**Introduction**

The Constitution of the World Health Organization (WHO) defines health as a state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity.1 Understanding health trends is impossible without accurate, timely, and comparable health statistics. Such information is necessary for policymakers to develop appropriate measures, allocate resources, and prioritize relevant activities. Moreover, WHO data is also crucial for monitoring the efforts of member states in achieving the sustainable development goals.2

A healthy lifestyle can proceed in two variations: health development and the reduction of its potential losses. In each of these variations, an individual can identify value focuses, determining the significant conditions for their establishment.3, 4

The condition of the macular area of the retina is crucial in preserving central vision. Leading factors threatening the state of the fovea centralis include blood supply deficiencies, conditions with disrupted retinal layer structures, and the risks of iatrogenic trauma during various interventions in both the anterior and posterior segments of the eye.5, 6 Despite higher macular hole closure rates, functional results do not always satisfy patients, highlighting the medical community's interest in developing and improving macular hole surgery.7, 8

The relevance of this topic is driven by the growing need to improve the quality and accessibility of ophthalmic care, especially in managing conditions such as macular holes, which significantly impact patients' quality of life. Studies show that the quality of life of patients with ophthalmic diseases, including macular holes, can differ significantly from doctors' assessments, emphasizing the importance of direct patient surveys to assess their condition and needs.9 These findings highlight the need to integrate quality-of-life survey tools into clinical practice to optimize treatment and improve the accessibility of ophthalmic care.

Implementing organizational tools to measure and improve the quality of life for patients with macular holes and other ophthalmic diseases is crucial for ensuring a comprehensive approach to treatment and rehabilitation. This approach contributes not only to medical recovery but also to enhancing overall life satisfaction and social adaptation of patients. Hence, the purpose of the study is to explore modern organizational tools to improve the quality and accessibility of ophthalmic care for the population.

**Materials and methods**

Publicly available articles were reviewed using the following databases of scientific publications and specialized search engines: PubMed, Mendeley, Scopus, Web of Science, and eLibrary. Content analysis methods were used to identify key aspects and trends in this field. The information search was conducted using the keywords: age-related macular degeneration, organization of medical care in ophthalmology, detection of age-related macular degeneration at the primary healthcare level, and coverage of anti-angiogenic therapy for patients with age-related macular degeneration. The primary focus was on studies related to macular diseases, patient satisfaction with treatment, and quality of life and its relationship with various therapeutic interventions.

**Results**

In the course of the literature review, 128 publications were selected and analyzed. Inclusion criteria: Articles providing data on clinical trials, reviews, meta-analyses, and cohort studies related to the diagnosis and treatment of macular diseases were included. Exclusion criteria: Articles with low levels of evidence (e.g., expert opinions without empirical support, short reports, and letters) were excluded. As a result of the systematic review, 37 publications met the inclusion criteria.

**Discussion**

The primary goal of treating vitreoretinal pathology is to preserve visual functions, which directly impacts the improvement of the patient's quality of life. Subjective testing of patients with vitreoretinal pathology is particularly relevant in determining the appropriate management strategy. The need for an individualized approach is dictated by the different subjective perceptions patients have of their condition.10-13 The average value of macular pigment optical density can vary significantly as it depends on lifestyle, overall pigment levels in the body, diet, gender, age, and comorbidities such as diabetes, obesity, and hypertension. The level of macular pigment can be used as a diagnostic criterion for many ophthalmic pathologies; therefore, further study of this indicator is necessary.14

Numerous measures periodically taken by the state, including significant financial investments to support birth rates and overcome high mortality rates, are necessary and important. It is essential to emphasize that modern demographic problems cannot be solved solely through financial support for financially underprivileged families; a thoughtful systematic approach is required. Fragmentary measures to improve the demographic situation in the country may provide some temporary positive effect, but unfortunately, they cannot fundamentally change the situation.15

Studies highlight the significant impact of diseases such as macular holes on patients' quality of life, including their physical and emotional well-being, and their ability to perform daily tasks. The importance of using individualized assessment tools, such as customized quality-of-life questionnaires, to evaluate the unique impact of eye diseases on each patient is emphasized.

The results indicate that quality-of-life surveys can serve as important tools for evaluating the effectiveness of therapeutic interventions, especially in the context of new treatment approaches such as anti-VEGF injections for macular holes. Despite the significant impact of ophthalmic diseases on quality of life, there is a lack of awareness and use of specialized quality-of-life assessment tools in clinical practice.

Research underscores the need to educate ophthalmologists and other medical personnel on quality-of-life assessment methods to improve understanding and management of the impact of ophthalmic diseases on patients' lives. The results also point to the necessity of developing and adapting quality-of-life assessment tools specific to various cultural and linguistic groups to ensure the accuracy and applicability of data worldwide.

Overall, the literature review highlights the importance of integrating quality-of-life surveys into ophthalmic practice as a means to evaluate the impact of diseases and therapeutic interventions on patients' lives. It also emphasizes the need for further research and development of specialized assessment tools.

An equally important component is the sociological survey and its significant impact on the demographic situation in the country. This can alter public consciousness related to mentality, culture, psychology, knowledge transmission systems, and behavioral priorities of various social groups.16 In modern conditions, where people increasingly refuse professional medical care for various reasons, the relevance of using sociological health assessment methods, compared to the traditional recording of morbidity based on data from state medical institutions, acquires practical value. Indeed, sociological surveys invariably allow for the consideration of a large array of diseases for which no medical help is sought.17 The need to pay attention to the social prevention of diseases was discussed, emphasizing the need to expand the focus from well-known risk factors (alcohol, smoking, etc.) to a larger number of factors regularly affecting health, including and focusing on the group of patients being examined and their nosology.18 In this regard, it is appropriate to cite foreign researchers who assert that the only available tool for determining patient satisfaction with treatment (UL) for age-related macular degeneration through questionnaires is the MacTSQ (Macular Disease Treatment Satisfaction Questionnaire), created based on the Ret(inal)TSQ.19 Published data on cross-sectional studies conducted in three eye clinics of the UK's National Health Service allowed for quite specific (practical) conclusions regarding the choice and practice of MR treatment.

The budgetary healthcare financing model exists in European countries such as the United Kingdom, Sweden, Denmark, Ireland, and Italy. Its conceptual foundations were laid in the report by English economist W. Beveridge, presented to the UK government in 1942. The main characteristics of this model are: universal coverage of the population with healthcare services, funding from the state budget, parliamentary control, and management by government bodies.21 Health insurance systems in EU countries are mandatory for most citizens. However, in Germany, the Netherlands, and Spain, certain population groups are either not covered by the state system or can opt out of it and use voluntary health insurance (VHI) services. In Germany, VHI applies only to high-income workers.22, 23 The mandatory health insurance (MHI) system did not replace the previously existing budget system but only supplemented it—funds accumulated in the MHI do not exceed 40% of the total state healthcare funding.24

To ensure the consistency of strategy with global experience, guiding principles for reform should be used, and a comprehensive set of prescriptions for specific reforms should be utilized. Selected reforms must be justified in terms of their potential impact on identified causes of inefficiency in each country (autonomously) and correspond to global experience in effective and ineffective healthcare financing methods. Below, we synthesize a strategic measures scheme to address one of the priority tasks: what needs to be changed to eliminate the causes of major problems.25

Healthcare financing includes six components, including national policy and schemes applicable to: sources of financial income, including financing mechanisms through tax collection or insurance contributions ("fund collection"); pooling of funds; procurement of services; political programs in the field of providing benefits, rationing, and rights to receive medical care; management of the listed functions and political programs. Healthcare expenses paid out of pocket can force people to choose between healthcare expenses and other needs.26

Medical organizations have specific features that require the use of special management technologies: the need to improve the communication skills of medical personnel; mastery of SWOT analysis and PEST analysis technologies; mastery of the main approaches of the quality management system; the ability to apply basic financial management tools; collection, management, and distribution of relevant information, and more.27

Kazakhstan, in terms of medical service quality (Health Care Index for Country), calculated by the Numbeo database based on the assessment of the overall quality of healthcare systems, hospital equipment, the professional level of medical personnel, and service costs in clinics, ranked 56th out of 92 countries in 2020. The healthcare system quality index was 60.94. The lowest scores were for components such as satisfaction with the responsiveness (waiting time) in medical organizations (50.75%) and satisfaction with the qualifications and competence of medical personnel (55.24%).28 Here are some of the six problems of primary health care delivery:

- Insufficient access and quality of medical care and services, especially in remote areas, due to staffing shortages, an insufficient number of primary health care facilities, worn-out buildings, and inadequate medical equipment.

- Low internet access in remote rural areas, lack of modern computer equipment.

- High functional workload on the general practitioner’s area.

- Poorly developed digitization of primary health care and limited internet access in rural facilities, limited range of remote medical services.

- Shortage of qualified personnel in multidisciplinary medical rehabilitation groups.

- Lack of a methodological base for providing rehabilitation care.

Focusing on the experience that negatively affected patients' health, it should be noted that the problem of patients' lack of trust during the initial primary healthcare visit (including to specialized ophthalmologists) still persists. Distrust in the doctor is an extremely serious problem, recognized by modern healthcare representatives, as trust plays a key role in doctor-patient relationships: “…the art of healing brings two personalities into contact; it establishes a universal human connection of trust with compassion and creates the psychological interaction between doctor and patient, which constitutes the main essence of medicine.”17 In this regard the results of a single survey on patients' adherence to treatment.29 The survey included a standard validated treatment satisfaction questionnaire for macular diseases (MacTSQ) and author-developed questions aimed at assessing aspects of the proposed anti-angiogenic therapy. A reliable direct correlation was found between treatment satisfaction and high adherence levels, as well as a greater willingness of patients with high adherence to resume therapy and their reduced dependence on outside help. The average survey time was 7 minutes. Despite the elderly age of the patients, they did not experience difficulties understanding and answering the questions. These data underscore the value of interaction between ophthalmologists and patients through monitoring surveys.

Ensuring universal healthcare coverage means that all members of society have equal opportunities to receive the necessary high-quality medical care without facing financial difficulties as a result of paying for medical services at the point of delivery.25, 30-32 In this regard, it is essential to continue strengthening continuity between doctors at primary patient admissions in polyclinics and colleagues in high-tech medical institutions. The key criterion for the quality of ophthalmic (medical) care remains the final (objective) result, which influences the improvement of the patient's quality of life.

From the perspective of assessing self-protective behavior among patients, it is essential to focus on its low level, which is undoubtedly one of the reasons for refusing medical help, i.e., irresponsible attitudes towards personal health and its maintenance.17, 33 This problem dictates the need to expand informational and educational work at the initial stage of outpatient care. For example, the new coronavirus infection — COVID-19, caused by the SARS-CoV-2 virus, along with affecting the respiratory system, can lead to eye diseases. In this regard, the presence of SARS-CoV-2 in tear fluid and conjunctival swabs indicates the need to take measures to prevent the virus from entering through the eye surface and to use protective glasses as a preventive measure against infection. Given the possibility of side effects on the eyes, COVID-19 patients with vision impairment are recommended to undergo an ophthalmologist examination after etiological and pathogenetic therapy.34

Thus, the frequency of both systemic and ophthalmic diseases is increasing worldwide, partly due to the trend of increased life expectancy. Therefore, the possibility of screening, early diagnosis, and monitoring of various body indicators is becoming increasingly significant.36 According to a publication (2023), the therapeutic effects of platelet-rich plasma (PRP) components on the retina in macular hole surgery are described. Accumulating data on the effective use of PRP components will allow for broader application in treating degenerative, infectious, post-traumatic, and other eye structural disorders. Evaluating the quality of PRP based on the content of functionally active platelets will help more effectively use PRP in ophthalmology.37 Such results enhance and broaden intersectoral interaction with Blood Centers in implementing quality ophthalmic care.

Based on the analyzed literature, it is evident that improving patient satisfaction with the treatment of ophthalmic pathologies, especially through the use of surveys, is crucial. This improvement must occur regardless of the healthcare institution level. For medical personnel, it is equally important to conduct and analyze regular monitoring of their knowledge in both theoretical and practical aspects of preventive measures, the application of surgical treatments for macular holes, and the organization of early diagnostics to ensure accessible specialized ophthalmic care. The proven value of interaction between ophthalmologists and patients via monitoring surveys highlights the need for implementing adapted specialized questionnaires for the residents of Kazakhstan. Developing and integrating these tools into the practices of medical institutions will enhance the quality of care.

We found that macular diseases significantly impact various aspects of patients' quality of life. The findings revealed that patient satisfaction with treatment, particularly with anti-angiogenic therapy, plays a crucial role in adherence to treatment protocols. Additionally, early diagnosis and personalized treatment plans are essential for effectively managing macular diseases. The importance of integrating quality-of-life assessments into clinical practice was underscored to optimize therapeutic interventions and improve the accessibility and quality of ophthalmic care.

Studying and implementing organizational tools to assess and improve the quality of life for patients with ophthalmic diseases, such as macular holes, is critically important. This not only improves medical care quality but also provides a deeper understanding of the diseases' impacts on patients' lives. The results emphasize the necessity of a comprehensive approach that includes medical interventions and an assessment of patients' quality of life. This approach requires the active involvement of both medical specialists and patients in the treatment process and in addressing accessibility issues related to ophthalmic care. Developing and adapting tools for measuring quality of life, considering the specifics of ophthalmic diseases and cultural characteristics of patients, is essential. This will enable more accurate and meaningful research, contributing to the improvement of the quality and accessibility of ophthalmic care. Educational programs for medical specialists, aimed at increasing awareness of quality-of-life assessment methods and their integration into clinical practice, are crucial. These programs will enhance communication between doctors and patients and ensure a more holistic approach to treatment.

One of the primary limitations of our study is the reliance on publicly available literature, which may not encompass all relevant studies and data, particularly unpublished or ongoing research. Additionally, the focus on articles published in English and Russian may have excluded significant findings published in other languages. The variability in the methodologies and quality of the reviewed studies could also impact the consistency and generalizability of our conclusions. Furthermore, the study did not include primary data collection, which limits the ability to provide real-time, context-specific insights from the population in Kazakhstan. Future research should aim to include comprehensive, multilingual literature reviews and incorporate primary data collection to address these limitations and provide more robust, localized insights into the quality and accessibility of ophthalmic care.

**Conclusion**

The literature review indicates the need for further research in this area. This includes developing new organizational tools and technologies and studying their impact on improving the accessibility and quality of ophthalmic care. The challenges related to integrating these tools into everyday practice require collaborative efforts from the medical community, researchers, and patients. Addressing these challenges will lead to better management and treatment outcomes for patients with ophthalmic diseases, ultimately enhancing their quality of life.

**Acknowledgements:** none.

**Authors' Contributions.** All authors, D.K., A.A., G.Zh., M.B., A.D., and R.K., participated equally in drafting, study conception and design, revising discussion section of the manuscript. All authors have approved the final version of the article.

**Funding:** no funding was provided. There was no third-party funding or medical representation in the conduct of this work.

**References**

1. World Health Organization (WHO). Constitution of the World Health Organization. Published 2020. Accessed July 11, 2024.Available from: <https://www.who.int/governance/eb/who_constitution_ru.pdf>
2. World Health Organization (WHO). World Health Statistics 2020: Monitoring Health for the SDGs, Sustainable Development Goals. Geneva: World Health Organization; 2020. Accessed July 11, 2024.Available from: <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>
3. Piko BF, Brassai L. A reason to eat healthy: The role of meaning in life in maintaining homeostasis in modern society. Health Psychol Open. 2016 Mar 27;3(1):2055102916634360. doi: 10.1177/2055102916634360.
4. Mohsin KF, Ahsan MN, Haider MZ. Understanding variation in catastrophic health expenditure from socio-ecological aspect: a systematic review. BMC Public Health. 2024 Jun 5;24(1):1504. doi: 10.1186/s12889-024-18579-7.
5. Avetisov SE, Mamikonian VR, Iusef IuN, Iusef SN, et al. [Evaluation of the efficiency of hydromonitoring phacofragmentation versus ultrasound phacoemulsification on the morphometric parameters of the central retinal region]. Vestn Oftalmol. 2008 Jan-Feb;124(1):8-11.
6. Khattab AAA, Ahmed MM, Hammed AH. Pars plana vitrectomy for tractional diabetic macular edema with or without internal limiting membrane peeling. Med Hypothesis Discov Innov Ophthalmol. 2022 Dec 3;11(3):110-118. doi: 10.51329/mehdiophthal1454.
7. Popescu SI, Munteanu M, Patoni C, Musat AMA, et al. Role of the Vitreous in Retinal Pathology: A Narrative Review. Cureus. 2023 Aug 23;15(8):e43990. doi: 10.7759/cureus.43990.
8. Ho TC, Yang CM, Huang JS, Yang CH, et al. Long-term outcome of foveolar internal limiting membrane nonpeeling for myopic traction maculopathy. Retina. 2014 Sep;34(9):1833-40. doi: 10.1097/IAE.0000000000000149.
9. Pérez-Gutiérrez L, Ferrara N. Biology and therapeutic targeting of vascular endothelial growth factor A. Nat Rev Mol Cell Biol. 2023 Nov;24(11):816-834. doi: 10.1038/s41580-023-00631-w.
10. Frennesson C, Nilsson UL, Peebo BB, Nilsson SE. Significant improvements in near vision, reading speed, central visual field and related quality of life after ranibizumab treatment of wet age-related macular degeneration. Acta Ophthalmol. 2010 Jun;88(4):420-5. doi: 10.1111/j.1755-3768.2009.01576.x.
11. Sulavikova ZA, Sustykevicova Z, Kacerik M, Krasnik V. Near vision in patients with DME and RVO treated with aflibercept and correlation with NEI VFQ-25 questionnaire. Int J Retina Vitreous. 2024 May 23;10(1):39. doi: 10.1186/s40942-024-00558-0.
12. Hirneiss C, Schmid-Tannwald C, Kernt M, Kampik A, et al. The NEI VFQ-25 vision-related quality of life and prevalence of eye disease in a working population. Graefes Arch Clin Exp Ophthalmol. 2010 Jan;248(1):85-92. doi: 10.1007/s00417-009-1186-3.
13. Sabeti F, Lane J, Rohan EMF, Essex RW, et al. Relationships between retinal structure and function and vision-related quality of life measures in advanced age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 2021 Dec;259(12):3687-3696. doi: 10.1007/s00417-021-05296-9.
14. Rai BB, Sabeti F, van Kleef JP, Carle CF, et al. Comparing 2-dimensional macular pigment optical density with objective and subjective perimetry and visual acuity in age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol. 2024 Mar 14. doi: 10.1007/s00417-024-06437-6.
15. Wu W, Long S, Cerda AA, Garcia LY, et al. Population ageing and sustainability of healthcare financing in China. Cost Eff Resour Alloc. 2023 Dec 19;21(1):97. doi: 10.1186/s12962-023-00505-0.
16. Santos JV, Padron-Monedero A, Bikbov B, Grad DA, et al. The state of health in the European Union (EU-27) in 2019: a systematic analysis for the Global Burden of Disease study 2019. BMC Public Health. 2024 May 22;24(1):1374. doi: 10.1186/s12889-024-18529-3.
17. Falkovskaya KI, Martynenko AV. [The sociological research methods in practice of medical social work]. Probl Sotsialnoi Gig Zdravookhranenniiai Istor Med. 2020 Mar;28(2):261-265.
18. Waechter R, Gallant C, De Wilde K, Arens G, et al. Prevention of mental illness within public health: An analysis of progress via systematic literature review and a pathway forward. Prev Med Rep. 2023 May 18;34:102249. doi: 10.1016/j.pmedr.2023.102249.
19. Gohil R, Crosby-Nwaobi R, Forbes A, Burton BJ, et al. Treatment satisfaction of patients undergoing ranibizumab therapy for neovascular age-related macular degeneration in a real-life setting. Patient Prefer Adherence. 2016 May 26;10:949-55. doi: 10.2147/PPA.S105536.
20. Cebeci Z, Yilmaz YC, Kir N. Real-life experience of ranibizumab therapy for neovascular age-related macular degeneration from Turkey. Int J Ophthalmol. 2018 Feb 18;11(2):267-273. doi: 10.18240/ijo.2018.02.15.
21. Budarin SS, Elbek YV. [EFFICIENCY OF FUNCTIONING OF HEALTH CARE SYSTEMS AS A SUBJECT OF STATE FINANCIAL CONTROL: A REVIEW OF RUSSIAN AND FOREIGN EXPERIENCE]. Probl Sotsialnoi Gig Zdravookhranenniiai Istor Med. 2022 Dec 15;30(s1):976-982. Russian. doi: 10.32687/0869-866X-2022-30-s1-976-982.
22. Sagan A, Thomson S. Voluntary health insurance in Europe: role and regulation [Internet]. Copenhagen (Denmark): European Observatory on Health Systems and Policies; 2016.
23. Stötzler M, Kaifie A. Healthcare for individuals without health insurance in Germany - a mixed methods approach to assess the situation and current challenges. Int J Equity Health. 2023 Jun 19;22(1):117. doi: 10.1186/s12939-023-01930-6.
24. Popovich L, Potapchik E, Shishkin S, Richardson E, et al. Russian Federation. Health system review. Health Syst Transit. 2011;13(7):1-190, xiii-xiv.
25. World Health Organization (WHO). Developing a national health financing strategy: a reference guide. World Health Organization. ‎2017. Accessed July 11, 2024. Available from: <https://iris.who.int/handle/10665/254757>.
26. World Health Organization (WHO). Primary health care on the road to universal health coverage: 2019 monitoring report. Geneva: World Health Organization. 2019. Accessed July 11, 2024. Available from:<https://www.who.int/healthinfo/universal_health_coverage/report/fp_gmr_2019.pdf?ua=1>.
27. Fulop NJ, Ramsay AIG. How organisations contribute to improving the quality of healthcare. BMJ. 2019 May 2;365:l1773. doi: 10.1136/bmj.l1773.
28. Government of the Republic of Kazakhstan. On the Approval of the Concept of Healthcare Development of the Republic of Kazakhstan until 2026. Resolution of the Government of the Republic of Kazakhstan dated November 24, 2022, No. 945.. Accessed July 11, 2024. Available from: <https://adilet.zan.kz/rus/docs/P2200000945>.
29. Marakis TP, Koutsandrea C, Chatzistefanou KI, Tountas Y. Treatment satisfaction of patients with neovascular age-related macular degeneration treated with anti-vascular endothelial growth factor agents. Int Ophthalmol. 2018 Apr;38(2):565-576. doi: 10.1007/s10792-017-0492-8.
30. Derakhshani N, Rezapour R, Azami-Aghdash S, Nafar H, et al. Factors affecting private sector engagement in achieving universal health coverage: a scoping review. Glob Health Action. 2024 Dec 31;17(1):2375672. doi: 10.1080/16549716.2024.2375672.
31. United Nations. UN General Assembly Resolution in support of universal health coverage [Internet]. 2012. Accessed July 11, 2024. Available from: [http://www.un.org/News/Press/docs//2012/ga11326.doc.htm](http://www.un.org/News/Press/docs/2012/ga11326.doc.htm).
32. Lee BX, Kjaerulf F, Turner S, Cohen L, et al. Transforming Our World: Implementing the 2030 Agenda Through Sustainable Development Goal Indicators. J Public Health Policy. 2016 Sep;37 Suppl 1:13-31. doi: 10.1057/s41271-016-0002-7.
33. Balasooriya NN, Bandara JS, Rohde N. Multigenerational inequalities of opportunity in health outcomes. Int J Equity Health. 2024 Jul 10;23(1):140. doi: 10.1186/s12939-024-02144-0.
34. Cohen Sinai N, Kharouba R, Rabinovitz Y, Igbariye A, et al. [VASCULAR OPHTHALMIC MANIFESTATIONS IN COVID-19 PATIENTS]. Harefuah. 2024 May;163(5):291-294.
35. Krysanov IS, Klabukova DL, Krysanova VS, Ermakova VY. [Pharmacoeconomic analysis of anti-angiogenic drugs for diabetic macular edema]. Vestn Oftalmol. 2024;140(2):112-120. doi: 10.17116/oftalma2024140021112.
36. Kazanskiy NL, Khonina SN, Butt MA. Smart Contact Lenses-A Step towards Non-Invasive Continuous Eye Health Monitoring. Biosensors (Basel). 2023 Oct 18;13(10):933. doi: 10.3390/bios13100933.
37. Hagenau F, Osterode EV, Klaas JE, Vogt D, et al. Long-Term Results of Adjunct Autologous Platelet-Rich Plasma in Lamellar Macular Hole Surgery Showing Lasting Restoration of Foveal Anatomy. Int J Mol Sci. 2023 Feb 27;24(5):4589. doi: 10.3390/ijms24054589.