** is widely used in the treatment of alcoholic liver disease and has been shown in RCT to improve survival in patients with alcoholic cirrhosis of Child — Pugh classes A and B* [329, 330]. *According to experts, ademetionine** can also be used for treating NAFLD patients with a concomitant risk factor of excessive alcohol consumption* [328].

3.4. Surgical treatment

Surgical treatment of obesity is considered in patients with NAFLD and BMI > 35 kg/m^2 when non-surgical therapy of obesity in combination with NAFLD is ineffective.

In addition, patients with LC associated with NASH may undergo liver transplantation and surgical interventions for portal hypertension. These aspects are discussed in the CPG "Liver Fibrosis and Cirrhosis", and their implementation has no special features for this etiology of LC.

• For patients with BMI > 35 kg/m^2 and NAFLD who have not achieved positive results with lifestyle changes and/or pharmacotherapy, it is recommended to consider bariatric surgery for reducing body weight, hepatic steatosis,

inflammation, and fibrosis, and diminishing metabolic complications [177, 178, 331, 332].

Grade of recommendation — B;
level of evidence — 2.

Comments. Bariatric surgery can reduce hepatic steatosis, inflammation and fibrosis, provide sustained weight loss of up to 30 %, treatment of type 2 DM and reduction of all-cause morbidity and mortality. Bariatric treatment is not contraindicated in patients with obesity and NAFLD or NASH (without verified cirrhosis), while data on the possibility of this treatment in patients with LC are limited [1, 177]. *According to a meta-analysis that included 32 cohort studies and assessed 3,093 biopsies, bariatric surgery resulted in a reduction in liver inflammation activity, as well as resolution of steatosis and fibrosis (in 66 and 40 % of patients, respectively). A significantly smaller proportion of patients (12 %) experienced worsening of histological characteristics of NAFLD after bariatric surgery* [333]. *Another meta-analysis reported a reduction in steatosis in 88 % and fibrosis in 30 % of patients* [334]. *The most recent meta-analysis of 37 clinical studies shows a liver biopsy-confirmed reduction in steatosis in 56 % of patients, inflammation in 45 %, and fibrosis in 25 % of patients after bariatric surgery. Roux-en-Y gastric bypass is most effective in terms of reducing steatosis, while sleeve gastrectomy — in terms of fibrosis regression* [335].

Indications and methods of bariatric intervention should be determined on an individual basis by a multidisciplinary team, including a surgeon.

4. Medical rehabilitation and sanatorium-resort therapy, medical indications and contraindications for the use of rehabilitation methods, including those based on the use of natural healing factors

There are no specific rehabilitation measures for patients with NAFLD. Sanatorium-resort treatment with the gastroenterological profile using physiotherapy procedures, regular physical activity, walking in the fresh air, and abstinence from alcohol may be recommended.

5. Prevention and follow-up monitoring, medical indications and contraindications for the use of prevention methods

The following issues should be considered in preventive measures:

— prevention of NAFLD development;
— timely detection of NAFLD and NASH;
— prevention of progression of NAFLD/NASH to LC;
— prevention of HCC.

NAFLD patients should be monitored by related specialists depending on the comorbidity profile (gastroenterologists, endocrinologists, cardiologists, nutritionists). Clinical efforts should be aimed at preventing NAFLD and associated cardiometabolic diseases.

• If NAFLD is suspected, it is recommended to see a general practitioner or a gastroenterologist to establish a diagnosis, prescribe examinations and treatment [1].

Grade of recommendation — C;
level of evidence — 5.

• To prevent the development of NAFLD, measures aimed at developing a healthy lifestyle, correcting eating habits, physical activity, and abstaining from alcohol are recommended [336].

Grade of recommendation — C;
level of evidence — 5.

• Patients with cardiometabolic risk factors without the NAFLD diagnosis are recommended to undergo screening examination (determination of platelets, ALT, AST in the blood serum, ultrasound of the abdominal organs, FIB-4 calculation) once every 3–5 years for the timely detection of NAFLD [337].

Grade of recommendation — C;
level of evidence — 5.

Comments. The diagnosis of NAFLD suggests the presence of cardiometabolic risk factors based on metabolic dysfunction. Accordingly, patients with any of its manifestations (obesity, dyslipidemia, type 2 DM, etc.) are considered a risk group of developing NAFLD. Most patients with NAFLD are asymptomatic or have nonspecific symptoms. This often results in the disease remaining undetected. The optimal frequency of follow-up care has not been established, but according to European experts, patients with metabolic risk factors without signs of NAFLD should be monitored once every 3–5 years [337].

• For NAFLD patients without laboratory or instrumental signs of progressive course/fibrosis, without type 2 DM and with one cardiometabolic risk factor, follow-up care with an assessment of non-invasive fibrosis indices (FIB-4) is recommended once every 2 years for the timely detection of disease progression [337].

Grade of recommendation — C;
level of evidence — 5.

Comments. According to a meta-analysis of clinical studies with paired biopsies, fibrosis progression is observed in 1/3 of patients with NAFLD, with its progression from stage F0 to F1 occurring on average in 14.3 years with initially simple steatosis and in 7.1 years with NASH [4]. *The optimal frequency of follow-up care has*

not been established, but according to European experts, patients with NAFLD without laboratory or instrumental signs of progressive course should be observed once every 2 years [337].

• Patients with NAFLD and prediabetes, type 2 DM and more than two cardiometabolic risk factors, as well as patients with laboratory or instrumental signs of progressive course (fibrosis), are recommended to have follow-up care with an assessment of non-invasive fibrosis indices (FIB-4) once a year for timely detection and assessment of disease progression [1].

Grade of recommendation — C;
level of evidence — 5.

Comments. Type 2 DM and other cardiometabolic risk factors contribute to the progressive course of NAFLD and development of NASH. In approximately 1/4 of patients with established NASH, the disease progresses to cirrhosis with the risk of developing HCC [65]. *According to experts, in patients with type 2 DM or several cardiometabolic risk factors, an assessment of the possible development/progression of fibrosis should be performed once every 1–2 years* [1].

• Patients with NAFLD are recommended to change their lifestyle (diet correction, increased physical activity) to prevent the progression of NAFLD, development and progression of comorbid conditions [132, 219, 338].

Grade of recommendation — B;
level of evidence — 1.

Comments. Lifestyle changes, discussed in detail in Section 3.1 "Non-pharmacological therapy of NAFLD", not only serve for treating NAFLD, but are also among the most effective measures for its prevention and progression, and have a positive effect on most comorbid conditions [131, 219].

It should be noted that the lack of a clear opinion on the possibility of non-pharmacological prevention of NAFLD progression is associated with the relative short-term nature of the randomized trials conducted (1–2 years), while convincing data to identify differences in mortality between NAFLD patients and the population can be obtained with observation from 8 to 28 years [155]. *Nevertheless, lifestyle changes should currently be considered the main method for preventing the unfavorable course of the disease.*

• NAFLD patients are recommended drug and non-drug correction of comorbid conditions to prevent unfavorable course of NAFLD [339].

Grade of recommendation — C;
level of evidence — 5.

Comments. NAFLD and many comorbid diseases aggravate each other. This suggests that correction of comorbid diseases may have a positive effect on preventing the unfavorable course of NAFLD [339]. *There is evidence that individual drugs used in the treatment of NAFLD in combination with DM and dyslipidemia reduce the risk of developing HCC. Thus, according to several meta-analyses, #metformin** is able to reduce the risk of developing HCC by approximately 50 % regardless of the etiology of liver disease* [340–342]. *In a meta-analysis of 10 studies including 4,298 patients with HCC in a total population of 1,459,417 patients, use of statins was associated with a significant reduction in the risk of developing this tumor, especially in Asian populations* [343]. *When interpreting the data obtained, it should be taken into account that most of these studies were not focused on NAFLD/NASH patients.*

• NAFLD patients at the stage of severe fibrosis (F3) or cirrhosis are recommended to undergo ultrasound examination of the abdominal organs once every 6 months for the purpose of screening for HCC [344, 345].

Grade of recommendation — B;
level of evidence — 2.

Comments. The proportion of HCC caused by NAFLD has been increasing in recent decades and now accounts for 15 % of all HCC cases with incidence rates of 0.44 per 1,000 person-years (0.29–0.66) in a cohort of NAFLD patients [346–348]. *Most often, HCC develops at the stage of severe fibrosis and LC due to NASH but can also occur with simple steatosis* [349–351].

It is assumed that HCC development risk in NAFLD is highest in patients with DM, in old age and with simultaneous alcohol consumption, as well as in individuals with the PNPLA3 I148M (rs738409) gene polymorphism [345]. *Patients at high risk of developing HCC should be included in continuous monitoring groups* [345]. *It was shown that patients with NASH-LC who did not participate in the HCC screening program were more likely to have a more advanced stage of cancer than those who participated in the screening program* [352].

Patients with NAFLD-HCC tend to have lower alpha-fetoprotein levels than patients with viral HCC [353].

Monitoring of patients should include regular ultrasound examination of the abdominal cavity performed once every 6 months [344, 345]. *The ultrasound effectiveness in detecting HCC is 94 %, in detecting early HCC — 63 %* [344].

The need for monitoring patients with NAFLD without cirrhosis has not yet been determined [345].

• Patients with NAFLD are recommended to quit drinking alcohol and smoking tobacco to reduce the risk of developing HCC [321, 354].

Grade of recommendation — C;
level of evidence — 5.

Comments. In 2/3 of HCC cases, several risk factors for its development are identified, with alcohol and smoking being proven risk factors. An increased risk of developing HCC has been shown in NAFLD patients who consume alcohol [321] *and smoke* [354]. *This recommendation is most relevant for patients with severe fibrosis and cirrhosis, since they have the highest risk of developing HCC* [349–351].

• Screening examination of first-degree relatives of patients with severe fibrosis and LC due to NASH is recommended for the timely detection of NAFLD and progressive liver fibrosis [1].

Grade of recommendation — C;
level of evidence — 5.

Comments. First-degree relatives of patients with LC due to NASH have a 12-fold increased risk of developing advanced liver fibrosis [355].

• Regular coffee consumption is recommended for NAFLD patients in the absence of contraindications to reduce the risk of fibrosis and HCC [356–358].

Grade of recommendation — B;
level of evidence — 2.

Comments. According to a number of meta-analyses, regular coffee consumption is associated with a reduction in the severity of fibrosis in NAFLD [359–362]. *According to other meta-analyses and large epidemiological studies, coffee reduced the risk of developing fibrosis in NAFLD and the occurrence of NAFLD itself* [356, 357, 363]. *In addition, coffee consumption has been shown to be associated with a reduced risk of developing HCC* [358].

The protective properties of coffee against NAFLD and HCC are maintained regardless of the presence of caffeine. A dose-dependent effect of coffee in preventing HCC has been demonstrated in a number of epidemiological studies conducted in different populations and a dose-response meta-analysis [364–367]. *However, the optimal daily dose of coffee is still unclear.*

6. Organization of medical care

Most NAFLD patients are monitored and treated on an outpatient basis.

There are no indications for emergency hospitalization for NAFLD.

Indications for planned hospitalization of NAFLD patients are the following:

- lack of effect from treatment at the outpatient stage or atypical course of the disease;
- need to perform diagnostic procedures that cannot be done on an outpatient basis (e.g., liver biopsy);
- need to perform differential diagnostic measures for excluding other causes of liver damage that cannot be done on an outpatient basis (e.g., liver biopsy);
- a combination of NAFLD with cardiometabolic conditions that complicate the course of the disease, requiring multidisciplinary patient management and/or 24-hour monitoring.

Criteria for hospital discharge: performance of planned diagnostic/differential diagnostic measures.

7. Additional information (including factors influencing the outcome of the disease or condition)

No additional information is available.

Criteria for assessing the quality of medical care

No.	Quality criterion	Performance evaluation
1	An initial appointment (examination, consultation) with a gastroenterologist or general practitioner has been completed	Yes/no
2	An assessment of cardiometabolic risk factors has been carried out	Yes/no
3	A general (clinical) blood test has been performed	Yes/no
4	A general therapeutic biochemical blood assay has been performed (ALT, AST, ALP, GGT, glucose, total bilirubin, creatinine, total cholesterol, LDL cholesterol, HDL cholesterol, TG)	Yes/no
5	Ultrasound of abdominal organs (complex) has been performed	Yes/no
6	BMI calculation and waist circumference measurement have been performed.	Yes/no
7	FIB-4 or NFS calculation has been performed	Yes/no
8	Recommendations for lifestyle changes (diet, physical activity) have been issued	Yes/no
9	A follow-up examination (follow-up monitoring) has been carried out	Yes/no

Appendix A2.
Methodology for the development of clinical guidelines

The purpose of the proposed recommendations is to convey to practicing physicians modern ideas about the etiology and pathogenesis of NAFLD, to introduce them to the currently used algorithms for diagnosis, prognosis assessment and treatment.

Target audience of these clinical guidelines:

1) gastroenterologists;
2) general practitioners (family doctors);
3) general physicians;
4) cardiologists;
5) endocrinologists;
6) oncologists;

Table 1. Level of evidence (LoE) rating scale for diagnostic methods (diagnostic interventions)

LoE	Explanation
1	Systematic reviews of reference-controlled studies or systematic reviews of randomized clinical trials using meta-analysis
2	Individual reference-controlled studies or individual randomized clinical trials and systematic reviews of studies of any design except randomized clinical trials using meta-analysis
3	Studies without consistent control by a reference method or studies with a reference method that is not independent of the method explored, or non-randomized comparative studies, including cohort studies
4	Non-comparative studies, case report
5	Only action mechanism validation or expert opinion is available

Table 2. Levels of evidence (LoE) with indication of the classification used

LoE	Explanation
1	Systematic reviews of reference-controlled studies or systematic reviews of randomized clinical trials using meta-analysis
2	Individual reference-controlled studies or individual randomized clinical trials and systematic reviews of studies of any design except randomized clinical trials using meta-analysis
3	Studies without consistent control by a reference method or studies with a reference method that is not independent of the method explored, or non-randomized comparative studies, including cohort studies
4	Non-comparative studies, case report
5	Only action mechanism validation or expert opinion is available

Table 3. Grades of recommendation (GR) with indication of the classification used

GR	Explanation
A	Strong recommendation (all efficacy endpoints (outcomes) considered are important, all studies are of high or satisfactory methodological quality, and their conclusions on the outcomes of interest are consistent)
B	Conditional recommendation (not all efficacy endpoints (outcomes) considered are important, not all studies are of high or satisfactory methodological quality and/or their conclusions on the outcomes of interest are not consistent)
C	Weak recommendation (lack of evidence of adequate quality, all efficacy endpoints (outcomes) considered are unimportant, all studies are of low methodological quality and their conclusions on the outcomes of interest are not consistent)

Procedure for updating clinical guidelines

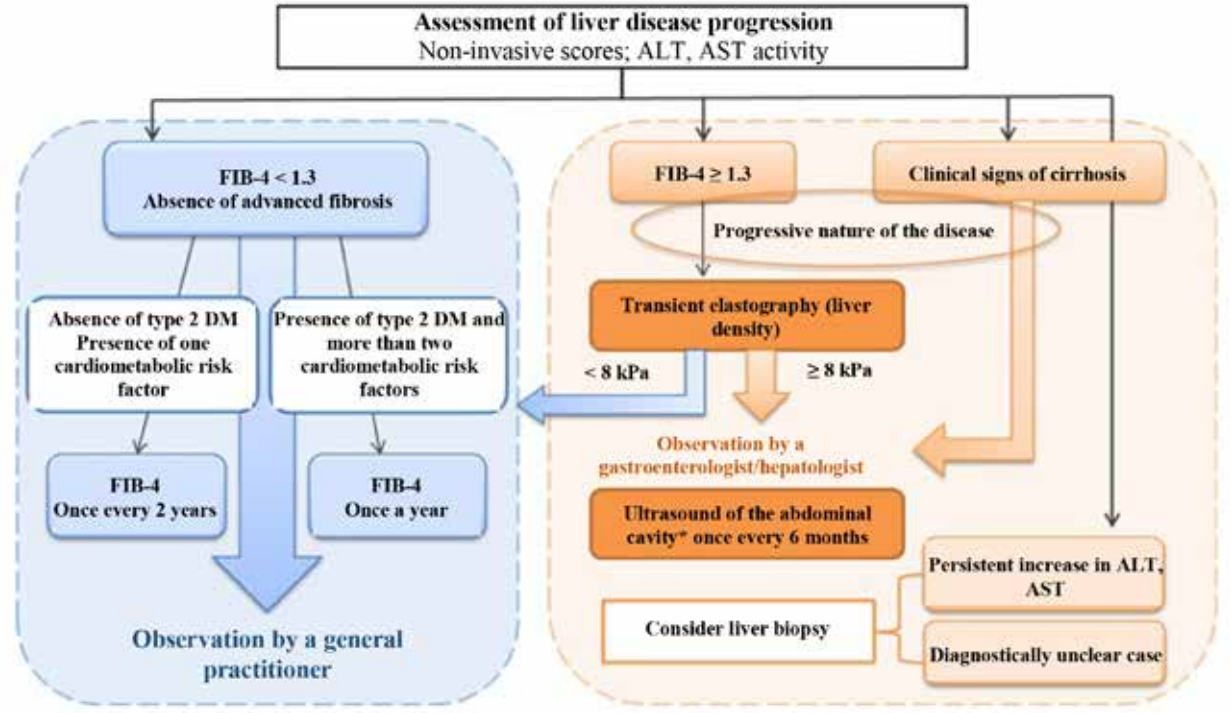
The mechanism of updating clinical guidelines provides for their systematic updating at least once every three years, as soon as new evidence-based data appears on diagnosis, treatment, prevention and rehabilitation of specific diseases, and upon availability of justified additions/comments to previously approved CG, but no more than semi-annually.

Appendix A3. Reference materials, including compliance of indications for use and contraindications, methods of administration and dosages of drugs, instructions for use of the drug

These clinical guidelines were developed taking into account the following regulatory documents:

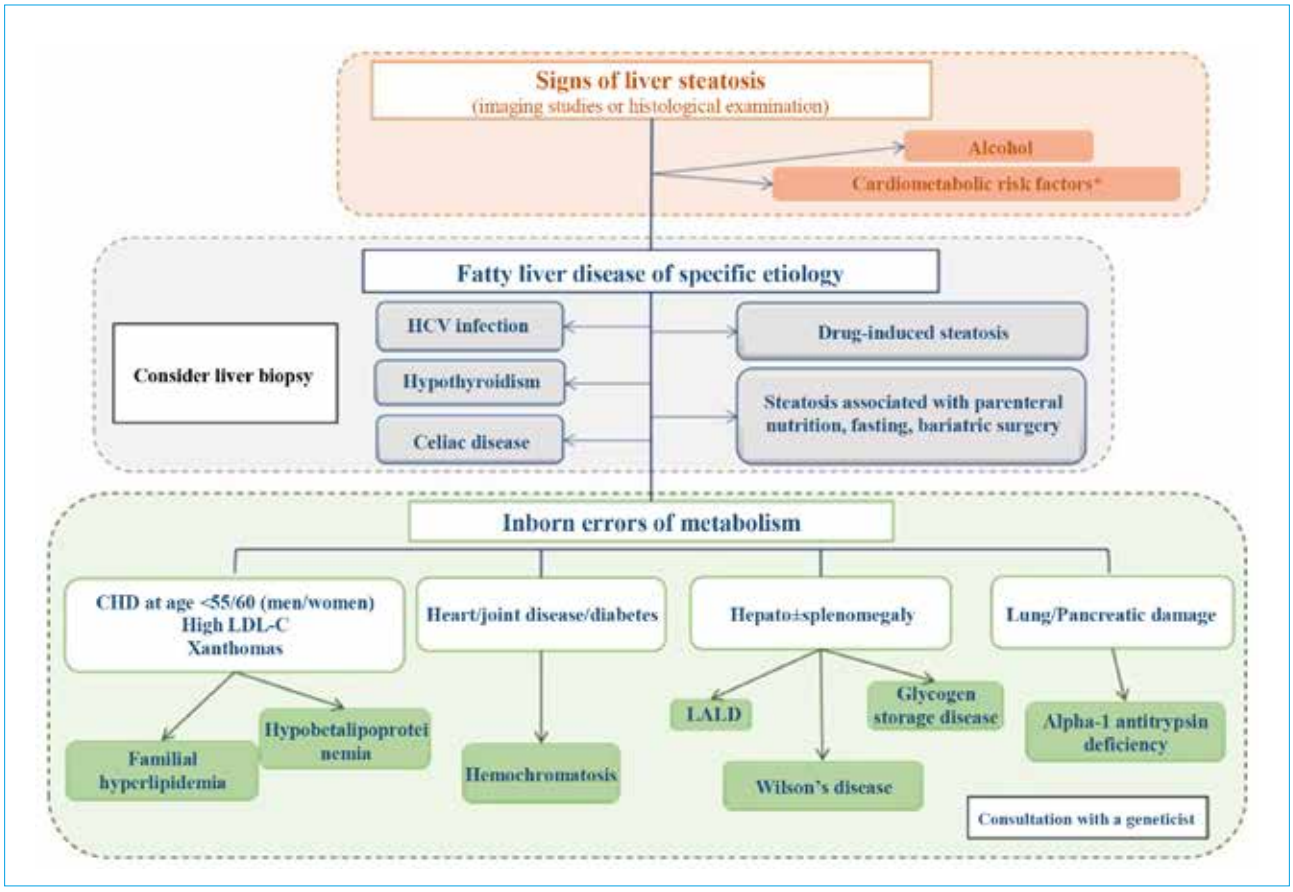
1. Order of the Ministry of Health and Social Development of the Russian Federation d/d November 12, 2012, No. 906n "On approval of the procedure for providing medical care to the population in the field of "Gastroenterology".
2. Order of the Ministry of Health of the Russian Federation d/d May 10, 2017, No. 203n "On approval of criteria for assessing the quality of medical care".
3. Order of the Ministry of Health of the Russian Federation d/d November 9, 2012, No. 772n "On approval of the medical care standard for other liver diseases".

Appendix B. Algorithm for monitoring NAFLD patients



Note: * – for the purpose of timely diagnosis of HCC.

Algorithms of physicians' actions
Algorithm for differential diagnosis of fatty liver disease causes



Note: * — a) BMI > 25 kg/m2 (Caucasians) or 23 kg/m2 (Asians) or waist circumference > 94 cm in men and > 80 cm in women; b) fasting glucose > 5.6 mmol/L, or postprandial glucose > 7.8 mmol/L, or HbA1c > 5.7 %, or already diagnosed type 2 DM or ongoing treatment for type 2 DM; c) blood pressure > 130/85 mmHg or pharmacotherapy for already diagnosed AH; d) plasma TG ≥ 1.70 mmol/L or lipid-lowering treatment; e) plasma HDL-C < 1.0 mmol/L in men and < 1.3 mmol/L in women, or lipid-lowering treatment. LALD — lysosomal acid lipase deficiency.

Appendix C.
Patient information

The key to success in treating NAFLD:
– healthy eating;
– physical activity.
- Reduce the size of the portions you eat. Eat as often as possible, but in small portions.
- Avoid food rich in simple carbohydrates (sweets, pastries) in your regular diet and try to consume them once in a while, in small quantities.
- Try to eat vegetables and fruit several times a day.
- Replace sugary and carbonated drinks with water or unsweetened beverages.
- Eat fiber-rich food, including whole grains.
- Avoid saturated fats, use extra virgin olive oil as your main source of added fat in meals.
- Eat fish 2–3 times a week.
- Avoid processed foods and fast foods.
- Read food labels to find hidden fat, sugar, and sodium.
- Try to do some kind of physical activity for at least 60 minutes a day. It doesn't have to be all at once. Walk more, exercise, and go upstairs, if possible.

Appendix D1–D4. Rating scales, questionnaires and other patient assessment instruments provided in clinical guidelines

Appendix D1. NAS Score (NAFLD Activity Score)

(*Bedossa P.* Current histological classification of NAFLD: Strength and limitations. *Hepatol Int*. 2013;7(Suppl. 2):765–70. DOI: 10.1007/s12072-013-9446-z)

Title in Russian: Шкала оценки активности НАЖБП (NAFLD activity score)
Source: Consensus of morphological experts CRN (Clinical Research Network, 2005).
Intended use: for semi-quantitative assessment of the severity and stage of NAFLD.
Contents (template): the score evaluates the degree of morphological changes in points (0 to 8), severity of liver steatosis, intralobular (lobular) inflammation, ballooning degeneration of hepatocytes and fibrosis stage.

Steatosis (%)	Lobular inflammation*	Ballooning degeneration
< 5 (0 points)	None (0 points)	None (0 points)
5–33 (1 point)	< 2 foci per field of vision (1 point)	Weak (1 point)
34–66 (2 points)	2–4 foci (2 points)	Moderate/severe (2 points)
Liver fibrosis (stages)	1a, 1b — zone 3 of the acinus; 1c — portal fibrosis; 2 — zone 3 of the acinus + portal/periportal fibrosis; 3 — fibrous septa; 4 — pseudolobules, disruption of liver tissue architecture (cirrhosis)	

Note: ** — the presence of clusters of inflammatory infiltrate cells at ×20 magnification.*

Key (interpretation):
- NAS 0–2: NASH diagnosis is unlikely;
- NAS 3–4: "gray zone", the patient may have NASH;
- NAS ≥ 5: provisional NASH diagnosis.

Appendix D2. SAF Score

(*Bedossa P.* Utility and appropriateness of the fatty liver inhibition of progression (FLIP) algorithm and steatosis, activity, and fibrosis (SAF) score in the evaluation of biopsies of nonalcoholic fatty liver disease. *Hepatology*. 2014;60(2):565–75. DOI: 10.1002/hep.27173)

Title in Russian: Шкала для полуколичественной оценки тяжести НАЖБП (Score of semi-quantitative assessment of NAFLD severity).
Source: FLIP Pathology Consortium (2014).
Purpose: for semi-quantitative assessment of NAFLD severity.
Contents (template): the scale includes such histological characteristics of NAFLD as the severity of steatosis (S — steatosis), ballooning degeneration and lobular inflammation (A — activity) and the stage of liver fibrosis (F — fibrosis).

Parameter	Severity of changes	Score
S — steatosis (0–3)	< 5	0
	5–33	1
	33–66	2
	> 66*	3
A — activity (0–4)	Ballooning degeneration	
	No	0
	Clusters of hepatocytes with normal size but rounded in shape and with pale cytoplasm	1
	The same, but there are also enlarged cells, and there are at least 2 times more of them than normal ones.	2
	Lobular inflammation (≥ 2 inflammatory cells at ×20 magnification	
	No	0
	<2 foci within 1 lobule	1
	>2 foci within 1 lobule	2
F — fibrosis (0–4)	No	0
	Perisinusoidal or portal fibrosis	1
	Perisinusoidal and portal fibrosis without bridging fibrosis	2
	The same and bridging fibrosis	3
	Cirrhosis	4
Total points		0–11

Note: ** — the presence of (sub)total hepatic steatosis in young patients, especially without signs of metabolic syndrome, requires assessment of lysosomal acid lipase activity to rule out cholesterol ester storage disease/Wolman disease or patient examination for Wilson disease. A rarer cause may be carriership of recessive mutations of POLG (DNA Polymerase Subunit Gamma), DGUOK (Deoxyguanosine Kinase) or MPV17 (Mitochondrial Inner Membrane Protein MPV17), which are characteristic of mitochondrial diseases.*

Key (interpretation): The assessment result is recorded in the form of an index: S1A2F3, S2A1F1, etc.

Appendix D3. Fibrosis-4 index, FIB-4

(*Sterling R.K., Lissen E., Clumeck N., Sola R., Correa M.C., Montaner J., et al.* Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. *Hepatology*. 2006;43(6):1317–25. DOI: 10.1002/hep.21178)

Title in Russian: Индекс фиброза-4 (Fibrosis Index-4).
Purpose: noninvasive assessment of potential fibrosis in NAFLD.
Contents (template):
FIB-4 = age ([years] × AST [U/L]) / ((platelets [109/L]) × (ALT [U/L])(1/2)).
Key (interpretation):
- > 1.3 — risk of advanced fibrosis;
- > 3.25 — high risk of advanced fibrosis.

Appendix D4. NAFLD Fibrosis Score, NFS

(*Angulo P., Hui J.M., Marchesini G., Bugianesi E., George J., Farrell G.C., et al.* The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD. *Hepatology*. 2007;45(4):846–54. DOI: 10.1002/hep.21496

Title in Russian: оценка фиброза при неалкогольной жировой болезни печени (fibrosis assessment in nonalcoholic fatty liver disease).
Purpose: noninvasive assessment of potential fibrosis in NAFLD.
Contents (template):
NFS = –1.675 + 0.037 × age (years) + 0.094 × BMI (kg/m^2) + 1.13 × (impaired glucose tolerance or diabetes mellitus [yes = 1, no = 0]) + 0.99 × (AST/ALT ratio) – 0.013 × platelets (×10^9/L) – 0.66 × albumin (g/dL).
Key (interpretation):
- < 1.455 — low risk of advanced fibrosis;
- 1.455–0.67 — inconclusive result;
- > 1.455 — high risk of advanced fibrosis

Литература / References

1. *Rinella M.E., Neuschwander-Tetri B.A., Siddiqui M.S., Abdelmalek M.F., Caldwell S., Barb D., et al.* AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology.* 2023;77(5):1797–835. DOI: 10.1097/HEP.0000000000000323
2. *Rinella M.E., Lazarus J.V., Ratziu V., Francque S.M., Sanyal A.J., Kanwal F., et al.* A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *Hepatology.* 2023;78(6):1966–86. DOI: 10.1097/HEP.0000000000000520
3. *ICD-11.* International Classification of Diseases 11th Revision. URL: https://icd.who.int
4. *Singh S., Allen A.M., Wang Z., Prokop L.J., Murad M.H., Loomba R.* Fibrosis progression in nonalcoholic fatty liver vs nonalcoholic steatohepatitis: A systematic review and meta-analysis of paired-biopsy studies. *Clin Gastroenterol Hepatol.* 2015;13(4):643–54.e1–9. DOI: 10.1016/j.cgh.2014.04.014
5. *Райхельсон К.Л., Маевская М.В., Жаркова М.С., Гречишникова В.Р., Оковитый С.В., Деева Т.А. и др.* Жировая болезнь печени: новая номенклатура и ее адаптация в Российской Федерации. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2024;34(2):35–44. [*Raikhelson K.L., Maevskaya M.V., Zharkova M.S., Grechishnikova V.R., Okovityi S.V., Deeva T.A., et al.* Steatotic liver disease: New nomenclature and its localization in the Russian Federation. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2024;34(2):35–44. (In Russ.)]. DOI: 10.22416/1382-4376-2024-961
6. *Day C.P., James O.F.* Steatohepatitis: A tale of two "hits"? *Gastroenterology.* 1998;114(4):842–5. DOI: 10.1016/s0016-5085(98)70599-2
7. *Byrne C.D., Targher G.* NAFLD: A multisystem disease. *J Hepatol.* 2015;62(Suppl. 1):S47–64. DOI: 10.1016/j.jhep.2014.12.012
8. *Xian Y.X., Weng J.P., Xu F.* MAFLD vs. NAFLD: Shared features and potential changes in epidemiology, pathophysiology, diagnosis, and pharmacotherapy. *Chin Med J (Engl).* 2020;134(1):8–19. DOI: 10.1097/CM9.0000000000001263
9. *Parthasarathy G., Revelo X., Malhi H.* Pathogenesis of nonalcoholic steatohepatitis: An overview. *Hepatol Commun.* 2020;4(4):478–92. DOI: 10.1002/hep4.1479
10. *Haas J.T., Francque S., Staels B.* Pathophysiology and mechanisms of nonalcoholic fatty liver disease. *Annu Rev Physiol.* 2016;78:181–205. DOI: 10.1146/annurev-physiol-021115-105331
11. *Basaranoglu M., Basaranoglu G., Bugianesi E.* Carbohydrate intake and nonalcoholic fatty liver disease: Fructose as a weapon of mass destruction. *Hepatobiliary Surg Nutr.* 2015;4(2):109–16. DOI: 10.3978/j.issn.2304-3881.2014.11.05
12. *Jensen T., Abdelmalek M.F., Sullivan S., Nadeau K.J., Green M., Roncal C., et al.* Fructose and sugar: A major mediator of non-alcoholic fatty liver disease. *J Hepatol.* 2018;68(5):1063–75. DOI: 10.1016/j.jhep.2018.01.019
13. *Birkenfeld A.L., Shulman G.I.* Nonalcoholic fatty liver disease, hepatic insulin resistance, and type 2 diabetes. *Hepatology.* 2014;59(2):713–23. DOI: 10.1002/hep.26672
14. *Ipsen D.H., Lykkesfeldt J., Tveden-Nyborg P.* Molecular mechanisms of hepatic lipid accumulation in non-alcoholic fatty liver disease. *Cell Mol Life Sci.* 2018;75(18):3313–27. DOI: 10.1007/s00018-018-2860-6
15. *Lambert J.E., Ramos-Roman M.A., Browning J.D., Parks E.J.* Increased de novo lipogenesis is a distinct characteristic of individuals with nonalcoholic fatty liver disease. *Gastroenterology.* 2014;146(3):726–35. DOI: 10.1053/j.gastro.2013.11.049
16. *Ter Horst K.W., Serlie M.J.* Fructose consumption, lipogenesis, and non-alcoholic fatty liver disease. *Nutrients.* 2017;9(9):981. DOI: 10.3390/nu9090981
17. *Shen J., Sakaida I., Uchida K., Terai S., Okita K.* Leptin enhances TNF-alpha production via p38 and JNK MAPK in LPS-stimulated Kupffer cells. *Life Sci.* 2005;77(13):1502–15. DOI: 10.1016/j.lfs.2005.04.004
18. *Subichin M., Clanton J., Makuszewski M., Bohon A., Zografakis J.G., Dan A.* Liver disease in the morbidly obese: A review of 1000 consecutive patients undergoing weight loss surgery. *Surg Obes Relat Dis.* 2015;11(1):137–41. DOI: 10.1016/j.soard.2014.06.015
19. *Sasaki A., Nitta H., Otsuka K., Umemura A., Baba S., Obuchi T., et al.* Bariatric surgery and non-alcoholic fatty liver disease: Current and potential future treatments. *Front Endocrinol (Lausanne).* 2014;5:164. DOI: 10.3389/fendo.2014.00164
20. *Stojsavljević S., Gomerčić Palčić M., Virović Jukić L., Smirčić Duvnjak L., Duvnjak M.* Adipokines and proinflammatory cytokines, the key mediators in the pathogenesis of nonalcoholic fatty liver disease. *World J Gastroenterol.* 2014;20(48):18070–91. DOI: 10.3748/wjg.v20.i48.18070
21. *Osborn O., Olefsky J.M.* The cellular and signaling networks linking the immune system and metabolism in disease. *Nat Med.* 2012;18(3):363–74. DOI: 10.1038/nm.2627
22. *Yan F.J., Wang X., Wang S.E., Hong H.T., Lu J., Ye Q., et al.* C-Jun/C7ORF41/NF-κB axis mediates hepatic inflammation and lipid accumulation in NAFLD. *Biochem J.* 2020;477(3):691–708. DOI: 10.1042/BCJ20190799
23. *Jin S., Li Y., Xia T., Liu Y., Zhang S., Hu H., et al.* Mechanisms and therapeutic implications of selective autophagy in nonalcoholic fatty liver disease. *J Adv Res.* 2025:67:317–29. DOI: 10.1016/j.jare.2024.01.027
24. *Prerna K., Dubey V.K.* Beclin1-mediated interplay between autophagy and apoptosis: New understanding. *Int J Biol Macromol.* 2022;204:258–73. DOI: 10.1016/j.ijbiomac.2022.02.005
25. *Fromenty B., Roden M.* Mitochondrial alterations in fatty liver diseases. *J Hepatol.* 2023;78(2):415–29. DOI: 10.1016/j.jhep.2022.09.020
26. *Ferré P., Foufelle F.* SREBP-1c transcription factor and lipid homeostasis: Clinical perspective. *Horm Res.* 2007;68(2):72–82. DOI: 10.1159/000100426
27. *Miserez A.R., Muller P.Y., Barella L., Barella S., Staehelin H.B., Leitersdorf E., et al.* Sterol-regulatory element-binding protein (SREBP)-2 contributes to polygenic hypercholesterolaemia. *Atherosclerosis.* 2002;164(1):15–26. DOI: 10.1016/s0021-9150(01)00762-6
28. *Iizuka K., Takao K., Yabe D.* ChREBP-mediated regulation of lipid metabolism: Involvement of the gut microbiota, liver, and adipose tissue. *Front Endocrinol (Lausanne).* 2020;11:587189. DOI: 10.3389/fendo.2020.587189
29. *Ma M., Xie W., Li X.* Identification of autophagy-related genes in the progression from non-alcoholic fatty liver to non-alcoholic steatohepatitis. *Int J Gen Med.* 2021;14:3163–76. DOI: 10.2147/IJGM.S317785
30. *Barrientos-Riosalido A., Real M., Bertran L., Aguilar C., Martínez S., Parada D., et al.* Increased hepatic ATG7 mRNA and ATG7 protein expression in nonalcoholic steatohepatitis associated with obesity. *Int J Mol Sci.* 2023;24(2):1324. DOI: 10.3390/ijms24021324
31. *Syed-Abdul M.M.* Lipid metabolism in metabolic-associated steatotic liver disease (MASLD). *Metabolites.* 2023;14(1):12. DOI: 10.3390/metabo14010012
32. *Branković M., Dukić M., Gmizić T., Popadić V., Nikolić N., Sekulić A., et al.* New therapeutic approaches for the treatment of patients with metabolic dysfunction-associated steatotic liver disease (MASLD) and increased cardiovascular risk. *Diagnostics (Basel).* 2024;14(2):229. DOI: 10.3390/diagnostics14020229
33. *Zhao Y., Zhou Y., Wang D., Huang Z., Xiao X., Zheng Q., et al.* Mitochondrial dysfunction in metabolic dysfunction fatty liver disease (MAFLD). *Int J Mol Sci.* 2023;24(24):17514. DOI: 10.3390/ijms242417514
34. *Chen Z., Tian R., She Z., Cai J., Li H.* Role of oxidative stress in the pathogenesis of nonalcoholic fatty liver disease. *Free Radic Biol Med.* 2020;152:116–41. DOI: 10.1016/j.freeradbiomed.2020.02.025

35. *Thomson A.W., Knolle P.A.* Antigen-presenting cell function in the tolerogenic liver environment. *Nat Rev Immunol*. 2010;10(11):753–66. DOI: 10.1038/nri2858
36. *Lotze M.T., Zeh H.J., Rubartelli A., Sparvero L.J., Amoscato A.A., Washburn N.R., et al.* The grateful dead: Damage-associated molecular pattern molecules and reduction/oxidation regulate immunity. *Immunol Rev*. 2007;220:60–81. DOI: 10.1111/j.1600-065X.2007.00579.x
37. *Szabo G., Csak T.* Inflammasomes in liver diseases. *J Hepatol*. 2012;57(3):642–54. DOI: 10.1016/j.jhep.2012.03.035
38. *Luedde T., Schwabe R.F.* NF-κB in the liver — linking injury, fibrosis and hepatocellular carcinoma. *Nat Rev Gastroenterol Hepatol*. 2011;8(2):108–18. DOI: 10.1038/nrgastro.2010.213
39. *Klein I., Cornejo J.C., Polakos N.K., John B., Wuensch S.A., Topham D.J., et al.* Kupffer cell heterogeneity: Functional properties of bone marrow derived and sessile hepatic macrophages. *Blood*. 2007;110(12):4077–85. DOI: 10.1182/blood-2007-02-073841
40. *Fang Y.L., Chen H., Wang C.L., Liang L.* Pathogenesis of non-alcoholic fatty liver disease in children and adolescence: From "two hit theory" to "multiple hit model". *World J Gastroenterol*. 2018;24(27):2974–83. DOI: 10.3748/wjg.v24.i27.2974
41. *Tomita K., Tamiya G., Ando S., Ohsumi K., Chiyo T., Mizutani A., et al.* Tumour necrosis factor alpha signalling through activation of Kupffer cells plays an essential role in liver fibrosis of non-alcoholic steatohepatitis in mice. *Gut*. 2006;55(3):415–24. DOI: 10.1136/gut.2005.071118
42. *Kremer M., Hines I.N., Milton R.J., Wheeler M.D.* Favored T helper 1 response in a mouse model of hepatosteatosis is associated with enhanced T cell-mediated hepatitis. *Hepatology*. 2006;44(1):216–27. DOI: 10.1002/hep.21221
43. *Ghazarian M., Revelo X.S., Nøhr M.K., Luck H., Zeng K., Lei H., et al.* Type I interferon Responses drive intrahepatic T cells to promote metabolic syndrome. *Sci Immunol*. 2017;2(10):eaai7616. DOI: 10.1126/sciimmunol.aai7616
44. *Wang M., Li L., Xu Y., Du J., Ling C.* Roles of hepatic stellate cells in NAFLD: From the perspective of inflammation and fibrosis. *Front Pharmacol*. 2022;13:958428. DOI: 10.3389/fphar.2022.958428
45. *Li Z., Yuan H., Chu H., Yang L.* The crosstalk between gut microbiota and bile acids promotes the development of non-alcoholic fatty liver disease. *Microorganisms*. 2023;11(8):2059. DOI: 10.3390/microorganisms11082059
46. *Clemente M.G., Mandato C., Poeta M., Vajro P.* Pediatric non-alcoholic fatty liver disease: Recent solutions, unresolved issues, and future research directions. *World J Gastroenterol*. 2016;22(36):8078–93. DOI: 10.3748/wjg.v22.i36.8078
47. *Ulluwishewa D., Anderson R.C., McNabb W.C., Moughan P.J., Wells J.M., Roy N.C.* Regulation of tight junction permeability by intestinal bacteria and dietary components. *J Nutr*. 2011;141(5):769–76. DOI: 10.3945/jn.110.135657
48. *Paolella G., Mandato C., Pierri L., Poeta M., Di Stasi M., Vajro P.* Gut-liver axis and probiotics: Their role in non-alcoholic fatty liver disease. *World J Gastroenterol*. 2014;20(42):15518–31. DOI: 10.3748/wjg.v20.i42.15518
49. *Zorn A.M., Wells J.M.* Vertebrate endoderm development and organ formation. *Annu Rev Cell Dev Biol*. 2009;25:221–51. DOI: 10.1146/annurev.cellbio.042308.113344
50. *Fairfield C.J., Drake T.M., Pius R., Bretherick A.D., Campbell A., Clark D.W., et al.* Genome-wide association study of NAFLD using electronic health records. *Hepatol Commun*. 2022;6(2):297–308. DOI: 10.1002/hep4.1805
51. *Anstee Q.M., Darlay R., Cockell S., Meroni M., Govaere O., Tiniakos D., et al.* Genome-wide association study of non-alcoholic fatty liver and steatohepatitis in a histologically characterised cohort. *J Hepatol*. 2020;73(3):505–15. DOI: 10.1016/j.jhep.2020.04.003
52. *Куртанов Х.А., Сыдыкова Л.А., Павлова Н.И., Филиппова Н.П., Додохов В.В., Ансолихова Г.А. и др.* Полиморфизм гена адипонутрина (*PNPLA3*) у коренных жителей Республики Саха (Якутия), страдающих сахарным диабетом 2-го типа. *Альманах клинической медицины*. 2018;46(3):258–63. [*Kurtanov K.A., Sydykova L.A., Pavlova N.I., Filippova N.P., Dodokhov V.V., Apsolikhova G.A., et al.* Polymorphism of the adiponutrin gene (*PNPLA3*) in the indigenous inhabitants of the Republic of Sakha (Yakutia) with type 2 diabetes mellitus. *Almanac of Clinical Medicine*. 2018;46(3):258–63 (In Russ.)]. DOI: 10.18786/2072-0505-2018-46-3-258-263
53. *Кролевец Т.С., Ливзан М.А., Ахмедов В.А., Новиков Д.Г.* Исследование полиморфизма гена *PNPLA3* у пациентов с неалкогольной жировой болезнью печени и различной стадией фиброза. *Экспериментальная и клиническая гастроэнтерология*. 2018;11:24–32. [*Krolevets T.S., Livzan M.A., Akhmedov V.A., Novikov D.G.* Study of *PNPLA3* gene polymorphism in patients with non-alcoholic fatty liver disease and various stages of fibrosis. *Experimental and Clinical Gastroenterology*. 2018;11:24–32. (In Russ.)].
54. *Райхельсон К.Л., Ковязина В.П., Сидоренко Д.В., Назаров В.Д., Лапин С.В., Эмануэль В.Л. и др.* Влияние полиморфизма гена *PNPLA3* на течение неалкогольной жировой болезни печени. *РМЖ*. 2019;12:85–8. [*Raikhelson K.L., Kovyazina V.P., Sidorenko D.V., Nazarov V.D., Lapin S.V., Emanuel V.L., et al. PNPLA3* gene polymorphism impact on the nonalcoholic fatty liver disease course. *RMJ*. 2019;12:85–8. (In Russ.)].
55. *Дьяконова А.Т., Куртанов Х.А., Павлова Н.И., Соловьева Н.А., Соловьева Ю.А., Филиппова Н.П. и др.* Полиморфизм rs58542926 гена *TM6SF2* при хронических неинфекционных болезнях печени в якутской популяции. *Современные проблемы науки и образования*. 2019;6:133. [*Dyakonova A.T., Kurtanov K.A., Pavlova N.I., Soloveva N.A., Soloveva Yu.A., Filippova N.P., et al.* Polymorphism rs58542926 of the *TM6SF2* gene in chronic non-infectious liver diseases in the Yakut population. *Modern Problems of Science and Education*. 2019;6:133. (In Russ.)]. DOI: 10.17513/spno.29334
56. *Cusi K., Isaacs S., Barb D., Basu R., Caprio S., Garvey W.T., et al.* American Association of Clinical Endocrinology Clinical Practice Guideline for the diagnosis and management of nonalcoholic fatty liver disease in primary care and endocrinology clinical settings: Co-sponsored by the American Association for the Study of Liver Diseases (AASLD). *Endocr Pract*. 2022;28(5):528–62. DOI: 10.1016/j.eprac.2022.03.010
57. *Lonardo A., Ballestri S., Mantovani A., Nascimbeni F., Lugari S., Targher G.* Pathogenesis of hypothyroidism-induced NAFLD: Evidence for a distinct disease entity? *Dig Liver Dis*. 2019;51(4):462–70. DOI: 10.1016/j.dld.2018.12.014
58. *Ramanathan R., Patwa S.A., Ali A.H., Ibdah J.A.* Thyroid hormone and mitochondrial dysfunction: Therapeutic implications for metabolic dysfunction-associated steatotic liver disease (MASLD). *Cells*. 2023;12(24):2806. DOI: 10.3390/cells12242806
59. *Younossi Z.M., Henry L.* Understanding the burden of nonalcoholic fatty liver disease: Time for action. *Diabetes Spectr*. 2024;37(1):9–19. DOI: 10.2337/dsi23-0010
60. *Jichitu A., Bungau S., Stanescu A.M.A., Vesa C.M., Toma M.M., Bustea C., et al.* Non-alcoholic fatty liver disease and cardiovascular comorbidities: Pathophysiological links, diagnosis, and therapeutic management. *Diagnostics (Basel)*. 2021;11(4):689. DOI: 10.3390/diagnostics11040689
61. *Драпкина О.М., Ивашкин В.Т.* Эпидемиологические особенности неалкогольной жировой болезни печени в России (результаты открытого многоцентрового проспективного исследования-наблюдения DIREG L 01903). *Российский журнал гастроэнтерологии, гепатологии, колопроктологии*. 2014;24(4):32–8. [*Drapkina O.M., Ivashkin V.T.* Epidemiological features of non-alcoholic fatty liver disease in Russia (results of an open multi-

center prospective observational study DIREG L 01903). *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2014;24(4):32–8. (In Russ.)].
62. *Ивашкин В.Т., Драпкина О.М., Маев И.В., Трухманов А.С., Блинов Д.В., Пальгова Л.К. и др.* Распространенность неалкогольной жировой болезни печени у пациентов амбулаторно-поликлинической практики в Российской Федерации: результаты исследования DIREG 2. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2015;25(6):31–41. [*Ivashkin V.T., Drapkina O.M., Mayev I.V., Trukhmanov A.S., Blinov D.V., Palgova L.K., et al.* Prevalence of non-alcoholic fatty liver disease in out-patients of the Russian Federation: DIREG 2 study results. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2015;25(6):31–41. (In Russ.)].
63. *Евстифеева С.Е., Шальнова С.А., Куценко В.А., Яровая Е.Б., Баланова Ю.А., Имаева А.Э. и др.* Распространенность неалкогольной жировой болезни печени среди населения трудоспособного возраста: ассоциации с социально-демографическими показателями и поведенческими факторами риска (данные ЭССЕ-РФ-2). *Кардиоваскулярная терапия и профилактика.* 2022;21(9):3356. [*Evstifeeva S.E., Shalnova S.A., Kutsenko V.A., Yarovaya E.V., Balanova Yu.A., Imaeva A.E., et al.* Prevalence of non-alcoholic fatty liver disease among the working-age population: Associations with socio-demographic indicators and behavioral risk factors (ESSE RF-2 data). *Cardiovascular Therapy and Prevention.* 2022;21(9):3356. (In Russ.)]. DOI: 10.15829/1728-8800-2022-3356
64. *Маев И.В., Андреев Д.Н., Кучерявый Ю.А.* Распространенность неалкогольной жировой болезни печени в России: метаанализ. *Consilium Medicum.* 2023;25(5):313–19. [*Maev I.V., Andreev D.N., Kucheryavyy Yu.A.* Prevalence of non-alcoholic fat disease liver in Russian Federation: Meta-analysis. *Consilium Medicum.* 2023;25(5):313–19. (In Russ.)]. DOI: 10.26442/20751753.2023.5.202155
65. *Povsic M., Wong O.Y., Perry R., Bottomley J.* A structured literature review of the epidemiology and disease burden of non-alcoholic steatohepatitis (NASH). *Adv Ther.* 2019;36(7):1574–94. DOI: 10.1007/s12325-019-00960-3
66. *Harrison S.A., Gawrieh S., Roberts K., Lisanti C.J., Schwope R.B., Cebe K.M., et al.* Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort. *J Hepatol.* 2021;75(2):284–91. DOI: 10.1016/j.jhep.2021.02.034
67. *Estes C., Anstee Q.M., Arias-Loste M.T., Bantel H., Bellentani S., Caballeria J., et al.* Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016–2030. *J Hepatol.* 2018;69(4):896–904. DOI: 10.1016/j.jhep.2018.05.036
68. *Huang D.Q., Terrault N.A., Tacke F., Gluud L.L., Arrese M., Bugianesi E., et al.* Global epidemiology of cirrhosis – aetiology, trends and predictions. *Nat Rev Gastroenterol Hepatol.* 2023;20(6):388–98. DOI: 10.1038/s41575-023-00759-2
69. *Huang D.Q., El-Serag H.B., Loomba R.* Global epidemiology of NAFLD-related HCC: Trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol.* 2021;18(4):223–38. DOI: 10.1038/s41575-020-00381-6
70. *Ивашкин В.Т., Маевская М.В., Жаркова М.С., Жигалова С.Б., Киценко Е.А., Манукьян Г.В. и др.* Цирроз и фиброз печени: клинические рекомендации. М.; 2021. [*Ivashkin V.T., Maevskaya M.V., Zharkova M.S., Zhigalova S.B., Kitsenko E.A., Manukyan G.V., et al.* Liver cirrhosis and fibrosis: Clinical guidelines. Moscow; 2021. (In Russ.)].
71. *Muthiah M.D., Cheng Han N., Sanyal A.J.* A clinical overview of non-alcoholic fatty liver disease: A guide to diagnosis, the clinical features, and complications – What the non-specialist needs to know. *Diabetes Obes Metab.* 2022;24(Suppl. 2):3–14. DOI: 10.1111/dom.14521
72. *Cook N., Geier A., Schmid A., Hirschfield G., Kautz A., Schattenberg J.M., et al.* The patient perspectives on future therapeutic options in NASH and patient needs. *Front Med (Lausanne).* 2019;6:61. DOI: 10.3389/fmed.2019.00061
73. *Liebe R., Esposito I., Bock H.H., Vom Dahl S., Stindt J., Baumann U., et al.* Diagnosis and management of secondary causes of steatohepatitis. *J Hepatol.* 2021;74(6):1455–71. DOI: 10.1016/j.jhep.2021.01.045
74. *Ивашкин В.Т.* Пропедевтика внутренних болезней: учебник. 2-е изд. М.: ГЭОТАР-Медиа; 2023. [*Ivashkin V.T.* Propaedeutics of internal diseases: textbook. 2nd ed. Moscow: GEOTAR-Media Publ.; 2023. (In Russ.)].
75. *Ивашкин В.Т., Маевская М.В., Жаркова М.С., Котовская Ю.В., Ткачева О.Н., Трошина Е.А. и др.* Клинические рекомендации Российского общества по изучению печени, Российской гастроэнтерологической ассоциации, Российской ассоциации эндокринологов, Российской ассоциации геронтологов и гериатров и Национального общества профилактической кардиологии по диагностике и лечению неалкогольной жировой болезни печени. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2022;32(4):104–40. [*Ivashkin V.T., Maevskaya M.V., Zharkova M.S., Kotovskaya Yu.V., Tkacheva O.N., Troshina E.A., et al.* Clinical Practice Guidelines of the Russian Scientific Liver Society, Russian Gastroenterological Association, Russian Association of Endocrinologists, Russian Association of Gerontologists and Geriatricians and National Society for Preventive Cardiology on Diagnosis and Treatment of Non-Alcoholic Liver Disease. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2022;32(4):104–40. (In Russ)]. DOI: 10.22416/1382-4376-2022-32-4-104-140
76. *Obika M., Noguchi H.* Diagnosis and evaluation of nonalcoholic fatty liver disease. *Exp Diabetes Res.* 2012;2012:145754. DOI: 10.1155/2012/145754
77. *Павлов Ч.С., Глушенков Д.В., Коновалова О.Н., Ивашкин В.Т.* Сфера клинического применения неинвазивных методов оценки фиброза печени: результаты собственных исследований в многопрофильном стационаре. *Клиническая медицина.* 2009;87(11):40–5. [*Pavlov Ch.S., Glushenkov D.V., Konovalova O.N., Ivashkin V.T.* The scope of clinical application of noninvasive methods for assessing liver fibrosis: Results of our own studies in a multidisciplinary hospital. *Clinical Medicine.* 2009;87(11):40–5. (In Russ.)].
78. *Sorbi D., Boynton J., Lindor K.D.* The ratio of aspartate aminotransferase to alanine aminotransferase: Potential value in differentiating nonalcoholic steatohepatitis from alcoholic liver disease. *Am J Gastroenterol.* 1999;94(4):1018–22. DOI: 10.1111/j.1572-0241.1999.01006.x
79. *Дедов И.И., Шестакова М.В., Майоров А.Ю., Шамхалова М.Ш., Сухарева О.Ю., Галстян Г.Р. и др.* Сахарный диабет 2-го типа у взрослых: клинические рекомендации. М.; 2022. [*Dedov I.I., Shestakova M.V., Mayorov A.Yu., Shamkhalova M.Sh., Sukhareva O.Yu., Galstyan G.R., et al.* Type 2 diabetes mellitus in adults: Clinical guidelines. Moscow; 2022. (In Russ.)].
80. *Fujii H., Kawada N.; Japan Study Group Of Nafld Jsg-Nafld.* The role of insulin resistance and diabetes in nonalcoholic fatty liver disease. *Int J Mol Sci.* 2020;21(11):3863. DOI: 10.3390/ijms21113863
81. *Targher G., Day C.P., Bonora E.* Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. *N Engl J Med.* 2010;363(14):1341–50. DOI: 10.1056/NEJMra0912063
82. *Кутишенко Н.П., Марцевич С.Ю., Лерман О.В., Балашов И.С., Невзорова В.А., Резник И.И. и др.* Повышение эффективности гиполипидемической терапии у пациентов высокого сердечно-сосудистого риска с сочетанной патологией печени (результаты дополнительного анализа исследования РАКУРС). *Рациональная фармакотерапия в кардиологии.* 2015;11(3):297–303. [*Kutishenko N.P., Martsevich S.Yu., Lerman O.V., Balashov I.S., Nevzorova V.A., Reznik I.I., et al.* The improvement of lipid-lowering therapy effectiveness in patients with high cardiovascular risk and concomitant

liver disease (results of additional analysis of the RAKURS study). *Rational Pharmacotherapy in Cardiology*. 2015;11(3):297–303. (In Russ.)]. DOI: 10.20996/1819-6446-2015-11-3-297-303
83. *Ежов М.В., Кухарчук В.В., Сергиенко И.В., Алиева А.С., Анциферов М.Б., Аншелес А.А.* и др. Нарушения липидного обмена: клинические рекомендации. М.; 2023. [*Ezhov M.V., Kukharchuk V.V., Sergienko I.V., Alieva A.S., Antsiferov M.B., Ansheles A.A., et al.* Lipid metabolism disorders: Clinical guidelines. Moscow; 2023. (In Russ.)].
84. *Spinosa M., Stine J.G.* Nonalcoholic fatty liver disease — evidence for a thrombophilic state? *Curr Pharm Des*. 2020;26(10):1036–44. DOI: 10.2174/1381612826666200131101553
85. *Verrijken A., Francque S., Mertens I., Prawitt J., Caron S., Hubens G., et al.* Prothrombotic factors in histologically proven nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. *Hepatology*. 2014;59(1):121–9. DOI: 10.1002/hep.26510
86. *Balta G., Altay C., Gurgey A.* PAI-1 gene 4G/5G genotype: A risk factor for thrombosis in vessels of internal organs. *Am J Hematol*. 2002;71(2):89–93. DOI: 10.1002/ajh.10192
87. *Northup P.G., Argo C.K., Shah N., Caldwell S.H.* Hypercoagulation and thrombophilia in nonalcoholic fatty liver disease: Mechanisms, human evidence, therapeutic implications, and preventive implications. *Semin Liver Dis*. 2012;32(1):39–48. DOI: 10.1055/s-0032-1306425
88. *Skurk T., Hauner H.* Obesity and impaired fibrinolysis: Role of adipose production of plasminogen activator inhibitor-1. *Int J Obes Relat Metab Disord*. 2004;28(11):1357–64. DOI: 10.1038/sj.ijo.0802778
89. *Kotronen A., Joutsi-Korhonen L., Sevastianova K., Bergholm R., Hakkarainen A., Pietiläinen K.H., et al.* Increased coagulation factor VIII, IX, XI and XII activities in non-alcoholic fatty liver disease. *Liver Int*. 2011;31(2):176–83. DOI: 10.1111/j.1478-3231.2010.02375.x
90. *Ciardullo S., Ballabeni C., Trevisan R., Perseghin G.* Liver stiffness, albuminuria and chronic kidney disease in patients with NAFLD: A systematic review and meta-analysis. *Biomolecules*. 2022;12(1):105. DOI: 10.3390/biom12010105
91. *Sun D.Q., Jin Y., Wang T.Y., Zheng K.I., Rios R.S., Zhang H.Y., et al.* MAFLD and risk of CKD. *Metabolism*. 2021;115:154433. DOI: 10.1016/j.metabol.2020.154433
92. *Бобкова И.Н., Ватазин А.В., Ветчинникова О.Н., Волгина Г.В., Голубев Р.В., Горелова Е.А. и др.* Хроническая болезнь почек (ХБП): клинические рекомендации. М.; 2021. [*Bobkova I.N., Vatazin A.V., Vetchinnikova O.N., Volgina G.V., Golubev R.V., Gorelova E.A., et al.* Chronic kidney disease (CKD): Clinical guidelines. Moscow; 2021. (In Russ.)].
93. *Маевская М.В., Котовская Ю.В., Ивашкин В.Т., Ткачева О.Н., Трошина Е.А., Шестакова М.В. и др.* Национальный Консенсус для врачей по ведению взрослых пациентов с неалкогольной жировой болезнью печени и ее основными коморбидными состояниями. *Терапевтический архив*. 2022;94(2):216–53. [*Maevskaya M.V., Kotovskaya Yu.V., Ivashkin V.T., Tkacheva O.N., Troshina E.A., Shestakova M.V., et al.* The National Consensus statement on the management of adult patients with non-alcoholic fatty liver disease and main comorbidities. *Terapevticheskii Arkhiv*. 2022;94(2):216–53. (In Russ.)]. DOI: 10.26442/00403660.2022.02.201363
94. *Darmawan G., Hamijoyo L., Hasan I.* Association between serum uric acid and non-alcoholic fatty liver disease: A meta-analysis. *Acta Med Indones*. 2017;49(2):136–47.
95. *Lombardi R., Pisano G., Fargion S.* Role of serum uric acid and ferritin in the development and progression of NAFLD. *Int J Mol Sci*. 2016;17(4):548. DOI: 10.3390/ijms17040548
96. *Аверкина Н.А., Багаева М.Э., Батышева Т.Т., Быкова О.В., Вашакмадзе Н.Д., Волынец Г.В. и др.* Нарушения обмена меди (болезнь Вильсона): клинические рекомендации. М.; 2021. [*Averkina N.A., Bagaeva M.E., Batysheva T.T., Bykova O.V., Vashakmadze N.D., Volynets G.V., et al.* Copper metabolism disorders (Wilson's disease): Clinical guidelines. Moscow; 2021. (In Russ.)].
97. *Ивашкин В.Т., Ющук Н.Д., Богомолов П.О., Волчкова Е.В., Дмитриев А.С., Жаркова М.С. и др.* Хронический вирусный гепатит С: клинические рекомендации. М.; 2021. [*Ivashkin V.T., Yushchuk N.D., Bogomolov P.O., Volchkova E.V., Dmitriev A.S., Zharkova M.S., et al.* Chronic viral hepatitis C: Clinical recommendations. Moscow; 2021. (In Russ.)].
98. *Ивашкин В.Т., Маевская М.В., Жаркова М.С., Тихонов И.Н., Федосьина Е.А., Павлов Ч.С.* Алгоритмы диагностики и лечения в гепатологии: справочные материалы. М.: МЕДпресс-информ; 2016. [*Ivashkin V.T., Maevskaya M.V., Zharkova M.S., Tikhonov I.N., Fedosina E.A., Pavlov Ch.S.* Algorithms for diagnosis and treatment in hepatology: Reference materials. Moscow: MEDpress-inform Publ.; 2016. (In Russ.)].
99. *Petzold G.* Role of ultrasound methods for the assessment of NAFLD. *J Clin Med*. 2022;11(15):4581. DOI: 10.3390/jcm11154581
100. *Ferraioli G., Soares Monteiro L.B.* Ultrasound-based techniques for the diagnosis of liver steatosis. *World J Gastroenterol*. 2019;25(40):6053–62. DOI: 10.3748/wjg.v25.i40.6053
101. *Hernaez R., Lazo M., Bonekamp S., Kamel I., Brancati F.L., Guallar E., et al.* Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: A meta-analysis. *Hepatology*. 2011;54(3):1082–90. DOI: 10.1002/hep.24452
102. *European Association for the Study of the Liver.* EASL Clinical Practice Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis — 2021 update. *J Hepatol*. 2021;75(3):659–89. DOI: 10.1016/j.jhep.2021.05.025
103. *Petroff D., Blank V., Newsome P.N., Shalimar, Voican C.S., Thiele M., et al.* Assessment of hepatic steatosis by controlled attenuation parameter using the M and XL probes: An individual patient data meta-analysis. *Lancet Gastroenterol Hepatol*. 2021;6(3):185–98. DOI: 10.1016/S2468-1253(20)30357-5
104. *Pu K., Wang Y., Bai S., Wei H., Zhou Y., Fan J., et al.* Diagnostic accuracy of controlled attenuation parameter (CAP) as a non-invasive test for steatosis in suspected non-alcoholic fatty liver disease: A systematic review and meta-analysis. *BMC Gastroenterol*. 2019;19(1):51. DOI: 10.1186/s12876-019-0961-9
105. *Gu J., Liu S., Du S., Zhang Q., Xiao J., Dong Q., et al.* Diagnostic value of MRI-PDFF for hepatic steatosis in patients with non-alcoholic fatty liver disease: A meta-analysis. *Eur Radiol*. 2019;29(7):3564–73. DOI: 10.1007/s00330-019-06072-4
106. *Verhaegh P., Bavalia R., Winkens B., Masclee A., Jonkers D., Koek G.* Noninvasive tests do not accurately differentiate nonalcoholic steatohepatitis from simple steatosis: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2018;16(6):837–61. DOI: 10.1016/j.cgh.2017.08.024
107. *Kleiner D.E., Brunt E.M.* Nonalcoholic fatty liver disease: Pathologic patterns and biopsy evaluation in clinical research. *Semin Liver Dis*. 2012;32(1):3–13. DOI: 10.1055/s-0032-1306421
108. *Kleiner D.E., Brunt E.M., Van Natta M., Behling C., Contos M.J., Cummings O.W., et al.* Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology*. 2005;41(6):1313–21. DOI: 10.1002/hep.20701
109. *Bedossa P.* Utility and appropriateness of the fatty liver inhibition of progression (FLIP) algorithm and steatosis, activity, and fibrosis (SAF) score in the evaluation of biopsies of nonalcoholic fatty liver disease. *Hepatology*. 2014;60(2):565–75. DOI: 10.1002/hep.27173
110. *Bedossa P.* Current histological classification of NAFLD: Strength and limitations. *Hepatol Int*. 2013;7(Suppl. 2):765–70. DOI: 10.1007/s12072-013-9446-z

111. *Harrison S.A., Torgerson S., Hayashi P., Ward J., Schenker S.* Vitamin E and vitamin C treatment improves fibrosis in patients with nonalcoholic steatohepatitis. *Am J Gastroenterol.* 2003;98(11):2485–90. DOI: 10.1111/j.1572-0241.2003.08699.x
112. *Xiao G., Zhu S., Xiao X., Yan L., Yang J., Wu G.* Comparison of laboratory tests, ultrasound, or magnetic resonance elastography to detect fibrosis in patients with nonalcoholic fatty liver disease: A meta-analysis. *Hepatology.* 2017;66(5):1486–501. DOI: 10.1002/hep.29302
113. *McPherson S., Hardy T., Dufour J.F., Petta S., Romero-Gomez M., Allison M., et al.* Age as a confounding factor for the accurate non-invasive diagnosis of advanced NAFLD fibrosis. *Am J Gastroenterol.* 2017;112(5):740–51. DOI: 10.1038/ajg.2016.453
114. *Bril F., McPhaul M.J., Caulfield M.P., Clark V.C., Soldevilla-Pico C., Firpi-Morell R.J., et al.* Performance of plasma biomarkers and diagnostic panels for nonalcoholic steatohepatitis and advanced fibrosis in patients with type 2 diabetes. *Diabetes Care.* 2020;43(2):290–7. DOI: 10.2337/dc19-1071
115. *Ratziu V., Massard J., Charlotte F., Messous D., Imbert-Bismut F., Bonyhay L., et al.* Diagnostic value of biochemical markers (FibroTest-FibroSURE) for the prediction of liver fibrosis in patients with nonalcoholic fatty liver disease. *BMC Gastroenterol.* 2006;6:6. DOI: 10.1186/1471-230X-6-6
116. *Vali Y., Lee J., Boursier J., Spijker R., Verheij J., Brosnan M.J., et al.* FibroTest for evaluating fibrosis in non-alcoholic fatty liver disease patients: A systematic review and meta-analysis. *J Clin Med.* 2021;10(11):2415. DOI: 10.3390/jcm10112415
117. *Papatheodoridi M., Hiriart J.B., Lupsor-Platon M., Bronte F., Boursier J., Elshaarawy O., et al.* Refining the Baveno VI elastography criteria for the definition of compensated advanced chronic liver disease. *J Hepatol.* 2021;74(5):1109–16. DOI: 10.1016/j.jhep.2020.11.050
118. *De Franchis R., Bosch J., Garcia-Tsao G., Reiberger T., Ripoll C.* Baveno VII – Renewing consensus in portal hypertension. *J Hepatol.* 2022;76(4):959–74. DOI: 10.1016/j.jhep.2021.12.022
119. *World Health Organization.* WHO guidelines on physical activity and sedentary behaviour. URL: https://iris.who.int/bitstream/handle/10665/336656/9789240015128-eng.pdf
120. *Keating S.E., Hackett D.A., George J., Johnson N.A.* Exercise and non-alcoholic fatty liver disease: A systematic review and meta-analysis. *J Hepatol.* 2012;57(1):157–66. DOI: 10.1016/j.jhep.2012.02.023
121. *Дедов И.И., Мокрышева Н.Г., Мельниченко Г.А., Трошина Е.А., Мазурина Н.В., Ершова Е.В. и др.* Ожирение: клинические рекомендации. М.; 2020. [*Dedov I.I., Mokrysheva N.G., Melnichenko G.A., Troshina E.A., Mazurina N.V., Ershova E.V., et al.* Obesity: Clinical guidelines. Moscow; 2020. (In Russ.)].
122. *Hashida R., Kawaguchi T., Bekki M., Omoto M., Matsuse H., Nago T., et al.* Aerobic vs. resistance exercise in non-alcoholic fatty liver disease: A systematic review. *J Hepatol.* 2017;66(1):142–52. DOI: 10.1016/j.jhep.2016.08.023
123. *Katsagoni C.N., Georgoulis M., Papatheodoridis G.V., Panagiotakos D.B., Kontogianni M.D.* Effects of lifestyle interventions on clinical characteristics of patients with non-alcoholic fatty liver disease: A meta-analysis. *Metabolism.* 2017;68:119–32. DOI: 10.1016/j.metabol.2016.12.006
124. *Golabi P., Locklear C.T., Austin P., Afdhal S., Byrns M., Gerber L., et al.* Effectiveness of exercise in hepatic fat mobilization in non-alcoholic fatty liver disease: Systematic review. *World J Gastroenterol.* 2016;22(27):6318–27. DOI: 10.3748/wjg.v22.i27.6318
125. *Smart N.A., King N., McFarlane J.R., Graham P.L., Dieberg G.* Effect of exercise training on liver function in adults who are overweight or exhibit fatty liver disease: A systematic review and meta-analysis. *Br J Sports Med.* 2018;52(13):834–43. DOI: 10.1136/bjsports-2016-096197
126. *Cheng S., Ge J., Zhao C., Le S., Yang Y., Ke D., et al.* Effect of aerobic exercise and diet on liver fat in prediabetic patients with non-alcoholic-fatty-liver-disease: A randomized controlled trial. *Sci Rep.* 2017;7(1):15952. DOI: 10.1038/s41598-017-16159-x
127. *Hallsworth K., Thoma C., Hollingsworth K.G., Cassidy S., Anstee Q.M., Day C.P., et al.* Modified high-intensity interval training reduces liver fat and improves cardiac function in non-alcoholic fatty liver disease: A randomized controlled trial. *Clin Sci (Lond).* 2015;129(12):1097–105. DOI: 10.1042/CS20150308
128. *Rector R.S., Thyfault J.P., Morris R.T., Laye M.J., Borengasser S.J., Booth F.W., et al.* Daily exercise increases hepatic fatty acid oxidation and prevents steatosis in Otsuka Long-Evans Tokushima Fatty rats. *Am J Physiol Gastrointest Liver Physiol.* 2008;294(3):G619–26. DOI: 10.1152/ajpgi.00428.2007
129. *Rinella M.E., Neuschwander-Tetri B.A., Siddiqui M.S., Abdelmalek M.F., Caldwell S., Barb D., et al.* AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology.* 2023;77(5):1797–835. DOI: 10.1097/HEP.0000000000000323
130. *Zelber-Sagi S., Salomone F., Mlynarsky L.* The Mediterranean dietary pattern as the diet of choice for non-alcoholic fatty liver disease: Evidence and plausible mechanisms. *Liver Int.* 2017;37(7):936–49. DOI: 10.1111/liv.13435
131. *Haigh L., Kirk C., El Gendy K., Gallacher J., Errington L., Mathers J.C., et al.* The effectiveness and acceptability of Mediterranean diet and calorie restriction in non-alcoholic fatty liver disease (NAFLD): A systematic review and meta-analysis. *Clin Nutr.* 2022;41(9):1913–31. DOI: 10.1016/j.clnu.2022.06.037
132. *Younossi Z.M., Corey K.E., Lim J.K.* AGA clinical practice update on lifestyle modification using diet and exercise to achieve weight loss in the management of nonalcoholic fatty liver disease: Expert review. *Gastroenterology.* 2021;160(3):912–8. DOI: 10.1053/j.gastro.2020.11.051
133. *Panchal S.K., Poudyal H., Brown L.* Quercetin ameliorates cardiovascular, hepatic, and metabolic changes in diet-induced metabolic syndrome in rats. *J Nutr.* 2012;142(6):1026–32. DOI: 10.3945/jn.111.157263
134. *Aller R., Izaola O., de la Fuente B., De Luis Román D.A.* Mediterranean diet is associated with liver histology in patients with non alcoholic fatty liver disease. *Nutr Hosp.* 2015;32(6):2518–24. DOI: 10.3305/nh.2015.32.6.10074
135. *Abenavoli L., Greco M., Nazionale I., Peta V., Milic N., Accattato F., et al.* Effects of Mediterranean diet supplemented with silybin-vitamin E-phospholipid complex in overweight patients with non-alcoholic fatty liver disease. *Expert Rev Gastroenterol Hepatol.* 2015;9(4):519–27. DOI: 10.1586/17474124.2015.1004312
136. *Ryan M.C., Itsiopoulos C., Thodis T., Ward G., Trost N., Hofferberth S., et al.* The Mediterranean diet improves hepatic steatosis and insulin sensitivity in individuals with non-alcoholic fatty liver disease. *J Hepatol.* 2013;59(1):138–43. DOI: 10.1016/j.jhep.2013.02.012
137. *Trovato F.M., Martines G.F., Brischetto D., Trovato G., Catalano D.* Neglected features of lifestyle: Their relevance in non-alcoholic fatty liver disease. *World J Hepatol.* 2016;8(33):1459–65. DOI: 10.4254/wjh.v8.i33.1459
138. *Lee D., Chiavaroli L., Ayoub-Charette S., Khan T.A., Zurbau A., Au-Yeung F., et al.* Important food sources of fructose-containing sugars and non-alcoholic fatty liver disease: A systematic review and meta-analysis of controlled trials. *Nutrients.* 2022;14(14):2846. DOI: 10.3390/nu14142846
139. *Liu W., Zhai D., Zhang T., Mudoti N.G., Chang Q., Liu Y., et al.* Meta-analysis of the association between major foods with added fructose and non-alcoholic fatty liver disease. *Food Funct.* 2023;14(12):5551–61. DOI: 10.1039/d3fo00882g

140. *Zhang X.L., Wang T.Y., Targher G., Byrne C.D., Zheng M.H.* Lifestyle interventions for non-obese patients both with, and at risk, of non-alcoholic fatty liver disease. *Diabetes Metab J*. 2022;46(3):391–401. DOI: 10.4093/dmj.2022.0048
141. *Wong V.W., Wong G.L., Chan R.S., Shu S.S., Cheung B.H., Li L.S., et al.* Beneficial effects of lifestyle intervention in non-obese patients with non-alcoholic fatty liver disease. *J Hepatol.* 2018;69(6):1349–56. DOI: 10.1016/j.jhep.2018.08.011
142. *Long M.T., Noureddin M., Lim J.K.* AGA clinical practice update: Diagnosis and management of nonalcoholic fatty liver disease in lean individuals: Expert review. *Gastroenterology.* 2022;163(3):764–74.e1. DOI: 10.1053/j.gastro.2022.06.023
143. *Francque S.M., Marchesini G., Kautz A., Walmsley M., Dorner R., Lazarus J.V., et al.* Non-alcoholic fatty liver disease: A patient guideline. *JHEP Rep*. 2021;3(5):100322. DOI: 10.1016/j.jhepr.2021.100322
144. *Jarvis H., O'Keefe H., Craig D., Stow D., Hanratty B., Anstee Q.M.* Does moderate alcohol consumption accelerate the progression of liver disease in NAFLD? A systematic review and narrative synthesis. *BMJ Open.* 2022;12(1):e049767. DOI: 10.1136/bmjopen-2021-049767
145. *Di Ciaula A., Bonfrate L., Krawczyk M., Frühbeck G., Portincasa P.* Synergistic and detrimental effects of alcohol intake on progression of liver steatosis. *Int J Mol Sci*. 2022;23(5):2636. DOI: 10.3390/ijms23052636
146. *Long M.T., Massaro J.M., Hoffmann U., Benjamin E.J., Naimi T.S.* Alcohol use is associated with hepatic steatosis among persons with presumed nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol*. 2020;18(8):1831–41.e5. DOI: 10.1016/j.cgh.2019.11.022
147. *El Hadi H., Di Vincenzo A., Vettor R., Rossato M.* Cardio-metabolic disorders in non-alcoholic fatty liver disease. *Int J Mol Sci.* 2019;20(9):2215. DOI: 10.3390/ijms20092215
148. *Lizardi-Cervera J., Aguilar-Zapata D.* Nonalcoholic fatty liver disease and its association with cardiovascular disease. *Ann Hepatol*. 2009;8(Suppl. 1):S40–3. DOI: 10.1016/S1665-2681(19)31825-3
149. *Angulo P., Kleiner D.E., Dam-Larsen S., Adams L.A., Bjornsson E.S., Charatcharoenwitthaya P., et al.* Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. *Gastroenterology.* 2015;149(2):389–97.e10. DOI: 10.1053/j.gastro.2015.04.043
150. *Kwo P.Y., Cohen S.M., Lim J.K.* ACG clinical guideline: Evaluation of abnormal liver chemistries. *Am J Gastroenterol.* 2017;112(1):18–35. DOI: 10.1038/ajg.2016.517
151. *Kim H.C., Nam C.M., Jee S.H., Han K.H., Oh D.K., Suh I.* Normal serum aminotransferase concentration and risk of mortality from liver diseases: Prospective cohort study. *BMJ*. 2004;328(7446):983. DOI: 10.1136/bmj.38050.593634.63
152. *Lee T.H., Kim W.R., Benson J.T., Therneau T.M., Melton L.J. 3rd.* Serum aminotransferase activity and mortality risk in a United States community. *Hepatology*. 2008;47(3):880–7. DOI: 10.1002/hep.22090
153. *Ruhl C.E., Everhart J.E.* Elevated serum alanine aminotransferase and gamma-glutamyltransferase and mortality in the United States population. *Gastroenterology.* 2009;136(2):477–85.e11. DOI: 10.1053/j.gastro.2008.10.052
154. *Ioannou G.N., Weiss N.S., Boyko E.J., Mozaffarian D., Lee S.P.* Elevated serum alanine aminotransferase activity and calculated risk of coronary heart disease in the United States. *Hepatology*. 2006;43(5):1145–51. DOI: 10.1002/hep.21171
155. *Buzzetti E., Linden A., Best L.M., Madden A.M., Roberts D., Chase T.J.G., et al.* Lifestyle modifications for nonalcohol-related fatty liver disease: A network meta-analysis. *Cochrane Database Syst Rev*. 2021;6(6):CD013156. DOI: 10.1002/14651858.CD013156.pub2
156. *Komolafe O., Buzzetti E., Linden A., Best L.M., Madden A.M., Roberts D., et al.* Nutritional supplementation for non-alcohol-related fatty liver disease: A network meta-analysis. *Cochrane Database Syst Rev*. 2021;7(7):CD013157. DOI: 10.1002/14651858.CD013157.pub2
157. *Romero-Gómez M., Zelber-Sagi S., Trenell M.* Treatment of NAFLD with diet, physical activity and exercise. *J Hepatol.* 2017;67(4):829–46. DOI: 10.1016/j.jhep.2017.05.016
158. *Peng L., Wang J., Li F.* Weight reduction for non-alcoholic fatty liver disease. *Cochrane Database Syst Rev*. 2011;6:CD003619. DOI: 10.1002/14651858.CD003619.pub3
159. *Xiang Z., Chen Y.P., Ma K.F., Ye Y.F., Zheng L., Yang Y.D., et al.* The role of ursodeoxycholic acid in non-alcoholic steatohepatitis: A systematic review. *BMC Gastroenterol*. 2013;13:140. DOI: 10.1186/1471-230X-13-140
160. *Simental-Mendía M., Sánchez-García A., Simental-Mendía L.E.* Effect of ursodeoxycholic acid on liver markers: A systematic review and meta-analysis of randomized placebo-controlled clinical trials. *Br J Clin Pharmacol*. 2020;86(8):1476–88. DOI: 10.1111/bcp.14311
161. *Laurin J., Lindor K.D., Crippin J.S., Gossard A., Gores G.J., Ludwig J., et al.* Ursodeoxycholic acid or clofibrate in the treatment of non-alcohol-induced steatohepatitis: A pilot study. *Hepatology*. 1996;23(6):1464–7. DOI: 10.1002/hep.510230624
162. *Ozel Coskun B.D., Yucesoy M., Gursoy S., Baskol M., Yurci A., Yagbasan A., et al.* Effects of ursodeoxycholic acid therapy on carotid intima media thickness, apolipoprotein A1, apolipoprotein B, and apolipoprotein B/A1 ratio in nonalcoholic steatohepatitis. *Eur J Gastroenterol Hepatol.* 2015;27(2):142–9. DOI: 10.1097/MEG.0000000000000264
163. *Ratziu V., de Ledinghen V., Oberti F., Mathurin P., Wartelle-Bladou C., Renou C., et al.* A randomized controlled trial of high-dose ursodesoxycholic acid for nonalcoholic steatohepatitis. *J Hepatol.* 2011;54(5):1011–9. DOI: 10.1016/j.jhep.2010.08.030
164. *Павлов Ч.С., Варганова Д.Л., Семенистая М.Ч., Кузнецова Е.А., Усанова А.А., Свистунов А.А.* Урсодезоксихолевая кислота: эффективность и безопасность в лечении неалкогольной жировой болезни печени (метаанализ). *Вестник Российской академии медицинских наук.* 2018;73(5):294–305. [*Pavlov Ch.S., Varganova D.L., Semenistaya M.Ch., Kuznetsova E.A., Usanova A.A., Svistunov A.A.* Ursodeoxycholic acid: Efficacy and safety in the treatment of nonalcoholic fatty liver disease (meta-analysis). *Annals of the Russian Academy of Medical Sciences*. 2018;73(5):294–305. (In Russ.)]. DOI: 10.15690/vramn975
165. *Zhang W., Tang Y., Huang J., Hu H.* Efficacy of ursodeoxycholic acid in nonalcoholic fatty liver disease: An updated meta-analysis of randomized controlled trials. *Asia Pac J Clin Nutr.* 2020;29(4):696–705. DOI: 10.6133/apjcn.202012_29(4).0004
166. *Lin X., Mai M., He T., Huang H., Zhang P., Xia E., et al.* Efficiency of ursodeoxycholic acid for the treatment of nonalcoholic steatohepatitis: A systematic review and meta-analysis. *Expert Rev Gastroenterol Hepatol*. 2022;16(6):537–45. DOI: 10.1080/17474124.2022.2083605
167. *Nadinskaia M., Maevskaya M., Ivashkin V., Kodzoeva K., Pirogova I., Chesnokov E., et al.* Ursodeoxycholic acid as a means of preventing atherosclerosis, steatosis and liver fibrosis in patients with nonalcoholic fatty liver disease. *World J Gastroenterol.* 2021;27(10):959–75. DOI: 10.3748/wjg.v27.i10.959
168. *Byrnes K., Blessinger S., Bailey N.T., Scaife R., Liu G., Khambu B.* Therapeutic regulation of autophagy in hepatic metabolism. *Acta Pharm Sin B*. 2022;12(1):33–49. DOI: 10.1016/j.apsb.2021.07.021
169. *Decuypere J.P., Parys J.B., Bultynck G.* Regulation of the autophagic bcl-2/beclin 1 interaction. *Cells*. 2012;1(3):284–312. DOI: 10.3390/cells1030284

170. *Carino A., Biagioli M., Marchianò S., Fiorucci C., Zampella A., Monti M.C., et al.* Ursodeoxycholic acid is a GPBAR1 agonist and resets liver/intestinal FXR signaling in a model of diet-induced dysbiosis and NASH. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2019;1864(10):1422–37. DOI: 10.1016/j.bbalip.2019.07.006
171. *Marchianò S., Biagioli M., Roselli R., Zampella A., Di Giorgio C., Bordoni M., et al.* Beneficial effects of UDCA and norUDCA in a rodent model of steatosis are linked to modulation of GPBAR1/FXR signaling. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2022;1867(11):159218. DOI: 10.1016/j.bbalip.2022.159218
172. *Karedath J., Javed H., Ahsan Talpur F., Lal B., Kumari A., Kivan H., et al.* Effect of vitamin E on clinical outcomes in patients with non-alcoholic fatty liver disease: A meta-analysis. *Cureus.* 2022;14(12):e32764. DOI: 10.7759/cureus.32764
173. *Bril F., Biernacki D.M., Kalavalapalli S., Lomonaco R., Subbarayan S.K., Lai J., et al.* Role of vitamin E for nonalcoholic steatohepatitis in patients with type 2 diabetes: A randomized controlled trial. *Diabetes Care*. 2019;42(8):1481–8. DOI: 10.2337/dc19-0167
174. *Xu R., Tao A., Zhang S., Deng Y., Chen G.* Association between vitamin E and non-alcoholic steatohepatitis: A meta-analysis. *Int J Clin Exp Med*. 2015;8(3):3924–34.
175. *Mazhar I.J., Yasir M., Sarfraz S., Shlaghya G., Narayana S.H., Mushtaq U., et al.* Vitamin E and pioglitazone: A comprehensive systematic review of their efficacy in non-alcoholic fatty liver disease. *Cureus*. 2023;15(8):e43635. DOI: 10.7759/cureus.43635
176. *Vilar-Gomez E., Vuppalanchi R., Gawrieh S., Ghabril M., Saxena R., Cummings O.W., et al.* Vitamin E improves transplant-free survival and hepatic decompensation among patients with nonalcoholic steatohepatitis and advanced fibrosis. *Hepatology.* 2020;71(2):495–509. DOI: 10.1002/hep.30368
177. *European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO).* EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*. 2016;64(6):1388–402. DOI: 10.1016/j.jhep.2015.11.004
178. *Chalasani N., Younossi Z., Lavine J.E., Charlton M., Cusi K., Rinella M., et al.* The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2018;67(1):328–57. DOI: 10.1002/hep.29367
179. *Sanyal A.J., Chalasani N., Kowdley K.V., McCullough A., Diehl A.M., Bass N.M., et al.* Pioglitazone, vitamin E, or placebo for nonalcoholic steatohepatitis. *N Engl J Med*. 2010;362(18):1675–85. DOI: 10.1056/NEJMoa0907929
180. *Ando Y., Jou J.H.* Nonalcoholic fatty liver disease and recent guideline updates. *Clin Liver Dis (Hoboken)*. 2021;17(1):23–8. DOI: 10.1002/cld.1045
181. *Bjelakovic G., Nikolova D., Gluud C.* Meta-regression analyses, meta-analyses, and trial sequential analyses of the effects of supplementation with beta-carotene, vitamin A, and vitamin E singly or in different combinations on all-cause mortality: Do we have evidence for lack of harm? *PLoS One.* 2013;8(9):e74558. DOI: 10.1371/journal.pone.0074558
182. *Miller E.R. 3rd, Pastor-Barriuso R., Dalal D., Riemersma R.A., Appel L.J., Guallar E.* Meta-analysis: High-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med.* 2005;142(1):37–46. DOI: 10.7326/0003-4819-142-1-200501040-00110
183. *Curtis A.J., Bullen M., Piccenna L., McNeil J.J.* Vitamin E supplementation and mortality in healthy people: A meta-analysis of randomised controlled trials. *Cardiovasc Drugs Ther.* 2014;28(6):563–73. DOI: 10.1007/s10557-014-6560-7
184. *Vivarelli F., Canistro D., Cirillo S., Papi A., Spisni E., Vornoli A., et al.* Co-carcinogenic effects of vitamin E in prostate. *Sci Rep.* 2019;9(1):11636. DOI: 10.1038/s41598-019-48213-1
185. *Podszun M., Frank J.* Vitamin E-drug interactions: Molecular basis and clinical relevance. *Nutr Res Rev.* 2014;27(2):215–31. DOI: 10.1017/S0954422414000146
186. *Noureddin M., Sander-Struckmeier S., Mato J.M.* Early treatment efficacy of S-adenosylmethionine in patients with intrahepatic cholestasis: A systematic review. *World J Hepatol.* 2020;12(2):46–63. DOI: 10.4254/wjh.v12.i2.46
187. *Райхельсон К.Л., Кондрашина Э.А.* Адеметионин в лечении повышенной утомляемости/слабости при заболеваниях печени: систематический обзор. *Терапевтический архив.* 2019;91(2):134–42. [*Raikhelson K.L., Kondrashina E.A.* Ademethionine in the treatment of fatigue in liver diseases: A systematic review. *Terapevticheskii Arkhiv*. 2019;91(2):134–42. (In Russ.)]. DOI: 10.26442/00403660.2019.02.000130
188. *Барановский А.Ю., Райхельсон К.Л., Марченко Н.В.* Применение S-аденозилметионина (Гептрала®) в терапии больных неалкогольным стеатогепатитом. *Клинические перспективы гастроэнтерологии, гепатологии.* 2010;9(1):3–10. [*Baranovsky A.Yu., Raykhelson K.L., Marchenko N.V.* Application of S-adenosylmethionine (Heptral®) in treatment of patients with non-alcoholic steatohepatitis. *Clinical Perspectives of Gastroenterology, Hepatology*. 2010;9(1):3–10. (In Russ.)].
189. *Shankar R., Virukalpattigopalratnam M.P., Singh T.* Heptral® (Ademetionine) in intrahepatic cholestasis due to chronic non-alcoholic liver disease: Subgroup analysis of results of a multicentre observational study in India. *J Clin Exp Hepatol*. 2014;4(Suppl. 2):S33. DOI: 10.1016/j.jceh.2014.02.071
190. *Li H., Liu N.N., Peng Z.G.* Effect of bicyclol on blood biomarkers of NAFLD: A systematic review and meta-analysis. *BMJ Open.* 2020;10(12):e039700. DOI: 10.1136/bmjopen-2020-039700
191. *Маевская М.В., Луньков В.Д., Гейвандова Н.И., Пальгова Л.К., Пирогова И.Ю., Прашнова М.К. и др.* Бициклол в лечении пациентов с хроническими диффузными заболеваниями печени. *Медицинский совет.* 2020;(15):78–89. [*Maevskaya M.V., Lunkov V.D., Geyvandova N.I., Palgova L.K., Pirogova I.Yu., Prashnova M.K., et al.* Bicyclol in the treatment of patients with chronic diffuse liver diseases. *Medical Council.* 2020;(15):78–89. (In Russ.)]. DOI: 10.21518/2079-701X-2020-15-78-89
192. *Pan S.Y., Dong H., Yu Z.L., Zhao X.Y., Xiang C.J., Wang H., et al.* Bicyclol, a synthetic dibenzocyclooctadiene derivative, decreases hepatic lipids but increases serum triglyceride level in normal and hypercholesterolaemic mice. *J Pharm Pharmacol.* 2007;59(12):1657–62. DOI: 10.1211/jpp.59.12.0007
193. *Pan S.Y., Yu Z.L., Dong H., Xiang C.J., Fong W.F., Ko K.M.* Ethanol extract of fructus schisandrae decreases hepatic triglyceride level in mice fed with a high fat/cholesterol diet, with attention to acute toxicity. *Evid Based Complement Alternat Med*. 2011;2011:729412. DOI: 10.1093/ecam/nep070
194. *Zhao W., Yan Y., Xiao Z., Wang M., Xu M., Wang Z., et al.* Bicyclol ameliorates nonalcoholic fatty liver disease in mice via inhibiting MAPKs and NF-κB signaling pathways. *Biomed Pharmacother.* 2021;141:111874. DOI: 10.1016/j.biopha.2021.111874
195. *Пирогова И.Ю., Яковлева С.В., Неуймина Т.В., Синицын С.П., Чулков В.С., Шамаева Т.Н.* Эффективность и безопасность Бициклола при неалкогольной жировой болезни печени: результаты когортного исследования. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2018;28(4):66–75. [*Pirogova I.Yu., Yakovleva S.V., Neuymina T.V., Sinitsyn S.P., Chulkov V.S., Shamaeva T.N.* Efficacy and safety of bicyclol treatment for non-alcoholic fatty liver disease: Results of a cohort study. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2018;28(4):66–75. (In Russ.)]. DOI: 10.22416/1382-4376-2018-28-4-66-75

196. *Оковитый С.В., Приходько В.А., Безбородкина Н.Н., Кудрявцев Б.Н.* Гепатопротекторы: руководство для врачей. 2-е изд. М.: ГЭОТАР-Медиа; 2022. [*Okovity S.V., Prikhodko V.A., Bezborodkina N.N., Kudryavtsev B.N.* Hepatoprotectors: A guide for doctors. 2nd ed. Moscow: GEOTAR-Media Publ.; 2022. (In Russ.)]. DOI: 10.33029/9704-6689-6-LIV-1-240

197. *Семисерин В.А., Каракозов А.Г., Малькута М.А., Золотарева Л.А., Левченко О.Б., Калягин И.Е. и др.* Оценка эффективности гепатопротективной монотерапии неалкогольной жировой болезни печени в стадии стеатогепатита препаратом на основе янтарной кислоты и метионина. *Терапевтический архив.* 2016;88(2):58–63. [*Semiserin V.A., Karakozov A.G., Malkuta M.A., Zolotareva L.A., Levchenko O.B., Kalyagin I.E., et al.* Evaluation of the efficiency of hepatoprotective monotherapy using succinic acid and methionine for nonalcoholic fatty liver disease at the stage of steatohepatitis. *Terapevticheskii Arkhiv.* 2016;88(2):58–63. (In Russ.)]. DOI: 10.17116/terarkh201688258-63

198. *Стельмах В.В., Козлов В.К., Баранов В.Л., Латария Э.Л., Некрасова А.С.* Энерготропная патогенетически ориентированная терапия сукцинатсодержащими препаратами при неалкогольной жировой болезни печени: перспективы клинического применения. *Медицинский алфавит.* 2013;1(2):38–44. [*Stelmakh V.V., Kozlov V.K., Baranov V.L., Latariya E.L., Nekrasova A.S.* Energy-tropic pathogenetically oriented therapy with succinate-containing drugs in non-alcoholic fatty liver disease: Prospects for clinical use. *Medical Alphabet.* 2013;1(2):38–44. (In Russ.)].

199. *Дударенко С.В., Коваленко А.Л., Прокопенко С.М., Белогурова Е.В.* Применение ремаксола в терапии метаболического синдрома у пациентов с неалкогольным стеатогепатитом и сахарным диабетом 2 типа. *Экспериментальная и клиническая гастроэнтерология.* 2016;6:89–94. [*Dudorenko S.V., Kovalenko A.L., Prokopenko S.M., Belogurova E.V.* The use of remaxol in the treatment of metabolic syndrome in patients with nonalcoholic steatohepatitis and diabetes mellitus 2 type. *Experimental and Clinical Gastroenterology.* 2016;6:89–94. (In Russ.)].

200. *Шиповская А.А., Дуданова О.П.* Внутрипеченочный холестаз при неалкогольной жировой болезни печени. *Терапевтический архив.* 2018;90(2):69–74. [*Shipovskaya A.A., Dudanova O.P.* Intrahepatic cholestasis in nonalcoholic fatty liver disease. *Terapevticheskii Arkhiv.* 2018;90(2):69–74. (In Russ.)]. DOI: 10.26442/terarkh201890269-74

201. *Pennisi G., Pipitone R.M., Grimaudo S., Spatola F., Di Martino V., Cammà C., et al.* A cholestatic pattern predicts liver outcomes in patients with nonalcoholic fatty liver disease. *Dig Liver Dis.* 2021;53(Suppl. 1):S27. DOI: 10.1016/j.dld.2020.12.069

202. *Широкова Е.Н.* Внутрипеченочный холестаз при неалкогольной жировой болезни печени: патогенез и роль адеметионина в терапии. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2023;33(2):79–86. [*Shirokova Ye.N.* Intrahepatic cholestasis in non-alcoholic fatty liver disease: Pathogenesis and role of ademetionine in treatment. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2023;33(2):79–86. (In Russ.)]. DOI: 10.22416/1382-4376-2023-33-2-79-86

203. *Anstee Q.M., Day C.P.* S-adenosylmethionine (SAMe) therapy in liver disease: A review of current evidence and clinical utility. *J Hepatol.* 2012;57(5):1097–109. DOI: 10.1016/j.jhep.2012.04.041

204. *Butterworth R.F., Kircheis G., Hilger N., McPhail M.J.W.* Efficacy of l-ornithine l-aspartate for the treatment of hepatic encephalopathy and hyperammonemia in cirrhosis: Systematic review and meta-analysis of randomized controlled trials. *J Clin Exp Hepatol.* 2018;8(3):301–13. DOI: 10.1016/j.jceh.2018.05.004

205. *Ермолова Т.В., Ермолов С.Ю., Сологуб Т.В., Карев В.Е., Добкес А.Л., Апресян А.Г.* Нарушения портопеченочной гемодинамики при хронических заболеваниях печени на начальных стадиях фиброза и их коррекция. *Фарматека.* 2016;(15):58–66. [*Ermolova T.V., Ermolov S.Yu., Sologub T.V., Karev V.E., Dobkes A.L., Apresyan A.G.* Portohepatic hemodynamic disturbances in patients with chronic liver disease at the initial stages of fibrosis and their correction. *Farmateka.* 2016;(15):58–66. (In Russ.)].

206. *Зыкина Е.Ю., Симонова Ж.Г.* Гипераммониемия у пациентов со стабильной стенокардией и неалкогольной жировой болезнью печени на стадии стеатоза. *Экспериментальная и клиническая гастроэнтерология.* 2023;8:57–65. [*Zykina E.J., Simonova Zh.G.* Hyperammonemia in patients with stable angina pectoris and nonalcoholic fatty liver disease at the steatosis stage. *Experimental and Clinical Gastroenterology.* 2023;8:57–65. (In Russ.)]. DOI: 10.31146/1682-8658-ecg-216-8-57-65

207. *Гаранина Е.В.* Влияние курсового приема L-орнитин-L-аспартата на фиброз и стеатоз печени у больных ассоциированной с нарушениями метаболизма жировой болезнью печени (неалкогольной жировой болезнью печени), имеющих гипераммониемию. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2021;31(4):31–6. [*Garanina E.V.* Effect of L-ornithine-L-aspartate on liver fibrosis and steatosis in patients with metabolic-associated fatty liver disease (non-alcoholic fatty liver disease) and hyperammonaemia. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2021;31(4):31–6. (In Russ.)]. DOI: 10.22416/1382-4376-2021-31-4-31-36

208. *Kaiser S., Gerok W., Häussinger D.* Ammonia and glutamine metabolism in human liver slices: New aspects on the pathogenesis of hyperammonaemia in chronic liver disease. *Eur J Clin Invest.* 1988;18(5):535–42. DOI: 10.1111/j.1365-2362.1988.tb01053.x

209. *De Chiara F., Heebøll S., Marrone G., Montoliu C., Hamilton-Dutoit S., Ferrandez A., et al.* Urea cycle dysregulation in non-alcoholic fatty liver disease. *J Hepatol.* 2018;69(4):905–15. DOI: 10.1016/j.jhep.2018.06.023

210. *Алексеенко С.А., Агеева Е.А., Полковникова О.П.* Современные подходы к диагностике и лечению гипераммониемии у пациентов с хроническими заболеваниями печени на доцирротической стадии. *РМЖ. Медицинское обозрение.* 2018;2(7-1):19–23. [*Alekseenko S.A., Ageeva E.A., Polkovnikova O.P.* Modern approaches to diagnostics and treatment of hyperammonemia in patients with chronic liver disease at a precirrhotic stage. *RMJ. Medical Review.* 2018;2(7-1):19–23. (In Russ.)].

211. *Tian L.Y., Lu L.G., Tang C.W., Xie Y., Luo H.S., Tan S.Y., et al.* Aspartate-ornithine granules in the treatment of nonalcoholic steatohepatitis: A multiple-dose parallel controlled clinical trial. *Zhonghua Gan Zang Bing Za Zhi.* 2013;21(7):528–32. (In Chinese). DOI: 10.3760/cma.j.issn.1007-3418.2013.07.013

212. *Pichon C., Nachit M., Gillard J., Vande Velde G., Lanthier N., Leclercq I.A.* Impact of L-ornithine L-aspartate on non-alcoholic steatohepatitis-associated hyperammonemia and muscle alterations. *Front Nutr.* 2022;9:1051157. DOI: 10.3389/fnut.2022.1051157

213. *Приходько В.А., Сысоев Ю.И., Поверяева М.А., Бунят А.В., Карев В.Е., Ивкин Д.Ю. и др.* Влияние эмпаглифлозина и L-орнитина L-аспартата на поведенческо-когнитивные функции и физическую работоспособность при экспериментальном стеатогепатите. *Вестник РГМУ.* 2020;3:53–62. [*Prikhodko V.A., Sysoev Yu.I., Poveryaeva M.A., Bunyat A.V., Karev V.E., Ivkin D.Yu., et al.* Effects of empagliflozin and L-ornithine L-aspartate on behavior, cognitive functions, and physical performance in mice with experimentally induced steatohepatitis. *Bulletin of Russian State Medical University.* 2020;3:49–57. (In Russ.)]. DOI: 10.24075/brsmu.2020.034

214. *Оковитый С.В., Райхельсон К.Л., Приходько В.А.* Комбинированная гепатопротекторная фармакотерапия заболеваний печени. *Экспериментальная и клиническая гастроэнтерология.* 2022;7:5–20. [*Okovityi S.V.,*

Raikhelson K.L., Prikhodko V.A. Combined hepatoprotective pharmacotherapy for liver disease. *Experimental and Clinical Gastroenterology.* 2022;7:5–20. (In Russ.)]. DOI: 10.31146/1682-8658-ecg-203-7-5-20
215. *Dufour J.F., Oneta C.M., Gonvers J.J., Bihl F., Cerny A., Cereda J.M., et al.* Randomized placebo-controlled trial of ursodeoxycholic acid with vitamin E in nonalcoholic steatohepatitis. *Clin Gastroenterol Hepatol.* 2006;4(12):1537–43. DOI: 10.1016/j.cgh.2006.09.025
216. *Pietu F., Guillaud O., Walter T., Vallin M., Hervieu V., Scoazec J.Y., et al.* Ursodeoxycholic acid with vitamin E in patients with nonalcoholic steatohepatitis: Long-term results. *Clin Res Hepatol Gastroenterol.* 2012;36(2):146–55. DOI: 10.1016/j.clinre.2011.10.011
217. *Balmer M.L., Siegrist K., Zimmermann A., Dufour J.F.* Effects of ursodeoxycholic acid in combination with vitamin E on adipokines and apoptosis in patients with nonalcoholic steatohepatitis. *Liver Int.* 2009;29(8):1184–8. DOI: 10.1111/j.1478-3231.2009.02037.x
218. *Thomsen M.N., Skytte M.J., Samkani A., Carl M.H., Weber P., Astrup A., et al.* Dietary carbohydrate restriction augments weight loss-induced improvements in glycaemic control and liver fat in individuals with type 2 diabetes: A randomised controlled trial. *Diabetologia.* 2022;65(3):506–17. DOI: 10.1007/s00125-021-05628-8
219. *Vilar-Gomez E., Martinez-Perez Y., Calzadilla-Bertot L., Torres-Gonzalez A., Gra-Oramas B., Gonzalez-Fabian L., et al.* Weight loss through lifestyle modification significantly reduces features of nonalcoholic steatohepatitis. *Gastroenterology.* 2015;149(2):367–78.e5. DOI: 10.1053/j.gastro.2015.04.005
220. *Wong C., Lee M.H., Yaow C.Y.L., Chin Y.H., Goh X.L., Ng C.H., et al.* Glucagon-like peptide-1 receptor agonists for non-alcoholic fatty liver disease in type 2 diabetes: A meta-analysis. *Front Endocrinol (Lausanne).* 2021;12:609110. DOI: 10.3389/fendo.2021.609110
221. *Fan S., Shi X., Yao J., Zhong M., Feng P.* The efficacy of glucagon-like peptide 1 receptor agonists in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis of randomized controlled trials. *Rev Esp Enferm Dig.* 2020;112(8):627–35. DOI: 10.17235/reed.2020.6392/2019
222. *Newsome P.N., Buchholtz K., Cusi K., Linder M., Okanoue T., Ratziu V., et al.* A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. *N Engl J Med.* 2021;384(12):1113–24. DOI: 10.1056/NEJMoa2028395
223. *Zhu K., Kakkar R., Chahal D., Yoshida E.M., Hussaini T.* Efficacy and safety of semaglutide in non-alcoholic fatty liver disease. *World J Gastroenterol.* 2023;29(37):5327–38. DOI: 10.3748/wjg.v29.i37.5327
224. *Bandyopadhyay S., Das S., Samajdar S.S., Joshi S.R.* Role of semaglutide in the treatment of nonalcoholic fatty liver disease or non-alcoholic steatohepatitis: A systematic review and meta-analysis. *Diabetes Metab Syndr.* 2023;17(10):102849. DOI: 10.1016/j.dsx.2023.102849
225. *Gu Y., Sun L., Zhang W., Kong T., Zhou R., He Y., et al.* Comparative efficacy of 5 sodium-glucose cotransporter protein-2 (SGLT-2) inhibitor and 4 glucagon-like peptide-1 (GLP-1) receptor agonist drugs in non-alcoholic fatty liver disease: A GRADE-assessed systematic review and network meta-analysis of randomized controlled trials. *Front Pharmacol.* 2023;14:1102792. DOI: 10.3389/fphar.2023.1102792
226. *Parab P., Chaudhary P., Mukhtar S., Moradi A., Kodali A., Okoye C., et al.* Role of glucagon-like peptide-1 (GLP-1) receptor agonists in cardiovascular risk management in patients with type 2 diabetes mellitus: A systematic review. *Cureus.* 2023;15(9):e45487. DOI: 10.7759/cureus.45487
227. *Banerjee M., Pal R., Mukhopadhyay S., Nair K.* GLP-1 receptor agonists and risk of adverse cerebrovascular outcomes in type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *J Clin Endocrinol Metab.* 2023;108(7):1806–12. DOI: 10.1210/clinem/dgad076
228. *Gomes D.A., Presume J., de Araújo Gonçalves P., Almeida M.S., Mendes M., Ferreira J.* Association between the magnitude of glycemic control and body weight loss with GLP-1 receptor agonists and risk of atherosclerotic cardiovascular disease: A systematic review and meta-analyses of randomized diabetes cardiovascular outcomes trials. *Cardiovasc Drugs Ther.* 2024. DOI: 10.1007/s10557-024-07547-3
229. *Cusi K., Orsak B., Bril F., Lomonaco R., Hecht J., Ortiz-Lopez C., et al.* Long-term pioglitazone treatment for patients with nonalcoholic steatohepatitis and prediabetes or type 2 diabetes mellitus: A randomized trial. *Ann Intern Med.* 2016;165(5):305–15. DOI: 10.7326/M15-1774
230. *Musso G., Cassader M., Paschetta E., Gambino R.* Thiazolidinediones and advanced liver fibrosis in nonalcoholic steatohepatitis: A meta-analysis. *JAMA Intern Med.* 2017;177(5):633–40. DOI: 10.1001/jamainternmed.2016.9607
231. *Zhao Y., Zhao W., Wang H., Zhao Y., Bu H., Takahashi H.* Pioglitazone on nonalcoholic steatohepatitis: A systematic review and meta-analysis of 15 RCTs. *Medicine (Baltimore).* 2022;101(46):e31508. DOI: 10.1097/MD.0000000000031508
232. *Ndakotsu A., Vivekanandan G.* The role of thiazolidinediones in the amelioration of nonalcoholic fatty liver disease: A systematic review. *Cureus.* 2022;14(5):e25380. DOI: 10.7759/cureus.25380
233. *Budd J., Cusi K.* Role of agents for the treatment of diabetes in the management of nonalcoholic fatty liver disease. *Curr Diab Rep.* 2020;20(11):59. DOI: 10.1007/s11892-020-01349-1
234. *Государственный реестр лекарственных средств.* Пиоглар. Номер ЛС-001671, дата регистрации 16.07.2011. [*State Register of Medicines.* Pioglar. Number LS-001671, registration date 16.07.2011. (In Russ.)]. URL: https://grls.rosminzdrav.ru/Grls_View_v2.aspx?routingGuid=66ecaf50-2ba6-41a8-848f-de7e5b8c9220
235. *Gautam A., Agrawal P.K., Doneria J., Nigam A.* Effects of canagliflozin on abnormal liver function tests in patients of type 2 diabetes with non-alcoholic fatty liver disease. *J Assoc Physicians India.* 2018;66(8):62–6.
236. *Wei Q., Xu X., Guo L., Li J., Li L.* Effect of SGLT2 inhibitors on type 2 diabetes mellitus with non-alcoholic fatty liver disease: A meta-analysis of randomized controlled trials. *Front Endocrinol (Lausanne).* 2021;12:635556. DOI: 10.3389/fendo.2021.635556
237. *Приходько В.А., Оковитый С.В., Куликов А.Н.* Глифлозины при неалкогольной жировой болезни печени: перспективы применения за границами диабета, кардио- и нефропротекции. *Терапия.* 2023;9(7):130–41. [*Prikhodko V.A., Okovity S.V., Kulikov A.N.* Gliflozins in non-alcoholic fatty liver disease: Perspectives of use outside diabetes, cardiac and nephroprotection. *Therapy.* 2023;9(7):130–41. (In Russ.)]. DOI: 10.18565/therapy.2023.7.130-141
238. *Mo M., Huang Z., Liang Y., Liao Y., Xia N.* The safety and efficacy evaluation of sodium-glucose co-transporter 2 inhibitors for patients with non-alcoholic fatty liver disease: An updated meta-analysis. *Dig Liver Dis.* 2022;54(4):461–8. DOI: 10.1016/j.dld.2021.08.017
239. *Jin Z., Yuan Y., Zheng C., Liu S., Weng H.* Effects of sodium-glucose co-transporter 2 inhibitors on liver fibrosis in non-alcoholic fatty liver disease patients with type 2 diabetes mellitus: An updated meta-analysis of randomized controlled trials. *J Diabetes Complications.* 2023;37(8):108558. DOI: 10.1016/j.jdiacomp.2023.108558
240. *Ong Lopez A.M.C., Pajimna J.A.T.* Efficacy of sodium glucose cotransporter 2 inhibitors on hepatic fibrosis and steatosis in non-alcoholic fatty liver disease: An updated systematic review and meta-analysis. *Sci Rep.* 2024;14(1):2122. DOI: 10.1038/s41598-024-52603-5
241. *Sánchez-García A., Sahebkar A., Simental-Mendía M., Simental-Mendía L.E.* Effect of ursodeoxycholic acid on glycemic markers: A systematic review and meta-ana-

lysis of clinical trials. *Pharmacol Res.* 2018;135:144–9. DOI: 10.1016/j.phrs.2018.08.008
242. *Elhini S.H., Wahsh E.A., Elberry A.A., El Ameen N.F., Abdelfadil Saedii A., Refaie S.M., et al.* The impact of an SGLT2 inhibitor versus ursodeoxycholic acid on liver steatosis in diabetic patients. *Pharmaceuticals (Basel).* 2022;15(12):1516. DOI: 10.3390/ph15121516
243. *Houttu V., Csader S., Nieuwdorp M., Holleboom A.G., Schwab U.* Dietary interventions in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis. *Front Nutr.* 2021;8:716783. DOI: 10.3389/fnut.2021.716783
244. *Koutoukidis D.A., Astbury N.M., Tudor K.E., Morris E., Henry J.A., Noreik M., et al.* Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: A systematic review and meta-analysis. *JAMA Intern Med.* 2019;179(9):1262–71. DOI: 10.1001/jamainternmed.2019.2248
245. *Ezpeleta M., Gabel K., Cienfuegos S., Kalam F., Lin S., Pavlou V., et al.* Effect of alternate day fasting combined with aerobic exercise on non-alcoholic fatty liver disease: A randomized controlled trial. *Cell Metab.* 2023;35(1):56–70.e3. DOI: 10.1016/j.cmet.2022.12.001
246. *Haufe S., Engeli S., Kast P., Böhnke J., Utz W., Haas V., et al.* Randomized comparison of reduced fat and reduced carbohydrate hypocaloric diets on intrahepatic fat in overweight and obese human subjects. *Hepatology.* 2011;53(5):1504–14. DOI: 10.1002/hep.24242
247. *Asrih M., Jornayvaz F.R.* Diets and nonalcoholic fatty liver disease: The good and the bad. *Clin Nutr.* 2014;33(2):186–90. DOI: 10.1016/j.clnu.2013.11.003
248. *Lemstra M., Bird Y., Nwankwo C., Rogers M., Moraros J.* Weight loss intervention adherence and factors promoting adherence: A meta-analysis. *Patient Prefer Adherence.* 2016;10:1547–59. DOI: 10.2147/PPA.S103649
249. *Scragg J., Hallsworth K., Taylor G., Cassidy S., Haigh L., Boyle M., et al.* Factors associated with engagement and adherence to a low-energy diet to promote 10 % weight loss in patients with clinically significant non-alcoholic fatty liver disease. *BMJ Open Gastroenterol.* 2021;8(1):e000678. DOI: 10.1136/bmjgast-2021-000678
250. *Armstrong M.J., Gaunt P., Aithal G.P., Barton D., Hull D., Parker R., et al.* Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): A multicentre, double-blind, randomised, placebo-controlled phase 2 study. *Lancet.* 2016;387(10019):679–90. DOI: 10.1016/S0140-6736(15)00803-X
251. *Vilsbøll T., Christensen M., Junker A.E., Knop F.K., Gluud L.L.* Effects of glucagon-like peptide-1 receptor agonists on weight loss: Systematic review and meta-analyses of randomised controlled trials. *BMJ.* 2012;344:d7771. DOI: 10.1136/bmj.d7771
252. *Stokes C.S., Gluud L.L., Casper M., Lammert F.* Ursodeoxycholic acid and diets higher in fat prevent gallbladder stones during weight loss: A meta-analysis of randomized controlled trials. *Clin Gastroenterol Hepatol.* 2014;12(7):1090–100.e2. DOI: 10.1016/j.cgh.2013.11.031
253. *Fearon N.M., Kearns E.C., Kennedy C.A., Conneely J.B., Heneghan H.M.* The impact of ursodeoxycholic acid on gallstone disease after bariatric surgery: A meta-analysis of randomized control trials. *Surg Obes Relat Dis.* 2022;18(1):77–84. DOI: 10.1016/j.soard.2021.10.004
254. *Mulliri A., Menahem B., Alves A., Dupont B.* Ursodeoxycholic acid for the prevention of gallstones and subsequent cholecystectomy after bariatric surgery: A meta-analysis of randomized controlled trials. *J Gastroenterol.* 2022;57(8):529–39. DOI: 10.1007/s00535-022-01886-4
255. *Machado F.H.F., Castro Filho H.F., Babadopulos R.F.A.L., Rocha H.A.L., Rocha J.L.C., Moraes Filho M.O.* Ursodeoxycholic acid in the prevention of gallstones in patients subjected to Roux-en-Y gastric bypass1. *Acta Cir Bras.* 2019;34(1):e20190010000009. DOI: 10.1590/s0102-865020190010000009
256. *Johansson K., Sundström J., Marcus C., Hemmingsson E., Neovius M.* Risk of symptomatic gallstones and cholecystectomy after a very-low-calorie diet or low-calorie diet in a commercial weight loss program: 1-year matched cohort study. *Int J Obes (Lond).* 2014;38(2):279–84. DOI: 10.1038/ijo.2013.83
257. *European Association for the Study of the Liver (EASL).* EASL Clinical Practice Guidelines on the prevention, diagnosis and treatment of gallstones. *J Hepatol.* 2016;65(1):146–81. DOI: 10.1016/j.jhep.2016.03.005
258. *Uy M.C., Talingdan-Te M.C., Espinosa W.Z., Daez M.L., Ong J.P.* Ursodeoxycholic acid in the prevention of gallstone formation after bariatric surgery: A meta-analysis. *Obes Surg.* 2008;18(12):1532–8. DOI: 10.1007/s11695-008-9587-7
259. *Dongiovanni P., Petta S., Mannisto V., Mancina R.M., Pipitone R., Karja V., et al.* Statin use and non-alcoholic steatohepatitis in at risk individuals. *J Hepatol.* 2015;63(3):705–12. DOI: 10.1016/j.jhep.2015.05.006
260. *Zhou H., Toshiyoshi M., Zhao W., Zhao Y., Zhao Y.* Statins on nonalcoholic fatty liver disease: A systematic review and meta-analysis of 14 RCTs. *Medicine (Baltimore).* 2023;102(26):e33981. DOI: 10.1097/MD.0000000000033981
261. *Pastori D., Sciacqua A., Marcucci R., Del Ben M., Baratta F., Violi F., et al.* Non-alcoholic fatty liver disease (NAFLD), metabolic syndrome and cardiovascular events in atrial fibrillation. A prospective multicenter cohort study. *Intern Emerg Med.* 2021;16(8):2063–8. DOI: 10.1007/s11739-021-02682-3
262. *Mach F., Baigent C., Catapano A.L., Koskinas K.C., Casula M., Badimon L., et al.* 2019 ESC/EAS Guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. *Eur Heart J.* 2020;41(1):111–88. DOI: 10.1093/eurheartj/ehz455
263. *Pastori D., Pani A., Di Rocco A., Menichelli D., Gazzaniga G., Farcomeni A., et al.* Statin liver safety in non-alcoholic fatty liver disease: A systematic review and metanalysis. *Br J Clin Pharmacol.* 2022;88(2):441–51. DOI: 10.1111/bcp.14943
264. *Abdallah M., Brown L., Provenza J., Tariq R., Gowda S., Singal A.K.* Safety and efficacy of dyslipidemia treatment in NAFLD patients: A meta-analysis of randomized controlled trials. *Ann Hepatol.* 2022;27(6):100738. DOI: 10.1016/j.aohep.2022.100738
265. *Athyros V.G., Boutari C., Stavropoulos K., Anagnostis P., Imprialos K.P., Doumas M., et al.* Statins: An under-appreciated asset for the prevention and the treatment of NAFLD or NASH and the related cardiovascular risk. *Curr Vasc Pharmacol.* 2018;16(3):246–53. DOI: 10.2174/1570161115666170621082910
266. *Torres-Peña J.D., Martín-Piedra L., Fuentes-Jiménez F.* Statins in non-alcoholic steatohepatitis. *Front Cardiovasc Med.* 2021;8:777131. DOI: 10.3389/fcvm.2021.777131
267. *Aithal G.P., Watkins P.B., Andrade R.J., Larrey D., Molokhia M., Takikawa H., et al.* Case definition and phenotype standardization in drug-induced liver injury. *Clin Pharmacol Ther.* 2011;89(6):806–15. DOI: 10.1038/clpt.2011.58
268. *Марцевич С.Ю., Кутишенко Н.П., Дроздова Л.Ю., Лерман О.В., Невзорова В.А., Резник И.И. и др.* Исследование РАКУРС: повышение эффективности и безопасности терапии статинами у больных с заболеваниями печени, желчного пузыря и (или) желчевыводящих путей с помощью урсодеоксихолевой кислоты. *Терапевтический архив.* 2014;86(12):48–52. [*Martsevich S.Yu., Kutishenko N.P., Drozdova L.Yu., Lerman O.V., Nevzorova V.A., Reznik I.I., et al.* Ursodeoxycholic acid-enhanced efficiency and safety of statin therapy in patients with liver, gallbladder, and/or biliary tract diseases: The RACURS study. *Terapevticheskii Arkhiv.* 2014;86(12):48–52. (In Russ.)]. DOI: 10.17116/terarkh2014861248-52
269. *Nadinskaya M., Martsevich S., Kutishenko N., Balashov I., Lerman O.* P0624 Ursodeoxycholic acid influence on efficacy and safety of statin therapy in patients with high risk of cardiovascular events and nonalcoholic

fatty liver disease: The RACURS study (post-hoc analysis). *United European Gastroenterol J.* 2015;3(Suppl. 5):P0624. DOI: 10.1177/2050640615601623
270. *Cabezas Gelabert R.* Effect of ursodeoxycholic acid combined with statins in hypercholesterolemia treatment: A prospective clinical trial. *Rev Clin Esp.* 2004;204(12):632–5. (In Spanish). DOI: 10.1016/s0014-2565(04)71566-0
271. *Seo S.H., Lee D.H., Lee Y.S., Cho K.J., Park H.J., Lee H.W., et al.* Co-administration of ursodeoxycholic acid with rosuvastatin/ezetimibe in a non-alcoholic fatty liver disease model. *Gastroenterol Rep (Oxf).* 2022;10:goac037. DOI: 10.1093/gastro/goac037
272. *Nakade Y., Murotani K., Inoue T., Kobayashi Y., Yamamoto T., Ishii N., et al.* Ezetimibe for the treatment of non-alcoholic fatty liver disease: A meta-analysis. *Hepatol Res.* 2017;47(13):1417–28. DOI: 10.1111/hepr.12887
273. *Lee H.Y., Jun D.W., Kim H.J., Oh H., Saeed W.K., Ahn H., et al.* Ezetimibe decreased nonalcoholic fatty liver disease activity score but not hepatic steatosis. *Korean J Intern Med.* 2019;34(2):296–304. DOI: 10.3904/kjim.2017.194
274. *Cho Y., Rhee H., Kim Y.E., Lee M., Lee B.W., Kang E.S., et al.* Ezetimibe combination therapy with statin for non-alcoholic fatty liver disease: An open-label randomized controlled trial (ESSENTIAL study). *BMC Med.* 2022;20(1):93. DOI: 10.1186/s12916-022-02288-2
275. *Scorletti E., Bhatia L., McCormick K.G., Clough G.F., Nash K., Hodson L., et al.* Effects of purified eicosapentaenoic and docosahexaenoic acids in nonalcoholic fatty liver disease: Results from the Welcome* study. *Hepatology.* 2014;60(4):1211–21. DOI: 10.1002/hep.27289
276. *Maciejewska-Markiewicz D., Stachowska E., Hawryłkowicz V., Stachowska L., Prowans P.* The role of resolvins, protectins and marensins in non-alcoholic fatty liver disease (NAFLD). *Biomolecules.* 2021;11(7):937. DOI: 10.3390/biom11070937
277. *Bhatt D.L., Steg P.G., Miller M., Brinton E.A., Jacobson T.A., Ketchum S.B., et al.* Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. *N Engl J Med.* 2019;380(1):11–22. DOI: 10.1056/NEJMoa1812792
278. *Sanyal A.J., Abdelmalek M.F., Suzuki A., Cummings O.W., Chojkier M.* No significant effects of ethyl-eicosapentanoic acid on histologic features of nonalcoholic steatohepatitis in a phase 2 trial. *Gastroenterology.* 2014;147(2):377–84.e1. DOI: 10.1053/j.gastro.2014.04.046
279. *Lee C.H., Fu Y., Yang S.J., Chi C.C.* Effects of omega-3 polyunsaturated fatty acid supplementation on non-alcoholic fatty liver: A systematic review and meta-analysis. *Nutrients.* 2020;12(9):2769. DOI: 10.3390/nu12092769
280. *Musazadeh V., Karimi A., Malekahmadi M., Ahrabi S.S., Dehghan P.* Omega-3 polyunsaturated fatty acids in the treatment of non-alcoholic fatty liver disease: An umbrella systematic review and meta-analysis. *Clin Exp Pharmacol Physiol.* 2023;50(5):327–34. DOI: 10.1111/1440-1681.13750
281. *Yan J.H., Guan B.J., Gao H.Y., Peng X.E.* Omega-3 polyunsaturated fatty acid supplementation and non-alcoholic fatty liver disease: A meta-analysis of randomized controlled trials. *Medicine (Baltimore).* 2018;97(37):e12271. DOI: 10.1097/MD.0000000000012271
282. *Hilleman D.E., Wiggins B.S., Bottorff M.B.* Critical differences between dietary supplement and prescription omega-3 fatty acids: A narrative review. *Adv Ther.* 2020;37(2):656–70. DOI: 10.1007/s12325-019-01211-1
283. *Fernández-Miranda C., Pérez-Carreras M., Colina F., López-Alonso G., Vargas C., Solís-Herruzo J.A.* A pilot trial of fenofibrate for the treatment of non-alcoholic fatty liver disease. *Dig Liver Dis.* 2008;40(3):200–5. DOI: 10.1016/j.dld.2007.10.002
284. *Mahmoudi A., Moallem S.A., Johnston T.P., Sahebkar A.* Liver protective effect of fenofibrate in NASH/NAFLD animal models. *PPAR Res.* 2022;2022:5805398. DOI: 10.1155/2022/5805398
285. *Lawitz E.J., Bhandari B.R., Ruane P.J., Kohli A., Harting E., Ding D., et al.* Fenofibrate mitigates hypertriglyceridemia in nonalcoholic steatohepatitis patients treated with cilofexor/firsocostat. *Clin Gastroenterol Hepatol.* 2023;21(1):143–52.e3. DOI: 10.1016/j.cgh.2021.12.044
286. *Maev I.V., Samsonov A.A., Palgova L.K., Pavlov C.S., Shirokova E.N., Vovk E.I., et al.* Effectiveness of phosphatidylcholine as adjunctive therapy in improving liver function tests in patients with non-alcoholic fatty liver disease and metabolic comorbidities: Real-life observational study from Russia. *BMJ Open Gastroenterol.* 2020;7(1):e000368. DOI: 10.1136/bmjgast-2019-000368
287. *Dajani A.I, Popovic B.* Essential phospholipids for nonalcoholic fatty liver disease associated with metabolic syndrome: A systematic review and network meta-analysis. *World J Clin Cases.* 2020;8(21):5235–49. DOI: 10.12998/wjcc.v8.i21.5235
288. *Kuche K., Bhargavi N., Dora C.P., Jain S.* Drug-phospholipid complex – a go through strategy for enhanced oral bioavailability. *AAPS PharmSciTech.* 2019;20(2):43. DOI: 10.1208/s12249-018-1252-4
289. *Оковитый С.В., Болотова В.Ц., Анисимова Н.А., Ивкин Д.Ю., Титович И.А., Сысоев Ю.И. и др.* Перспективы применения растительных извлечений для коррекции нарушений жирового и углеводного обмена. *Фармация.* 2020;69(2):17–22. [*Okovityi S.V., Bolotova V.Ts., Anisimova N.A., Ivkin D.Yu., Titovich I.A., Sysoev Yu.I., et al.* Prospects for using plant extracts to correct fat and carbohydrate metabolism disorders. *Pharmacy.* 2020;69(2):17–22. (In Russ.)]. DOI: 10.29296/25419218-2020-02-03
290. *Dimakopoulou A., Sfikas G., Athyros V.* PCSK9 administration ameliorates non alcoholic fatty disease in patients with heterozygous familial hyperlipidemia. *Hell J Atheroscler.* 2018;9(2):12. DOI: 10.23803/HJA.V9I2.175.G150
291. *Rimbert A., Smati S., Dijk W., Le May C., Cariou B.* Genetic inhibition of PCSK9 and liver function. *JAMA Cardiol.* 2021;6(3):353–4. DOI: 10.1001/jamacardio.2020.5341
292. *Jang H.R., Kang D., Sinn D.H., Gu S., Cho S.J., Lee J.E., et al.* Nonalcoholic fatty liver disease accelerates kidney function decline in patients with chronic kidney disease: A cohort study. *Sci Rep.* 2018;8(1):4718. DOI: 10.1038/s41598-018-23014-0
293. *Musso G., Gambino R., Tabibian J.H., Ekstedt M., Kechagias S., Hamaguchi M., et al.* Association of non-alcoholic fatty liver disease with chronic kidney disease: A systematic review and meta-analysis. *PLoS Med.* 2014;11(7):e1001680. DOI: 10.1371/journal.pmed.1001680
294. *Targher G., Chonchol M., Bertolini L., Rodella S., Zenari L., Lippi G., et al.* Increased risk of CKD among type 2 diabetics with nonalcoholic fatty liver disease. *J Am Soc Nephrol.* 2008;19(8):1564–70. DOI: 10.1681/ASN.2007101155
295. *Heda R., Yazawa M., Shi M., Bhaskaran M., Aloor F.Z., Thuluvath P.J., et al.* Non-alcoholic fatty liver and chronic kidney disease: Retrospect, introspect, and prospect. *World J Gastroenterol.* 2021;27(17):1864–82. DOI: 10.3748/wjg.v27.i17.1864
296. *Monteillet L., Gjorgjieva M., Silva M., Verzieux V., Imikirene L., Duchampt A., et al.* Intracellular lipids are an independent cause of liver injury and chronic kidney disease in non alcoholic fatty liver disease-like context. *Mol Metab.* 2018;16:100–15. DOI: 10.1016/j.molmet.2018.07.006
297. *Shimano H., Sato R.* SREBP-regulated lipid metabolism: Convergent physiology – divergent pathophysiology. *Nat Rev Endocrinol.* 2017;13(12):710–30. DOI: 10.1038/nrendo.2017.91
298. *Marcuccilli M., Chonchol M.* NAFLD and chronic kidney disease. *Int J Mol Sci.* 2016;17(4):562. DOI: 10.3390/ijms17040562
299. *Kwon S.Y., Park J., Park S.H., Lee Y.B., Kim G., Hur K.Y., et al.* MAFLD and NAFLD in the pre-

diction of incident chronic kidney disease. *Sci Rep.* 2023;13(1):1796. DOI: 10.1038/s41598-023-27762-6
300. *Zhang X., Wong G.L., Yip T.C., Tse Y.K., Liang L.Y., Hui V.W., et al.* Angiotensin-converting enzyme inhibitors prevent liver-related events in nonalcoholic fatty liver disease. *Hepatology.* 2022;76(2):469–82. DOI: 10.1002/hep.32294
301. *Hirata T., Tomita K., Kawai T., Yokoyama H., Shimada A., Kikuchi M., et al.* Effect of telmisartan or losartan for treatment of nonalcoholic fatty liver disease: Fatty Liver Protection Trial by Telmisartan or Losartan Study (FANTASY). *Int J Endocrinol.* 2013:587140. DOI: 10.1155/2013/587140
302. *Georgescu E.F., Georgescu M.* Therapeutic options in non-alcoholic steatohepatitis (NASH). Are all agents alike? Results of a preliminary study. *J Gastrointestin Liver Dis.* 2007;16(1):39–46.
303. *Georgescu E.F., Ionescu R., Niculescu M., Mogoanta L., Vancica L.* Angiotensin-receptor blockers as therapy for mild-to-moderate hypertension-associated non-alcoholic steatohepatitis. *World J Gastroenterol.* 2009;15(8):942–54. DOI: 10.3748/wjg.15.942
304. *Yokohama S., Yoneda M., Haneda M., Okamoto S., Okada M., Aso K., et al.* Therapeutic efficacy of an angiotensin II receptor antagonist in patients with nonalcoholic steatohepatitis. *Hepatology.* 2004;40(5):1222–5. DOI: 10.1002/hep.20420
305. *Osterreicher C.H., Taura K., De Minicis S., Seki E., Penz-Osterreicher M., Kodama Y., et al.* Angiotensin-converting-enzyme 2 inhibits liver fibrosis in mice. *Hepatology.* 2009;50(3):929–38. DOI: 10.1002/hep.23104
306. *Ala M.* SGLT2 inhibition for cardiovascular diseases, chronic kidney disease, and NAFLD. *Endocrinology.* 2021;162(12):bqab157. DOI: 10.1210/endocr/bqab157
307. *Toyama T., Neuen B.L., Jun M., Ohkuma T., Neal B., Jardine M.J., et al.* Effect of SGLT2 inhibitors on cardiovascular, renal and safety outcomes in patients with type 2 diabetes mellitus and chronic kidney disease: A systematic review and meta-analysis. *Diabetes Obes Metab.* 2019;21(5):1237–50. DOI: 10.1111/dom.13648
308. *Sarafidis P., Ferro C.J., Morales E., Ortiz A., Malyszko J., Hojs R., et al.* SGLT-2 inhibitors and GLP-1 receptor agonists for nephroprotection and cardioprotection in patients with diabetes mellitus and chronic kidney disease. A consensus statement by the EURECA-m and the DIABESITY working groups of the ERA-EDTA. *Nephrol Dial Transplant.* 2019;34(2):208–30. DOI: 10.1093/ndt/gfy407
309. *Musso G., Cassader M., Cohney S., De Michieli F., Pinach S., Saba F., et al.* Fatty liver and chronic kidney disease: Novel mechanistic insights and therapeutic opportunities. *Diabetes Care.* 2016;39(10):1830–45. DOI: 10.2337/dc15-1182
310. *Heerspink H.J.L., Stefánsson B.V., Correa-Rotter R., Chertow G.M., Greene T., Hou F.F., et al.* Dapagliflozin in patients with chronic kidney disease. *N Engl J Med.* 2020;383(15):1436–46. DOI: 10.1056/NEJMoa2024816
311. *Herrington W.G., Staplin N., Wanner C., Green J.B., Hauske S.J., Emberson J.R., et al.* Empagliflozin in patients with chronic kidney disease. *N Engl J Med.* 2023;388(2):117–27. DOI: 10.1056/NEJMoa2204233
312. *Palmer S.C., Tendal B., Mustafa R.A., Vandvik P.O., Li S., Hao Q., et al.* Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: Systematic review and network meta-analysis of randomised controlled trials. *BMJ.* 2021;372:m4573. DOI: 10.1136/bmj.m4573
313. *Greco E.V., Russo G., Giandalia A., Viazzi F., Pontremoli R., De Cosmo S.* GLP-1 receptor agonists and kidney protection. *Medicina (Kaunas).* 2019;55(6):233. DOI: 10.3390/medicina55060233
314. *Marso S.P., Daniels G.H., Brown-Frandsen K., Kristensen P., Mann J.F., Nauck M.A., et al.* Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med.* 2016;375(4):311–22. DOI: 10.1056/NEJMoa1603827
315. *Marso S.P., Bain S.C., Consoli A., Eliaschewitz F.G., Jódar E., Leiter L.A., et al.* Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med.* 2016;375(19):1834–44. DOI: 10.1056/NEJMoa1607141
316. *Gerstein H.C., Colhoun H.M., Dagenais G.R., Diaz R., Lakshmanan M., Pais P., et al.* Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): A double-blind, randomised placebo-controlled trial. *Lancet.* 2019;394(10193):121–30. DOI: 10.1016/S0140-6736(19)31149-3
317. *Zhang Y., Jiang L., Wang J., Wang T., Chien C., Huang W., et al.* Network meta-analysis on the effects of finerenone versus SGLT2 inhibitors and GLP-1 receptor agonists on cardiovascular and renal outcomes in patients with type 2 diabetes mellitus and chronic kidney disease. *Cardiovasc Diabetol.* 2022;21(1):232. DOI: 10.1186/s12933-022-01676-5
318. *Ludwig J., Viggiano T.R., McGill D.B., Oh B.J.* Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. *Mayo Clin Proc.* 1980;55(7):434–8.
319. *Powell E.E., Cooksley W.G., Hanson R., Searle J., Halliday J.W., Powell L.W.* The natural history of nonalcoholic steatohepatitis: A follow-up study of forty-two patients for up to 21 years. *Hepatology.* 1990;11(1):74–80. DOI: 10.1002/hep.1840110114
320. *Ajmera V., Belt P., Wilson L.A., Gill R.M., Loomba R., Kleiner D.E., et al.* Among patients with nonalcoholic fatty liver disease, modest alcohol use is associated with less improvement in histologic steatosis and steatohepatitis. *Clin Gastroenterol Hepatol.* 2018;16(9):1511–20.e5. DOI: 10.1016/j.cgh.2018.01.026
321. *Kimura T., Tanaka N., Fujimori N., Sugiura A., Yamazaki T., Joshita S., et al.* Mild drinking habit is a risk factor for hepatocarcinogenesis in non-alcoholic fatty liver disease with advanced fibrosis. *World J Gastroenterol.* 2018;24(13):1440–50. DOI: 10.3748/wjg.v24.i13.1440
322. *Younossi Z.M., Stepanova M., Ong J., Yilmaz Y., Duseja A., Eguchi Y., et al.* Effects of alcohol consumption and metabolic syndrome on mortality in patients with nonalcoholic and alcohol-related fatty liver disease. *Clin Gastroenterol Hepatol.* 2019;17(8):1625–33.e1. DOI: 10.1016/j.cgh.2018.11.033
323. *Ekstedt M., Franzén L.E., Holmqvist M., Bendtsen P., Mathiesen U.L., Bodemar G., et al.* Alcohol consumption is associated with progression of hepatic fibrosis in non-alcoholic fatty liver disease. *Scand J Gastroenterol.* 2009;44(3):366–74. DOI: 10.1080/00365520802555991
324. *Sookoian S., Castaño G.O., Pirola C.J.* Modest alcohol consumption decreases the risk of non-alcoholic fatty liver disease: A meta-analysis of 43,175 individuals. *Gut.* 2014;63(3):530–2. DOI: 10.1136/gutjnl-2013-305718
325. *Cao G., Yi T., Liu Q., Wang M., Tang S.* Alcohol consumption and risk of fatty liver disease: A meta-analysis. *PeerJ.* 2016;4:e2633. DOI: 10.7717/peerj.2633
326. *Chang Y., Cho Y.K., Kim Y., Sung E., Ahn J., Jung H.S., et al.* Nonheavy drinking and worsening of noninvasive fibrosis markers in nonalcoholic fatty liver disease: A cohort study. *Hepatology.* 2019;69(1):64–75. DOI: 10.1002/hep.30170
327. *Blomdahl J., Nasr P., Ekstedt M., Kechagias S.* Moderate alcohol consumption is associated with significant fibrosis progression in NAFLD. *Hepatol Commun.* 2023;7(1):e0003. DOI: 10.1097/HC9.0000000000000003
328. *Ивашкин В.Т., Жаркова М.С., Корочанская Н.В., Хлынов И.Б., Успенский Ю.П.* Фенотипы неалкогольной жировой болезни печени в различных регионах Российской Федерации, диагностические и лечебные подходы в клинической практике. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии.* 2023;33(2):7–18. [*Ivashkin V.T., Zharkova M.S., Korochanskaya N.V., Khlynov I.B., Uspensky Yu.P.* Phenotypes of non-alcoholic fatty liver disease in different regions of the Russian Federation, diagnostic and therapeutic

approach in clinical practice. *Russian Journal of Gastroenterology, Hepatology, Coloproctology.* 2023;33(2):7–18. (In Russ.)]. DOI: 10.22416/1382-4376-2023-33-2-7-18
329. *Mato J.M., Cámara J., Fernández de Paz J., Caballería L., Coll S., Caballero A., et al.* S-adenosylmethionine in alcoholic liver cirrhosis: A randomized, placebo-controlled, double-blind, multicenter clinical trial. *J Hepatol.* 1999;30(6):1081–9. DOI: 10.1016/s0168-8278(99)80263-3
330. *Rambaldi A., Gluud C.* S-adenosyl-L-methionine for alcoholic liver diseases. *Cochrane Database Syst Rev.* 2006;2:CD002235. DOI: 10.1002/14651858.CD002235.pub2
331. *Lassailly G., Caiazzo R., Buob D., Pigeyre M., Verkindt H., Labreuche J., et al.* Bariatric surgery reduces features of nonalcoholic steatohepatitis in morbidly obese patients. *Gastroenterology.* 2015;149(2):379–88. DOI: 10.1053/j.gastro.2015.04.014
332. *Bower G., Toma T., Harling L., Jiao L.R., Efthimiou E., Darzi A., et al.* Bariatric surgery and non-alcoholic fatty liver disease: A systematic review of liver biochemistry and histology. *Obes Surg.* 2015;25(12):2280–9. DOI: 10.1007/s11695-015-1691-x
333. *Lee Y., Doumouras A.G., Yu J., Brar K., Banfield L., Gmora S., et al.* Complete resolution of nonalcoholic fatty liver disease after bariatric surgery: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2019;17(6):1040–60.e11. DOI: 10.1016/j.cgh.2018.10.017
334. *Fakhry T.K., Mhaskar R., Schwitalla T., Muradova E., Gonzalvo J.P., Murr M.M.* Bariatric surgery improves nonalcoholic fatty liver disease: A contemporary systematic review and meta-analysis. *Surg Obes Relat Dis.* 2019;15(3):502–11. DOI: 10.1016/j.soard.2018.12.002
335. *Zhou H., Luo P., Li P., Wang G., Yi X., Fu Z., et al.* Bariatric surgery improves nonalcoholic fatty liver disease: Systematic review and meta-analysis. *Obes Surg.* 2022;32(6):1872–83. DOI: 10.1007/s11695-022-06011-1
336. *Lazarus J.V., Mark H.E., Anstee Q.M., Arab J.P., Batterham R.L., Castera L., et al.* Advancing the global public health agenda for NAFLD: A consensus statement. *Nat Rev Gastroenterol Hepatol.* 2022;19(1):60–78. DOI: 10.1038/s41575-021-00523-4
337. *European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO).* EASL-EASD-EASO clinical practice guidelines for the management of non-alcoholic fatty liver disease. *Obes Facts.* 2016;9(2):65–90. DOI: 10.1159/000443344
338. *Fernández T., Viñuela M., Vidal C., Barrera F.* Lifestyle changes in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis. *PLoS One.* 2022;17(2):e0263931. DOI: 10.1371/journal.pone.0263931
339. *Glass L.M., Hunt C.M., Fuchs M., Su G.L.* Comorbidities and nonalcoholic fatty liver disease: The chicken, the egg, or both? *Fed Pract.* 2019;36(2):64–71.
340. *Singh S., Singh P.P., Singh A.G., Murad M.H., Sanchez W.* Anti-diabetic medications and the risk of hepatocellular cancer: A systematic review and meta-analysis. *Am J Gastroenterol.* 2013;108(6):881–91. DOI: 10.1038/ajg.2013.5
341. *Ma S., Zheng Y., Xiao Y., Zhou P., Tan H.* Meta-analysis of studies using metformin as a reducer for liver cancer risk in diabetic patients. *Medicine (Baltimore).* 2017;96(19):e6888. DOI: 10.1097/MD.0000000000006888
342. *Zhou Y.Y., Zhu G.Q., Liu T., Zheng J.N., Cheng Z., Zou T.T., et al.* Systematic review with network meta-analysis: Antidiabetic medication and risk of hepatocellular carcinoma. *Sci Rep.* 2016;6:33743. DOI: 10.1038/srep33743
343. *Singh S., Singh P.P., Singh A.G., Murad M.H., Sanchez W.* Statins are associated with a reduced risk of hepatocellular cancer: A systematic review and meta-analysis. *Gastroenterology.* 2013;144(2):323–32. DOI: 10.1053/j.gastro.2012.10.005
344. *Singal A., Volk M.L., Waljee A., Salgia R., Higgins P., Rogers M.A., et al.* Meta-analysis: Surveillance with ultrasound for early-stage hepatocellular carcinoma in patients with cirrhosis. *Aliment Pharmacol Ther.* 2009;30(1):37–47. DOI: 10.1111/j.1365-2036.2009.04014.x
345. *European Association for the Study of the Liver.* EASL clinical practice guidelines: Management of hepatocellular carcinoma. *J Hepatol.* 2018;69(1):182–236. DOI: 10.1016/j.jhep.2018.03.019
346. *Machado M.V.* The growing landscape of NAFLD-associated hepatocellular carcinoma and its impact in surveillance. *GE Port J Gastroenterol.* 2023;31(1):14–23. DOI: 10.1159/000531397
347. *Younossi Z., Stepanova M., Ong J.P., Jacobson I.M., Bugianesi E., Duseja A., et al.* Nonalcoholic steatohepatitis is the fastest growing cause of hepatocellular carcinoma in liver transplant candidates. *Clin Gastroenterol Hepatol.* 2019;17(4):748–55.e3. DOI: 10.1016/j.cgh.2018.05.057
348. *Ducreux M., Abou-Alfa G.K., Bekaii-Saab T., Berlin J., Cervantes A., de Baere T., et al.* The management of hepatocellular carcinoma. Current expert opinion and recommendations derived from the 24th ESMO/World Congress on Gastrointestinal Cancer, Barcelona, 2022. *ESMO Open.* 2023;8(3):101567. DOI: 10.1016/j.esmoop.2023.101567
349. *Adams L.A., Lymp J.F., St Sauver J., Sanderson S.O., Lindor K.D., Feldstein A., et al.* The natural history of nonalcoholic fatty liver disease: A population-based cohort study. *Gastroenterology.* 2005;129(1):113–21. DOI: 10.1053/j.gastro.2005.04.014
350. *Hashimoto E., Yatsuji S., Tobari M., Taniai M., Torii N., Tokushige K., et al.* Hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. *J Gastroenterol.* 2009;44(Suppl. 19):89–95. DOI: 10.1007/s00535-008-2262-x
351. *Ascha M.S., Hanouneh I.A., Lopez R., Tamimi T.A., Feldstein A.F., Zein N.N.* The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. *Hepatology.* 2010;51(6):1972–8. DOI: 10.1002/hep.23527
352. *Bertot L.C., Jeffrey G.P., Wallace M., MacQuillan G., Garas G., Ching H.L., et al.* Nonalcoholic fatty liver disease-related cirrhosis is commonly unrecognized and associated with hepatocellular carcinoma. *Hepatol Commun.* 2017;1(1):53–60. DOI: 10.1002/hep4.1018
353. *Than N.N., Ghazanfar A., Hodson J., Tehami N., Coldham C., Mergental H., et al.* Comparing clinical presentations, treatments and outcomes of hepatocellular carcinoma due to hepatitis C and non-alcoholic fatty liver disease. *QJM.* 2017;110(2):73–81. DOI: 10.1093/qjmed/hcw151
354. *Yoo J.J., Park M.Y., Cho E.J., Yu S.J., Kim S.G., Kim Y.J., et al.* Smoking increases the risk of hepatocellular carcinoma and cardiovascular disease in patients with metabolic-associated fatty liver disease. *J Clin Med.* 2023;12(9):3336. DOI: 10.3390/jcm12093336
355. *Caussy C., Soni M., Cui J., Bettencourt R., Schork N., Chen C.H., et al.* Nonalcoholic fatty liver disease with cirrhosis increases familial risk for advanced fibrosis. *J Clin Invest.* 2017;127(7):2697–704. DOI: 10.1172/JCI93465
356. *Wijarnpreecha K., Thongprayoon C., Ungprasert P.* Coffee consumption and risk of nonalcoholic fatty liver disease: A systematic review and meta-analysis. *Eur J Gastroenterol Hepatol.* 2017;29(2):e8–12. DOI: 10.1097/MEG.0000000000000776
357. *Hayat U., Siddiqui A.A., Okut H., Afroz S., Tasleem S., Haris A.* The effect of coffee consumption on the non-alcoholic fatty liver disease and liver fibrosis: A meta-analysis of 11 epidemiological studies. *Ann Hepatol.* 2021;20:100254. DOI: 10.1016/j.aohep.2020.08.071
358. *Kennedy O.J., Roderick P., Buchanan R., Fallowfield J.A., Hayes P.C., Parkes J.* Coffee, including caffeinated and decaffeinated coffee, and the risk of hepatocellular carcinoma: A systematic review and dose-response meta-analysis. *BMJ Open.* 2017;7(5):e013739. DOI: 10.1136/bmjopen-2016-013739
359. *Shen H., Rodriguez A.C., Shiani A., Lipka S., Shahzad G., Kumar A., et al.* Association between caffeine consumption and nonalcoholic fatty liver disease: A systemic review and meta-analysis. *Therap Adv Gastroenterol.* 2016;9(1):113–20. DOI: 10.1177/1756283X15593700

360. *Chen Y.P., Lu F.B., Hu Y.B., Xu L.M., Zheng M.H., Hu E.D.* A systematic review and a dose-response meta-analysis of coffee dose and nonalcoholic fatty liver disease. *Clin Nutr.* 2019;38(6):2552–7. DOI: 10.1016/j.clnu.2018.11.030
361. *Marventano S., Salomone F., Godos J., Pluchinotta F., Del Rio D., Mistretta A., et al.* Coffee and tea consumption in relation with non-alcoholic fatty liver and metabolic syndrome: A systematic review and meta-analysis of observational studies. *Clin Nutr.* 2016;35(6):1269–81. DOI: 10.1016/j.clnu.2016.03.012
362. *Ebadi M., Ip S., Bhanji R.A., Montano-Loza A.J.* Effect of coffee consumption on non-alcoholic fatty liver disease incidence, prevalence and risk of significant liver fibrosis: Systematic review with meta-analysis of observational studies. *Nutrients.* 2021;13(9):3042. DOI: 10.3390/nu13093042
363. *Birerdinc A., Stepanova M., Pawloski L., Younossi Z.M.* Caffeine is protective in patients with non-alcoholic fatty liver disease. *Aliment Pharmacol Ther.* 2012;35(1):76–82. DOI: 10.1111/j.1365-2036.2011.04916.x
364. *Inoue M., Yoshimi I., Sobue T., Tsugane S.* Influence of coffee drinking on subsequent risk of hepatocellular carcinoma: A prospective study in Japan. *J Natl Cancer Inst.* 2005;97(4):293–300. DOI: 10.1093/jnci/dji040
365. *Johnson S., Koh W.P., Wang R., Govindarajan S., Yu M.C., Yuan J.M.* Coffee consumption and reduced risk of hepatocellular carcinoma: Findings from the Singapore Chinese Health Study. *Cancer Causes Control.* 2011;22(3):503–10. DOI: 10.1007/s10552-010-9725-0
366. *Hu G., Tuomilehto J., Pukkala E., Hakulinen T., Antikainen R., Vartiainen E., et al.* Joint effects of coffee consumption and serum gamma-glutamyltransferase on the risk of liver cancer. *Hepatology.* 2008;48(1):129–36. DOI: 10.1002/hep.22320
367. *Tanaka K., Hara M., Sakamoto T., Higaki Y., Mizuta T., Eguchi Y., et al.* Inverse association between coffee drinking and the risk of hepatocellular carcinoma: A case-control study in Japan. *Cancer Sci.* 2007;98(2):214–8. DOI: 10.1111/j.1349-7006.2006.00368.x

Information about the authors

Vladimir T. Ivashkin — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, Head of the Department of Propaedeutics of Internal Diseases, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: ivashkin_v_t@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0002-6815-6015

Oksana M. Drapkina — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, Director, National Medical Research Center for Therapy and Preventive Medicine.
Contact information: drapkina@bk.ru;
101000, Moscow, Petroverginskiy lane, 10, build. 3.
ORCID: https://orcid.org/0000-0002-4453-8430

Marina V. Maevskaya — Dr. Sci. (Med.), Professor, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: maevskaya_m_v@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0001-8913-140X

Karina L. Raikhelson — Dr. Sci. (Med.), Professor of the Scientific, Clinical and Educational Centre of Gastroenterology and Hepatology, Saint Petersburg State University; Academician I.P. Pavlov First Saint Petersburg State Medical University.
Contact information: kraikhelson@mail.ru;
199034, Saint Petersburg, Universitetskaya embankment, 7/9.
ORCID: https://orcid.org/0000-0002-8821-6142

Sergey V. Okovityi — Dr. Sci. (Med.), Professor, Head of the Department of Pharmacology and Clinical Pharmacology, Saint Petersburg State Chemical Pharmaceutical University.

Сведения об авторах

Ивашкин Владимир Трофимович — доктор медицинских наук, профессор, академик РАН, заведующий кафедрой пропедевтики внутренних болезней, гастроэнтерологии и гепатологии, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: ivashkin_v_t@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0002-6815-6015

Драпкина Оксана Михайловна — доктор медицинских наук, профессор, академик РАН, директор, ФГБУ «Национальный медицинский исследовательский центр терапии и профилактической медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: drapkina@bk.ru;
101000, г. Москва, Петроверигский пер., 10, стр. 3.
ORCID: https://orcid.org/0000-0002-4453-8430

Маевская Марина Викторовна — доктор медицинских наук, профессор, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: maevskaya_m_v@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0001-8913-140X

Райхельсон Карина Леонидовна — доктор медицинских наук, профессор Научно-клинического и образовательного центра гастроэнтерологии и гепатологии, ФГБОУ ВО «Санкт-Петербургский государственный университет»; ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. академика И.П. Павлова» Министерства здравоохранения Российской Федерации.
Контактная информация: kraikhelson@mail.ru;
199034, г. Санкт-Петербург, Университетская наб., 7/9.
ORCID: https://orcid.org/0000-0002-8821-6142

Оковитый Сергей Владимирович — доктор медицинских наук, профессор, заведующий кафедрой фармакологии и клинической фармакологии, ФГБОУ ВО «Санкт-Петербургский государственный химико-фармацевтический университет» Министерства здравоохранения Российской Федерации.

Contact information: sergey.okovity@pharminnotech.com;
197022, Saint Petersburg, Professora Popova str., 14A.
ORCID: https://orcid.org/0000-0003-4294-5531

Maria S. Zharkova — Cand. Sci. (Med.), Head of the Hepatology Department, V.Kh. Vasilenko Clinic of Internal Disease Propaedeutics, Gastroenterology and Hepatology, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: zharkova_m_s@staff.sechenov.ru;
119048, Moscow, Trubetskaya str., 8/2.
ORCID: https://orcid.org/0000-0001-5939-1032

Vasilisa R. Grechishnikova* — Postgraduate, Teaching Assistant of the Department of Internal Disease Propaedeutics, Gastroenterology and Hepatology, N.V. Sklifosovsky Institute of Clinical Medicine, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: korneeva_v_r@staff.sechenov.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0002-3851-626X

Diana I. Abdulganieva — Dr. Sci. (Med.), Professor, Head of the Department of Hospital Therapy, Kazan State Medical University.
Contact information: diana_s@mail.ru;
420012, Kazan, Butlerova str., 49.
ORCID: https://orcid.org/0000-0001-7069-2725

Sergei A. Alekseenko — Dr. Sci. (Med.), Professor, Head of the Department of Hospital Therapy, Far-Eastern State Medical University.
Contact information: sa.alexeenko@gmail.com;
680000, Khabarovsk, Muravyova-Amurskogo str., 35.
ORCID: https://orcid.org/0000-0003-1724-9980

Maria D. Ardatskaya — Dr. Sci. (Med.), Professor, Central State Medical Academy of the Department of Presidential Affairs.
Contact information: ma@uni-med.ru;
121359, Moscow, Marshala Timoshenko str., 19, build. 1A.
ORCID: https://orcid.org/0000-0002-8069-0368

Igor G. Bakulin — Dr. Sci. (Med.), Professor, Head of the Department of Propaedeutics of Internal Medicine, Gastroenterology and Dietetics named after S.M. Ryss, North-Western State Medical University named after I.I. Mechnikov.
Contact information: igbakulin@yandex.ru;
191015, Saint Petersburg, Kirochnaya str., 41.
ORCID: https://orcid.org/0000-0002-6151-2021

Natalia V. Bakulina — Dr. Sci. (Med.), Head of the Department of Internal Medicine, Nephrology, General and Clinical Pharmacology with a course in Pharmacy, North-Western State Medical University named after I.I. Mechnikov.

Контактная информация: sergey.okovity@pharminnotech.com;
197022, г. Санкт-Петербург, ул. Профессора Попова, 14а.
ORCID: https://orcid.org/0000-0003-4294-5531

Жаркова Мария Сергеевна — кандидат медицинских наук, заведующая отделением гепатологии Клиники пропедевтики внутренних болезней, гастроэнтерологии, гепатологии им. В.Х. Василенко, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: zharkova_m_s@staff.sechenov.ru;
119048, г. Москва, ул. Трубецкая, 8, стр. 2.
ORCID: https://orcid.org/0000-0001-5939-1032

Гречишникова Василиса Романовна* — аспирант, ассистент кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии Института клинической медицины им. Н.В. Склифосовского, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: korneeva_v_r@staff.sechenov.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0002-3851-626X

Абдулганиева Диана Ильдаровна — доктор медицинских наук, профессор, заведующая кафедрой госпитальной терапии, ФГБОУ ВО «Казанский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: diana_s@mail.ru;
420012, г. Казань, ул. Бутлерова, 49.
ORCID: https://orcid.org/0000-0001-7069-2725

Алексеенко Сергей Алексеевич — доктор медицинских наук, профессор, заведующий кафедрой госпитальной терапии, ФГБОУ ВО «Дальневосточный государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: sa.alexeenko@gmail.com;
680000, г. Хабаровск, ул. Муравьева-Амурского, 35.
ORCID: https://orcid.org/0000-0003-1724-9980

Ардатская Мария Дмитриевна — доктор медицинских наук, профессор, ФГБУ ДПО «Центральная государственная медицинская академия» Управления делами Президента Российской Федерации.
Контактная информация: ma@uni-med.ru;
121359, г. Москва, ул. Маршала Тимошенко, 19, стр. 1А.
ORCID: https://orcid.org/0000-0002-8069-0368

Бакулин Игорь Геннадьевич — доктор медицинских наук, профессор, заведующий кафедрой пропедевтики внутренних болезней, гастроэнтерологии и диетологии им. С.М. Рысса, ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации.
Контактная информация: igbakulin@yandex.ru;
191015, г. Санкт-Петербург, ул. Кирочная, 41.
ORCID: https://orcid.org/0000-0002-6151-2021

Бакулина Наталья Валерьевна — доктор медицинских наук, профессор, проректор по науке и инновационной деятельности, заведующая кафедрой внутренних болезней, клинической фармакологии и нефрологии, ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации.

* Corresponding author / Автор, ответственный за переписку

Contact information: natalya.bakulina@szgmu.ru;
191015, Saint Petersburg, Kirochnaya str., 41.
ORCID: https://orcid.org/0000-0003-4075-4096

Pavel O. Bogomolov — Cand. Sci. (Med.), Associate Professor of the Department of Propaedeutics of Internal Medicine and Gastroenterology, Russian University of Medicine; Head of the Department of Hepatology, Moscow Regional Research Clinical Institute.
Contact information: Bpo73@list.ru;
129110, Moscow, Shchepkina str., 61/2.
ORCID: https://orcid.org/0000-0003-2346-1216

Valeriy V. Breder — Dr. Sci. (Med.), Head of the Department of Drug Treatment, National Medical Research Center of Oncology named after N.N. Blokhin.
Contact information: vbreder@yandex.ru;
115478, Moscow, Kashirskoe highway, 24.
ORCID: https://orcid.org/0000-0002-6244-4294

Elena V. Vinnitskaya — Dr. Sci. (Med.), Head of the Department of Hepatology, Loginov Moscow Clinical Scientific Center.
Contact information: evinn@mail.ru;
111123, Moscow, Entuziastov highway, 86.
ORCID: https://orcid.org/0000-0002-0344-8375

Natalia I. Geyvandova — Dr. Sci. (Med.), Professor of the Department of Hospital Therapy, Stavropol State Medical University.
Contact information: ngeyvandova@yandex.ru;
355017, Stavropol, Mira str., 310.
ORCID: https://orcid.org/0000-0001-5920-5703

Elena V. Golovanova — Dr. Sci. (Med.), Professor of the Department of Therapy and Preventive Medicine, Russian University of Medicine.
Contact information: golovanovaev@mail.ru;
127473, Moscow, Delegatskaya str., 20, build. 1.
ORCID: https://orcid.org/0000-0002-8034-5329

Vladimir B. Grinevich — Dr. Sci. (Med.), Professor, Head of the 2nd Department of Therapy, Kirov Military Medical Academy.
Contact information: vb_grinevich@mail.ru;
194044, Saint Petersburg, Akademika Lebedeva str., 6.
ORCID: https://orcid.org/0000-0002-1095-8787

Vladimir L. Doshchitsin — Dr. Sci. (Med.), Professor, Professor of the Department of Cardiology, N.I. Pirogov Russian National Research Medical University.
Contact information: vlad.dos@mail.ru;
117997, Moscow, Ostrovityanova str., 1.
ORCID: https://orcid.org/0000-0001-8874-4108

Контактная информация: natalya.bakulina@szgmu.ru;
191015, г. Санкт-Петербург, ул. Кирочная, 41.
ORCID: https://orcid.org/0000-0003-4075-4096

Богомолов Павел Олегович — кандидат медицинских наук, доцент кафедры пропедевтики внутренних болезней и гастроэнтерологии, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации; руководитель отделения и ведущий научный сотрудник гепатологического отделения, ГБУЗ МО «Московский областной научно-исследовательский клинический институт им. М.Ф. Владимирского» Министерства здравоохранения Российской Федерации.
Контактная информация: Bpo73@list.ru;
129110, г. Москва, ул. Щепкина, 61/2.
ORCID: https://orcid.org/0000-0003-2346-1216

Бредер Валерий Владимирович — доктор медицинских наук, заведующий отделом лекарственного лечения, ФГБУ «Национальный медицинский исследовательский центр онкологии им. Н.Н. Блохина» Министерства здравоохранения Российской Федерации.
Контактная информация: vbreder@yandex.ru;
115478, г. Москва, Каширское шоссе, 24.
ORCID: https://orcid.org/0000-0002-6244-4294

Винницкая Елена Владимировна — доктор медицинских наук, заведующая отделом гепатологии, ГБУЗ «Московский клинический научно-практический центр им. А.С. Логинова» Департамента здравоохранения города Москвы.
Контактная информация: evinn@mail.ru;
111123, г. Москва, шоссе Энтузиастов, 86.
ORCID: https://orcid.org/0000-0002-0344-8375

Гейвандова Наталья Иогановна — доктор медицинских наук, профессор, ФГБОУ ВО «Ставропольский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: ngeyvandova@yandex.ru;
355017, г. Ставрополь, ул. Мира, 310.
ORCID: https://orcid.org/0000-0001-5920-5703

Голованова Елена Владимировна — доктор медицинских наук, профессор кафедры терапии и профилактической медицины, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: golovanovaev@mail.ru;
127473, г. Москва, ул. Делегатская, 20, стр. 1.
ORCID: https://orcid.org/0000-0002-8034-5329

Гриневич Владимир Борисович — доктор медицинских наук, профессор, заведующий 2-й кафедрой (терапии усовершенствования врачей), ФГБВОУ ВО «Военно-медицинская академия им. С.М. Кирова» Министерства обороны Российской Федерации.
Контактная информация: vb_grinevich@mail.ru;
194044, г. Санкт-Петербург, ул. Академика Лебедева, 6.
ORCID: https://orcid.org/0000-0002-1095-8787

Дощицин Владимир Леонидович — доктор медицинских наук, профессор, профессор кафедры кардиологии, ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации.
Контактная информация: vlad.dos@mail.ru;
117997, г. Москва, ул. Островитянова, 1.
ORCID: https://orcid.org/0000-0001-8874-4108

Ekaterina N. Dudinskaya — Dr. Sci. (Med.), Head of the Laboratory of Age-Related Metabolic Endocrinological Disorders, Russian Gerontological Scientific and Clinical Center, Professor of the Department of Aging Diseases of the Faculty of Continuing Professional Education, N.I. Pirogov Russian National Research Medical University.
Contact information: katharina.gin@gmail.com;
129226, Moscow, 1-ya Leonova str., 16.
ORCID: https://orcid.org/0000-0001-7891-6850

Ekaterina V. Ershova — Cand. Sci. (Med.), Leading Researcher of the Department of Therapeutic Endocrinology, Endocrinology Research Centre.
Contact information: yu99pol06@rambler.ru;
117292, Moscow, Dmitriya Ulyanova str., 11.
ORCID: https://orcid.org/0000-0002-6220-4397

Khava B. Kodzoeva — Physician of the Therapeutic Department, National Medical Research Center for Transplantology and Artificial Organs named after Academician V.I. Shumakov.
Contact information: kod_eva@bk.ru;
119435, Moscow, Pogodinskaya str., 1, build. 1.
ORCID: https://orcid.org/0000-0001-7510-6553

Irina V. Kozlova — Dr. Sci. (Med.), Professor, Saratov State Medical University named after V.I. Razumovsky.
Contact information: kozlova@inbox.ru;
410012, Saratov, Bolshaya Kazachya str., 112.
ORCID: https://orcid.org/0000-0002-5056-4504

Kseniya A. Komshilova — Cand. Sci. (Med.), Endocrinologist at the Department of Therapy of Thyroid Gland Diseases, Adrenal Glands and Obesity, Department of Therapeutic Endocrinology, Endocrinology Research Centre.
Contact information: kom-ksusha@rambler.ru;
117292, Moscow, Dmitriya Ulyanova str., 11.
ORCID: https://orcid.org/0000-0002-6624-2374

Yuri V. Konev — Dr. Sci. (Med.), Professor of the Department of Outpatient Therapy, Russian University of Medicine.
Contact information: ukonev@rambler.ru;
127473, Moscow, Delegatskaya str., 20, build. 1.
ORCID: https://orcid.org/0000-0002-4786-2041

Natalia V. Korochanskaya — Dr. Sci. (Med.), Professor, Kuban State Medical University.
Contact information: nvk-gastro@mail.ru;
350063, Krasnodar, Mitrofana Sedina str., 4.
ORCID: https://orcid.org/0000-0002-5538-9418

Yulia V. Kotovskaya — Dr. Sci. (Med.), Professor, Deputy Director for Research, Russian Gerontological Scientific and Clinical Center, N.I. Pirogov Russian National Research Medical University.

Дудинская Екатерина Наильевна — доктор медицинских наук, заведующая лабораторией возрастных метаболических и эндокринных нарушений, обособленное структурное подразделение «Российский геронтологический научно-клинический центр», профессор кафедры болезней старения факультета дополнительного профессионального образования, ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации.
Контактная информация: katharina.gin@gmail.com;
129226, г. Москва, ул. 1-я Леонова, 16.
ORCID: https://orcid.org/0000-0001-7891-6850

Ершова Екатерина Владимировна — кандидат медицинских наук, ведущий научный сотрудник отдела терапевтической эндокринологии, ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации.
Контактная информация: yu99pol06@rambler.ru;
117292, г. Москва, ул. Дмитрия Ульянова, 11.
ORCID: https://orcid.org/0000-0002-6220-4397

Кодзоева Хава Багаудиновна — врач-терапевт терапевтического отделения, ФГБУ «Национальный медицинский исследовательский центр трансплантологии и искусственных органов им. академика В.И. Шумакова» Министерства здравоохранения Российской Федерации.
Контактная информация: kod_eva@bk.ru;
119435, г. Москва, ул. Погодинская, 1, стр. 1.
ORCID: https://orcid.org/0000-0001-7510-6553

Козлова Ирина Вадимовна — доктор медицинских наук, профессор, ФГБОУ ВО «Саратовский государственный медицинский университет им. В.И. Разумовского» Министерства здравоохранения Российской Федерации.
Контактная информация: kozlova@inbox.ru;
410012, г. Саратов, ул. Большая Казачья, 112.
ORCID: https://orcid.org/0000-0002-5056-4504

Комшилова Ксения Андреевна — кандидат медицинских наук, врач-эндокринолог отделения терапии заболеваний щитовидной железы, надпочечников и ожирения отдела терапевтической эндокринологии, ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации.
Контактная информация: kom-ksusha@rambler.ru;
117292, г. Москва, ул. Дмитрия Ульянова, 11.
ORCID: https://orcid.org/0000-0002-6624-2374

Конев Юрий Владимирович — доктор медицинских наук, профессор кафедры поликлинической терапии, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: ukonev@rambler.ru;
127473, г. Москва, ул. Делегатская, 20, стр. 1.
ORCID: https://orcid.org/0000-0002-4786-2041

Корочанская Наталья Всеволодовна — доктор медицинских наук, профессор, ФГБОУ ВО «Кубанский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: nvk-gastro@mail.ru;
350063, г. Краснодар, ул. Митрофана Седина, 4.
ORCID: https://orcid.org/0000-0002-5538-9418

Котовская Юлия Викторовна — доктор медицинских наук, профессор, заместитель директора по научной работе, обособленное структурное подразделение «Российский геронтологический научно-клинический центр», ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации.

Contact information: kotovskaya_yv@rgnkc.ru;
129226, Moscow, 1-ya Leonova str., 16.
ORCID: https://orcid.org/0000-0002-1628-5093

Yuri A. Kravchuk — Dr. Sci. (Med.), Professor, Kirov Military Medical Academy.
Contact information: kravchuk2003@mail.ru;
194044, Saint Petersburg, Akademika Lebedeva str., 6.
ORCID: https://orcid.org/0000-0001-8347-0531

Irina D. Loranskaya — Dr. Sci. (Med.), Professor, Dean of the Faculty of Therapy, Head of the Department of Gastroenterology of the Faculty of Therapy, Russian Medical Academy of Continuous Professional Education.
Contact information: gastrormapo@yandex.ru;
123242, Moscow, Barrikadnaya str., 2/1, build. 1.
ORCID: https://orcid.org/0000-0002-3681-4132

Igor V. Maev — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, Head of the Department of Internal Disease Propaedeutics and Gastroenterology, Russian University of Medicine.
Contact information: igormaev@rambler.ru;
127473, Moscow, Delegatskaya str., 20, build. 1.
ORCID: https://orcid.org/0000-0001-6114-564X

Anatoliy I. Martynov — Dr. Sci. (Med.), Academician of the Russian Academy of Sciences, Professor of the Department of Hospital Therapy No. 1 of the Faculty of Medicine, Russian University of Medicine.
Contact information: anatmartynov@mail.ru;
127473, Moscow, Delegatskaya str., 20, build. 1.
ORCID: https://orcid.org/0000-0003-2839-7292

Sabir N. Mekhtiev — Dr. Sci. (Med.), Professor, Academician I.P. Pavlov First Saint Petersburg State Medical University.
Contact information: sabirm@mail.ru;
197022, Saint Petersburg, L'va Tolstogo str., 6-8.
ORCID: https://orcid.org/0000-0001-7367-9219

Ekaterina E. Mishina — Cand. Sci. (Med.), Researcher, Endocrinologist, Endocrinology Research Centre.
Contact information: eka-mi@rambler.ru;
117292, Moscow, Dmitriya Ulyanova str., 11.
ORCID: https://orcid.org/0000-0002-5371-8708

Maria Yu. Nadinskaia — Cand. Sci. (Med.), Associate Professor of the Department of Propaedeutics of Internal Diseases, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: nadinskaya_m_yu@staff.sechenov.ru;
119048, Moscow, Trubetskaya str., 8/2.
ORCID: https://orcid.org/0000-0002-1210-2528

Контактная информация: kotovskaya_yv@rgnkc.ru;
129226, г. Москва, ул. 1-я Леонова, 16.
ORCID: https://orcid.org/0000-0002-1628-5093

Кравчук Юрий Алексеевич — доктор медицинских наук, профессор, ФГБВОУ ВО «Военно-медицинская академия им. С.М. Кирова» Министерства обороны Российской Федерации.
Контактная информация: kravchuk2003@mail.ru;
194044, г. Санкт-Петербург, ул. Академика Лебедева, 6.
ORCID: https://orcid.org/0000-0001-8347-0531

Лоранская Ирина Дмитриевна — доктор медицинских наук, профессор, декан терапевтического факультета, заведующая кафедрой гастроэнтерологии, ФГБОУ ДПО «Российская медицинская академия непрерывного профессионального образования» Министерства здравоохранения Российской Федерации.
Контактная информация: gastrormapo@yandex.ru;
123242, г. Москва, Баррикадная ул., 2/1, корп. 1.
ORCID: https://orcid.org/0000-0002-3681-4132

Маев Игорь Вениаминович — доктор медицинских наук, профессор, академик РАН, заведующий кафедрой пропедевтики внутренних болезней и гастроэнтерологии, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: igormaev@rambler.ru;
127473, г. Москва, ул. Делегатская, 20, стр. 1.
ORCID: https://orcid.org/0000-0001-6114-564X

Мартынов Анатолий Иванович — доктор медицинских наук, академик РАН, профессор кафедры госпитальной терапии № 1 лечебного факультета, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: anatmartynov@mail.ru;
127473, г. Москва, ул. Делегатская, 20, стр. 1.
ORCID: https://orcid.org/0000-0003-2839-7292

Мехтиев Сабир Насрединович — доктор медицинских наук, профессор, ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. академика И.П. Павлова» Министерства здравоохранения Российской Федерации.
Контактная информация: sabirm@mail.ru;
197022, г. Санкт-Петербург, ул. Льва Толстого, 6-8.
ORCID: https://orcid.org/0000-0001-7367-9219

Мишина Екатерина Евгеньевна — кандидат медицинских наук, научный сотрудник, врач-эндокринолог, ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации.
Контактная информация: eka-mi@rambler.ru;
117292, г. Москва, ул. Дмитрия Ульянова, 11.
ORCID: https://orcid.org/0000-0002-5371-8708

Надинская Мария Юрьевна — кандидат медицинских наук, доцент кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: nadinskaya_m_yu@staff.sechenov.ru;
119048, г. Москва, ул. Трубецкая, 8, стр. 2.
ORCID: https://orcid.org/0000-0002-1210-2528

Igor G. Nikitin — Dr. Sci. (Med.), Professor, Head of the Department of Hospital Therapy named after Academician G.I. Storozhakov, Institute of Clinical Medicine, N.I. Pirogov Russian National Research Medical University; National Medical Research Center "Treatment and Rehabilitation Center".
Contact information: igor.nikitin.64@mail.ru;
117997, Moscow, Ostrovityanova str., 1.
ORCID: https://orcid.org/0000-0003-1699-0881

Никитин Игорь Геннадьевич — доктор медицинских наук, профессор, заведующий кафедрой госпитальной терапии им. академика Г.И. Сторожакова Института клинической медицины, ФГАОУ ВО «Российский национальный исследовательский медицинский университет имени Н.И. Пирогова» Министерства здравоохранения Российской Федерации; ФГАУ «Национальный медицинский исследовательский центр «Лечебно-реабилитационный центр» Министерства здравоохранения Российской Федерации.
Контактная информация: igor.nikitin.64@mail.ru;
117997, г. Москва, ул. Островитянова, 1.
ORCID: https://orcid.org/0000-0003-1699-0881

Marina F. Osipenko — Dr. Sci. (Med.), Professor, Head of the Department of Internal Diseases Propedeutics, Novosibirsk State Medical University.
Contact information: ngma@bk.ru;
630091, Novosibirsk, Krasnyi ave., 52.
ORCID: https://orcid.org/0000-0002-5156-2842

Осипенко Марина Федоровна — доктор медицинских наук, профессор, заведующая кафедрой пропедевтики внутренних болезней, ФГБОУ ВО «Новосибирский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: ngma@bk.ru;
630091, г. Новосибирск, Красный просп., 52.
ORCID: https://orcid.org/0000-0002-5156-2842

Olga D. Ostroumova — Dr. Sci. (Med.), Professor, Head of the Department of Therapy and Polymorbid Pathology named after Academician M.S. Vovsi, Russian Medical Academy of Continuous Professional Education.
Contact information: ostroumova.olga@mail.ru;
123242, Moscow, Barrikadnaya str., 2/1, build. 1.
ORCID: https://orcid.org/0000-0002-0795-8225

Остроумова Ольга Дмитриевна — доктор медицинских наук, профессор, заведующая кафедрой терапии и полиморбидной патологии им. академика М.С. Вовси, ФГБОУ ДПО «Российская медицинская академия непрерывного профессионального образования» Министерства здравоохранения Российской Федерации.
Контактная информация: ostroumova.olga@mail.ru;
123242, г. Москва, Баррикадная ул., 2/1, корп. 1.
ORCID: https://orcid.org/0000-0002-0795-8225

Chavdar S. Pavlov — Dr. Sci. (Med.), Professor, Head of the Department of Therapy at the Institute of Professional Education, Deputy Director for Scientific and Organizational Work at the N.V. Sklifosovsky Institute of Clinical Medicine, I.M. Sechenov First Moscow State Medical University (Sechenov University); Head of the Therapy Clinic, Moscow Multidisciplinary Scientific and Clinical Center named after S.P. Botkin.
Contact information: chpavlov@mail.ru;
252844, Moscow, 2-y Botkinsky lane, 5.
ORCID: https://orcid.org/0000-0001-5031-9798

Павлов Чавдар Савов — доктор медицинских наук, профессор, заведующий кафедрой терапии Института профессионального образования, заместитель директора по научно-организационной работе Института клинической медицины им. Н.В. Склифосовского, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет); руководитель клиники терапии, ГБУЗ «Московский многопрофильный научно-клинический центр им. С.П. Боткина» Департамента здравоохранения города Москвы.
Контактная информация: chpavlov@mail.ru;
252844, г. Москва, 2-й Боткинский проезд, 5.
ORCID: https://orcid.org/0000-0001-5031-9798

Nana V. Pogosova — Dr. Sci. (Med.), Professor, Deputy Director General for Scientific and Analytical Work and Preventive Cardiology, National Medical Research Center of Cardiology named after Academician E.I. Chazov.
Contact information: nanapogosova@gmail.com;
121552, Moscow, Akademika Chazova str., 15a, build. 1.
ORCID: https://orcid.org/0000-0002-4165-804X

Погосова Нана Вачиковна — доктор медицинских наук, профессор, заместитель генерального директора по научно-аналитической работе и профилактической кардиологии, ФГБУ «Национальный медицинский исследовательский центр кардиологии им. академика Е.И. Чазова» Министерства здравоохранения Российской Федерации.
Контактная информация: nanapogosova@gmail.com;
121552, г. Москва, ул. Академика Чазова, 15а, стр. 1.
ORCID: https://orcid.org/0000-0002-4165-804X

Valery G. Radchenko — Dr. Sci. (Med.), Professor, Professor of the 2nd Department of Therapy, Kirov Military Medical Academy.
Contact information: radchenkovalery@mail.ru;
194044, Saint Petersburg, Akademika Lebedeva str., 6.
ORCID: https://orcid.org/0000-0002-2964-9167

Радченко Валерий Григорьевич — доктор медицинских наук, профессор, профессор 2-й кафедры (терапии усовершенствования врачей), ФГБВОУ ВО «Военно-медицинская академия им. С.М. Кирова» Министерства обороны Российской Федерации.
Контактная информация: radchenkovalery@mail.ru;
194044, г. Санкт-Петербург, ул. Академика Лебедева, 6.
ORCID: https://orcid.org/0000-0002-2964-9167

Grigory E. Roytberg — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, N.I. Pirogov Russian National Research Medical University.
Contact information: contact@medicina.ru;
117997, Moscow, Ostrovityanova str., 1.
ORCID: https://orcid.org/0000-0003-0514-9114

Ройтберг Григорий Ефимович — доктор медицинских наук, профессор, академик РАН, ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации.
Контактная информация: contact@medicina.ru;
117997, г. Москва, ул. Островитянова, 1.
ORCID: https://orcid.org/0000-0003-0514-9114

Rafik G. Saifutdinov — Dr. Sci. (Med.), Professor, Head of the Department of Hospital and Polyclinic Therapy, Kazan State Medical Academy — Branch Campus of the Russian Medical Academy of Continuous Professional Education.
Contact information: rgsbancorp@mail.ru;
420012, Kazan, Butlerova str., 36.
ORCID: https://orcid.org/0000-0003-2839-100X

Сайфутдинов Рафик Галимзянович — доктор медицинских наук, профессор, заведующий кафедрой госпитальной и поликлинической терапии, Казанская государственная медицинская академия — филиал ФГБОУ ДПО «Российская медицинская академия непрерывного профессионального образования» Министерства здравоохранения Российской Федерации.
Контактная информация: rgsbancorp@mail.ru;
420012, г. Казань, ул. Бутлерова, 36.
ORCID: https://orcid.org/0000-0003-2839-100X

Aleksey A. Samsonov — Dr. Sci. (Med.), Professor of the Department of Propaedeutics of Internal Medicine and Gastroenterology, Russian University of Medicine.
Contact information: aleksey.samsonov@gmail.com;
127473, Moscow, Delegatskaya str., 20, build. 1.
ORCID: https://orcid.org/0000-0001-5617-7110

Самсонов Алексей Андреевич — доктор медицинских наук, профессор кафедры пропедевтики внутренних болезней и гастроэнтерологии, ФГБОУ ВО «Российский университет медицины» Министерства здравоохранения Российской Федерации.
Контактная информация: aleksey.samsonov@gmail.com;
127473, г. Москва, ул. Делегатская, 20, стр. 1.
ORCID: https://orcid.org/0000-0001-5617-7110

Pavel V. Seliverstov — Cand. Sci. (Med.), Associate Professor of the 2nd Department of Therapy, Kirov Military Medical Academy.
Contact information: seliverstov-pv@yandex.ru;
194044, Saint Petersburg, Akademika Lebedeva str., 6.
ORCID: https://orcid.org/0000-0001-5623-4226

Селиверстов Павел Васильевич — кандидат медицинских наук, доцент 2-й кафедры (терапии усовершенствования врачей), ФГБВОУ ВО «Военно-медицинская академия им. С.М. Кирова» Министерства обороны Российской Федерации.
Контактная информация: seliverstov-pv@yandex.ru;
194044, г. Санкт-Петербург, ул. Академика Лебедева, 6.
ORCID: https://orcid.org/0000-0001-5623-4226

Stanislav I. Sitkin — Cand. Sci. (Med.), Associate Professor of the Department of Propaedeutics of Internal Medicine, Gastroenterology and Dietetics named after S.M. Ryss, North-Western State Medical University named after I.I. Mechnikov; Head of the Research Group of Epigenetics and Metagenomics of the Institute of Perinatology and Pediatrics, V.A. Almazov National Medical Research Center.
Contact information: sitkins@mail.ru;
197341, Saint Petersburg, Akkuratova str., 2.
ORCID: https://orcid.org/0000-0003-0331-0963

Ситкин Станислав Игоревич — кандидат медицинских наук, доцент кафедры пропедевтики внутренних болезней, гастроэнтерологии и диетологии им. С.М. Рысса, ФГБОУ ВО «Северо-Западный государственный медицинский университет им. И.И. Мечникова» Министерства здравоохранения Российской Федерации; заведующий научно-исследовательской группой эпигенетики и метагеномики Института перинатологии и педиатрии, ФГБУ «Национальный медицинский исследовательский центр им. В.А. Алмазова» Министерства здравоохранения Российской Федерации.
Контактная информация: sitkins@mail.ru;
197341, г. Санкт-Петербург, ул. Аккуратова, 2.
ORCID: https://orcid.org/0000-0003-0331-0963

Larisa V. Tarasova — Dr. Sci. (Med.), Professor, Chuvash State University named after I.N. Ulyanov.
Contact information: Tlarisagast18@mail.ru;
428015, Cheboksary, Moskovsky ave., 15.
ORCID: https://orcid.org/0000-0003-1496-0689

Тарасова Лариса Владимировна — доктор медицинских наук, профессор, ФГБОУ ВО «Чувашский государственный университет им. И.Н. Ульянова» Министерства здравоохранения Российской Федерации.
Контактная информация: Tlarisagast18@mail.ru;
428015, г. Чебоксары, Московский просп., 15.
ORCID: https://orcid.org/0000-0003-1496-0689

Aida I. Tarzimanova — Dr. Sci. (Med.), Professor of the Department of Faculty Therapy No. 2, I.M. Sechenov First Moscow State Medical University (Sechenov University).
Contact information: tarzimanova@mail.ru;
119048, Moscow, Efremova str., 24.
ORCID: https://orcid.org/0000-0001-9536-8307

Тарзиманова Аида Ильгизовна — доктор медицинских наук, профессор кафедры факультетской терапии № 2, ФГАОУ ВО «Первый Московский государственный медицинский университет им. И.М. Сеченова» Министерства здравоохранения Российской Федерации (Сеченовский Университет).
Контактная информация: tarzimanova@mail.ru;
119048, г. Москва, ул. Ефремова, 24.
ORCID: https://orcid.org/0000-0001-9536-8307

Olga N. Tkacheva — Dr. Sci. (Med.), Professor, Corresponding Member of the Russian Academy of Sciences, Director of the Russian Gerontological Scientific and Clinical Center, N.I. Pirogov Russian National Research Medical University; Chief Freelance Geriatrician of the Ministry of Health of the Russian Federation.
Contact information: tkacheva@rgnkc.ru;
129226, Moscow, 1-ya Leonova str., 16.
ORCID: https://orcid.org/0000-0002-4193-688X

Ткачева Ольга Николаевна — доктор медицинских наук, профессор, член-корреспондент РАН, директор Российского геронтологического научно-клинического центра, ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации; главный внештатный гериатр Министерства здравоохранения Российской Федерации.
Контактная информация: tkacheva@rgnkc.ru;
129226, г. Москва, ул. 1-я Леонова, 16.
ORCID: https://orcid.org/0000-0002-4193-688X

Evgeny I. Tkachenko — Dr. Sci. (Med.), Professor of the 2nd Department of Therapy, Kirov Military Medical Academy.
Contact information: tkachenkoe@mail.ru;
194044, Saint Petersburg, Akademika Lebedeva str., 6.
ORCID: https://orcid.org/0009-0006-4123-4649

Ткаченко Евгений Иванович — доктор медицинских наук, профессор, профессор 2-й кафедры (терапии усовершенствования врачей), ФГБВОУ ВО «Военно-медицинская академия имени С.М. Кирова» Министерства обороны Российской Федерации.
Контактная информация: tkachenkoe@mail.ru;
194044, г. Санкт-Петербург, ул. Академика Лебедева, 6.
ORCID: https://orcid.org/0009-0006-4123-4649

Ekaterina A. Troshina — Dr. Sci. (Med.), Professor, Corresponding Member of the Russian Academy of Sciences, Head of the Institute of Clinical Endocrinology, Deputy Director, Endocrinology Research Centre.
Contact information: troshina@inbox.com;
17292, Moscow, Dmitriya Ulyanova str., 11.
ORCID: https://orcid.org/0000-0002-8520-8702

Трошина Екатерина Анатольевна — доктор медицинских наук, профессор, член-корреспондент РАН, директор Института клинической эндокринологии, заместитель директора, ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации.
Контактная информация: troshina@inbox.com;
117292, г. Москва, ул. Дмитрия Ульянова, 11.
ORCID: https://orcid.org/0000-0002-8520-8702

Svetlana V. Turkina — Dr. Sci. (Med.), Professor, Volgograd State Medical University.
Contact information: turkinasv@rambler.ru;
400131, Volgograd, Pavshikh Bortsov square, 1.
ORCID: https://orcid.org/0000-0002-8844-2465

Туркина Светлана Владимировна — доктор медицинских наук, профессор, ФГБОУ ВО «Волгоградский государственный медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: turkinasv@rambler.ru;
400131, г. Волгоград, пл. Павших борцов, 1.
ORCID: https://orcid.org/0000-0002-8844-2465

Yury P. Uspenskiy — Dr. Sci. (Med.), Professor, Professor of the Department of Internal Diseases, Faculty of Dentistry, Academician I.P. Pavlov First Saint Petersburg State Medical University; Head of the Department of Faculty Therapy named after Professor V.A. Valdman, Saint Petersburg State Pediatric Medical University.
Contact information: uspenskiy65@mail.ru;
194100, Saint Petersburg, Litovskaya str., 2.
ORCID: https://orcid.org/0000-0001-6434-1267

Успенский Юрий Павлович — доктор медицинских наук, профессор, профессор кафедры внутренних болезней стоматологического факультета, ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. академика И.П. Павлова» Министерства здравоохранения Российской Федерации; заведующий кафедрой факультетской терапии им. профессора В.А. Вальдмана, ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: uspenskiy65@mail.ru;
194100, г. Санкт-Петербург, Литовская ул., 2.
ORCID: https://orcid.org/0000-0001-6434-1267

Yulia A. Fominykh — Dr. Sci. (Med.), Docent, Head of the Department of Propaedeutics of Internal Medicine with a Clinic, V.A. Almazov National Medical Research Center; Associate Professor of the Department of Internal Diseases of Dentistry Faculty, Academician I.P. Pavlov First Saint Petersburg State Medical University.
Contact information: jaf@mail.ru;
194100, Saint Petersburg, Litovskaya str., 2.
ORCID: https://orcid.org/0000-0002-2436-3813

Фоминых Юлия Александровна — доктор медицинских наук, доцент, заведующая кафедрой пропедевтики внутренних болезней с клиникой, ФГБУ «Национальный медицинский исследовательский центр им. В.А. Алмазова» Министерства здравоохранения Российской Федерации; доцент кафедры внутренних болезней стоматологического факультета, ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Министерства здравоохранения Российской Федерации.
Контактная информация: jaf@mail.ru;
194100, г. Санкт-Петербург, Литовская ул., 2.
ORCID: https://orcid.org/0000-0002-2436-3813

Olga V. Khlynova — Dr. Sci. (Med.), Professor, Corresponding Member of the Russian Academy of Sciences, Head of the Department of Hospital Therapy and Cardiology, Perm State Medical University named after Academician E.A. Wagner.
Contact information: olgakhlynova@mail.ru;
614990, Perm, Petropavlovskaya str., 26.
ORCID: https://orcid.org/0000-0003-4860-0112

Yulia V. Tsyganova — Cand. Sci. (Med.), Associate Professor of the Department of Hospital Therapy, Chuvash State University named after I.N. Ulyanov.
Contact information: aj_00001@mail.ru;
428015, Cheboksary, Moskovsky ave., 15.
ORCID: https://orcid.org/0000-0002-8339-9496

Minara Sh. Shamkhalova — Dr. Sci. (Med.), Professor, Head of the Department of Diabetic Kidney Disease and Post-Transplant Rehabilitation, Endocrinology Research Centre.
Contact information: shamkhalova@mail.ru;
117292, Moscow, Dmitriya Ulyanova str., 11.
ORCID: https://orcid.org/0000-0002-3433-0142

Olga O. Sharkhun — Dr. Sci. (Med.), Professor, N.I. Pirogov Russian National Research Medical University.
Contact information: olga_sharkhun@mail.ru;
117997, Moscow, Ostrovityanova str., 1.
ORCID: https://orcid.org/0000-0001-8527-4681

Marina V. Shestakova — Dr. Sci. (Med.), Professor, Academician of the Russian Academy of Sciences, Deputy Director, Endocrinology Research Centre.
Contact information: shestakova.mv@gmail.com;
117292, Moscow, Dmitriya Ulyanova str., 11.
ORCID: https://orcid.org/0000-0002-5057-127X

Хлынова Ольга Витальевна — доктор медицинских наук, профессор, член-корреспондент РАН, заведующая кафедрой госпитальной терапии и кардиологии, ФГБОУ ВО «Пермский государственный медицинский университет им. академика Е.А. Вагнера» Министерства здравоохранения Российской Федерации.
Контактная информация: olgakhlynova@mail.ru;
614990, г. Пермь, ул. Петропавловская, 26.
ORCID: https://orcid.org/0000-0003-4860-0112

Цыганова Юлия Вадимовна — кандидат медицинских наук, доцент кафедры госпитальной терапии, ФГБОУ ВО «Чувашский государственный университет им. И.Н. Ульянова» Министерства здравоохранения Российской Федерации.
Контактная информация: aj_00001@mail.ru;
428015, г. Чебоксары, Московский просп., 15.
ORCID: https://orcid.org/0000-0002-8339-9496

Шамхалова Минара Шамхаловна — доктор медицинских наук, профессор, заведующая отделением диабетической болезни почек и посттрансплантационной реабилитации, ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации.
Контактная информация: shamkhalova@mail.ru;
117292, г. Москва, ул. Дмитрия Ульянова, 11.
ORCID: https://orcid.org/0000-0002-3433-0142

Шархун Ольга Олеговна — доктор медицинских наук, профессор, ФГАОУ ВО «Российский национальный исследовательский медицинский университет им. Н.И. Пирогова» Министерства здравоохранения Российской Федерации.
Контактная информация: olga_sharkhun@mail.ru;
117997, г. Москва, ул. Островитянова, 1.
ORCID: https://orcid.org/0000-0001-8527-4681

Шестакова Марина Владимировна — доктор медицинских наук, профессор, академик РАН, заместитель директора, ФГБУ «Национальный медицинский исследовательский центр эндокринологии» Министерства здравоохранения Российской Федерации.
Контактная информация: shestakova.mv@gmail.com;
117292, г. Москва, ул. Дмитрия Ульянова, 11.
ORCID: https://orcid.org/0000-0002-5057-127X

Authors' contributions

Working group leaders: Ivashkin V.T., Drapkina O.M.
Preparation of questions for discussion, formulation of the provisions of the recommendations, preliminary version of the document, online approval: Maevskaya M.V., Raikhelson K.L., Okovity S.V., Zharkova M.S., Grechishnikova V.R.
Online voting using the Delphi method, discussion and critical assessment of the provisions of the recommendations: all authors equally.
Writing the final version of the document: Maevskaya M.V., Raikhelson K.L., Okovity S.V., Zharkova M.S., Grechishnikova V.R.
Final editing: Maevskaya M.V., Raikhelson K.L., Okovity S.V., Zharkova M.S., Grechishnikova V.R.
Proof checking and approval with authors: Grechishnikova V.R.

Вклад авторов

Руководители рабочей группы: Ивашкин В.Т., Драпкина О.М.
Подготовка вопросов для обсуждения, формулировка положений рекомендаций, предварительного варианта документа, он-лайн согласование: Маевская М.В., Райхельсон К.Л., Оковитый С.В., Жаркова М.С., Гречишникова В.Р.
Он-лайн голосование с применением метода Дельфи, обсуждение и критическая оценка положений рекомендаций: все авторы в равной степени.
Написание финального варианта документа: Маевская М.В., Райхельсон К.Л., Оковитый С.В., Жаркова М.С., Гречишникова В.Р.
Редактирование финального документа: Маевская М.В., Райхельсон К.Л., Оковитый С.В., Жаркова М.С., Гречишникова В.Р.
Проверка и согласование верстки с авторским коллективом: Гречишникова В.Р.

Submitted: 17.09.2024 Accepted: 30.10.2024 Published: 28.02.2025
Поступила: 17.09.2024 Принята: 30.10.2024 Опубликована: 28.02.2025