

GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 6 (339) Июнь 2023

ТБИЛИСИ - NEW YORK



ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press.
Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Tsitsino Abakelia, Ketevan Lashkhi, Sophio Kakhadze. BRIDGING GAP BETWEEN PRE AND POSTOPERATIVE PROSTATE BIOPSIES: PI RADS CORRELATION WITH FINAL HISTOPATHOLOGICAL DATA.....	6-12
Sopio Gvazava, Vladimer Margvelashvili, Nino Chikhladze, Diana Dulf, Corinne Peek-Asa. A RETROSPECTIVE STUDY OF THE MAXILLOFACIAL INJURIES IN TWO EMERGENCY DEPARTMENTS IN TBILISI, GEORGIA.....	13-19
Eraliyeva B.A, Paizova.M.K, Almakhanova A.N, Erkinbekova G.B, Nurgazieva G.Y, Tyndybay S.S. EXPENDITURE ON MEDICINES IN A MULTIDISCIPLINARY HOSPITAL IN ALMATY BASED ON ABC /VEN ANALYSIS.....	20-23
Tchernev G. NITROSOGENESIS OF SKIN CANCER: THE NITROSAMINE CONTAMINATION IN THE CALCIUM CHANNEL BLOCKERS (AMLODIPINE), BETA BLOCKERS (BISOPROLOL), SARTANS (VALSARTAN/LOSARTAN), ACE INHIBITORS (PERINDOPRIL/ ENALAPRIL), TRICYCLIC ANTIDEPRESSANTS (MELITRACEN), SSRIS (PAROXETINE), SNRIS (VENLAFAXINE) AND METFORMIN: THE MOST PROBABLE EXPLANATION FOR THE RISING SKIN CANCER INCIDENCE.....	24-32
Kachanov D.A, Karabanova A.V, Knyazeva M.B, Vedzizheva H.Kh, Makhtamerzaeva H.S, Ulikhanian E.G, Gukoyan A. A, Galdobina V.A, Dimakov D.A, Shakirianova A.V. INFLUENCE OF PROFICIENCY OF SYNTHETIC FOLIC ACID ON THE NEUROLOGICAL SYMPTOMS OF RATS.....	33-36
Zamzam AR. Aziz, Entedhar R. Sarhat, Zaidan J. Zaidan. ESTIMATION OF SERUM FERROPORTIN AND LIVER ENZYMES IN BREAST CANCER PATIENTS.....	37-41
Tereza Azatyan. THE RHOENCEPHALOGRAPHIC STUDY OF THE INTERHEMISPHERIC ASYMMETRY OF CEREBRAL BLOOD FLOW IN HEALTHY AND MENTALLY RETARDED CHILDREN.....	42-46
Ahmed T. Jihad, Entedhar R. Sarhat. ALTERED LEVELS OF ANTI-MULLERIAN HORMONE AND HEPcidIN AS POTENTIAL BIOMARKERS FOR POLYCYSTIC OVARY SYNDROME.....	47-51
L.V. Darbinyan, K.V. Simonyan, L.P. Manukyan, L.E. Hambarzumyan. EFFECTS OF DIMETHYL SULFOXIDE ON HIPPOCAMPAL ACTIVITY IN A ROTENONE-INDUCED RAT MODEL OF PARKINSON'S DISEASE.....	52-56
Labeeb H. Al-Alsadoon, Ghada A. Taqa, Maha T. AL-Saffar. EVALUATION OF PAIN-KILLING ACTION OF ACETYSALICYLIC ACID NANOPARTICLES ON THERMAL NOCICEPTION IN MICE.....	57-61
Olesia Kornus, Anatolii Kornus, Olha Skyba, Iryna Mazhak, Svitlana Budnik. FORECASTING THE POPULATION MORTALITY RATE FROM CARDIOVASCULAR DISEASES AS A CONDITION OF THE ECONOMIC SECURITY OF THE STATE.....	62-66
Saif K. Yahya, Haiman A. Tawfiq, Yasir Saber. STIMULATION OF B3-RECEPTOR-INDUCED CENTRAL NEUROGENIC EDEMA AND VITIATED ELECTROLYTE HOMEOSTASIS IN EXPERIMENTAL RODENT MODEL.....	67-70
M.A. Babakhanyan, V.A. Chavushyan, K.V. Simonyan, L.M. Ghalachyan, L.V.Darbinyan, A.G. Ghukasyan, Sh.S. Zaqaryan, L.E. Hovhannisyan. PRODUCTIVITY AND SELENIUM ENRICHMENT OF STEVIA IN HYDROPONIC AND SOIL CULTIVATION SYSTEMS IN THE ARARAT VALLEY.....	71-76
Ezzuldin Yaseen Aljumaily, Ali R. Al-Khatib. HARDNESS AND ELASTIC MODULUS ASSESSMENT FOR TWO ALIGNER MATERIALS BEFORE AND AFTER THERMOCYCLING: A COMPARATIVE STUDY.....	77-82
Tchernev G. NITROSOGENESIS OF CUTANEOUS MELANOMA: SIMULTANEOUSLY DEVELOPMENT OF PRIMARY CUTANEOUS THICK MELANOMA OF THE BREAST, THIN MELANOMA/ DYSPLASTIC MOLE OF THE BACK DURING PARALLEL INTAKE OF BISOPROLOL, AMLODIPINE AND VALSARTAN/ HCT: NITROSAMINE POLYCONTAMINATION IN THE MULTIMEDICATION AS THE MOST POWERFUL SKIN CANCER TRIGGER.....	83-88
Manish Tyagi, Uzma Noor Shah, Geetika Patel M, Varun Toshniwal, Rakesh AshokraoBhongade, Pravesh Kumar Sharma. THE IMPACT OF SLEEP ON PHYSICAL AND MENTAL HEALTH: IMPORTANCE OF HEALTHY SLEEP HABITS.....	89-94
Musayev S.A, Gurbanov E.F. DYNAMICS OF THE MECHANICAL FUNCTION OF THE LEFT ATRIUM IN PATIENTS WITH ISCHEMIC MITRAL VALVE REGURGITATION.....	95-98

Abrahamovych Orest, Abrahamovych Uliana, Chemes Viktoriia, Tsyhanyk Liliya, Mariia Ferko. INDICATORS OF BONE METABOLISM IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH IMPAIRED BONE MINERAL DENSITY: CHARACTERISTICS, THEIR FEATURES AND DIAGNOSTIC VALUE.....	99-104
Jagdish Kumar Arun, Ashok Kumar Singh, Shashidhar ES, Geetika M. Patel, Yogita Verma, Samir Sapkota. THE ROLE OF IMMUNOTHERAPY IN CANCER TREATMENT: CHECKPOINT INHIBITORS, CAR-T CELLS, AND VACCINES.....	105-112
L.G. Buinov, L.A. Sorokina, S.N. Proshin, N.A. Fedorov, M.N. Magradze, A.B. Shangin, S.V. Alekseev, T.V. Kot, P.A. Torkunov. A METHOD FOR IMPROVING THE PROFESSIONAL PERFORMANCE AND RELIABILITY OF PERSONS DRIVING HIGH-SPEED VEHICLES.....	113-116
Bhupesh Goyal, Sandeep Bishnoi, Suphiya Parveen, Devanshu Patel J, Yasmeen, Anupama Nanasahab Tarekar. MANAGING ARTHRITIS PAIN: MEDICATIONS AND LIFESTYLE CHANGES.....	117-122
Sergienko Ruslan, Vovchenko Anna, Kravchuk Lyudmila, Zinchenko Vitaliy, Ivanovska Olha. ANALYSIS THE RESULTS OF SURGICAL TREATMENT AND EARLY REHABILITATION OF PATIENTS WITH MASSIVE TEARS THE ROTATOR CUFF THE SHOULDER.....	123-128
Gulyaeva K.V, Fokin M.S, Kachanov D.A, Karabanova A.V, Dzhanbekova K.R, Zablotskaya P.Yu, Magomedov Sh. A, Gadzhiev M.B, Alilov A.A, Idiatullin R.M. NEURODEGENERATION AND NMDA.....	129-136
Dilshad Ahmad Usmani, Kavina Ganapathy, Devanshu Patel J, Anchal Saini, Jaya Gupta, Shalini Dixit. THE ROLE OF EXERCISE IN PREVENTING CHRONIC DISEASES: CURRENT EVIDENCE AND RECOMMENDATIONS.....	137-142
Tchernev G. Controversies and paradoxes in melanoma surgery: consolidating two surgical sessions into one and sparing the sentinel lymph node- a possible guarantee of recurrence-free survival.....	143-146

MANAGING ARTHRITIS PAIN: MEDICATIONS AND LIFESTYLE CHANGES

Bhupesh Goyal¹, Sandeep Bishnoi², Suphiya Parveen³, Devanshu Patel J⁴, Yasmeen⁵, Anupama Nanasaheb Tarekar⁶.

¹Professor, Department of Allied Healthcare & Sciences, Vivekananda Global University, Jaipur, India.

²Associate Professor, Department of Orthopaedics, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India.

³Assistant Professor, Department of Genetics, School of Sciences, JAIN (Deemed-to-be University), Karnataka, India.

⁴Associate Professor, Department of Pharmacology, Parul University, PO Limda, Tal. Waghodia, District Vadodara, Gujarat, India.

⁵Tutor, Department of Nursing, IIMT University, Meerut, Uttar Pradesh, India.

⁶Professor, Department of Ayurveda, Sanskriti University, Mathura, Uttar Pradesh, India.

Abstract.

This study aims to characterize and contrast the triennial rates at which doctors prescribe PT, determine patient, doctor, and practicing characteristics related to every therapy suggestion, and assess pain relievers, lifestyle counseling, and PT as effective treatments for knee osteoarthritis (OA). We analyzed the National Ambulatory Medical Care Survey. Nonsteroidal anti-inflammatory drugs (NSAID), narcotics prescriptions, physical therapy referrals, and primary care physician visits for knee OA have been determined and evaluated. The average yearly rate after three years of therapy was determined. Using multivariable logistic modeling with adjustments for complicated sample design, we analyzed the relationships among patient, physician, and practice characteristics and treatments. Over time the patients were prescribed physical therapy to improve their lifestyle whereas the percentage of patients who were prescribed NSAIDs or drugs. Physical therapy, lifestyle therapy, and drugs were prescribed at similar rates across time for basic care doctor visits. There was an association between nonclinical characteristics and treatment suggestions, such as provider type, practice setting, and geographic proximity. Physical therapy (PT) and lifestyle counseling (LC) seem underused in patients with knee OA, but prescriptions for pain medication rose over the studied period. The treatment decisions varied due to variables outside of medicine. Increased usage of physical therapy and lifestyle changes, as well as decreased treatment variance for knee OA, are important areas for further study.

Key words. Arthritis, medications of arthritis, lifestyle changes of arthritis.

Introduction.

The sensation of pain, deformed joints, diminished grasping power, and diminished ability to use one's hands are often cited as signs of a particularly prevalent OA Painful swelling, joint deformity, loss of joint function, and elevated impairment are all possible when rheumatoid arthritis strikes tiny joints. Drug and non-drug therapies, such as joint-protection regimens, aids, and activities, are all part of the conservative therapy of arthritis [1]. The present pandemic of morphine and drug misuse seems primarily due to the tardiness of the discovery of efficient therapies for optimum managing pain, which has trailed beyond fields like irritation reduction, including the oversight of immunology. The latest study has shown that Osteoarthritis accounts for roughly 10% of all prescription drugs made by general practitioners in Australia. Similarly, 12% of occurrence morphine exemptions in a study of Swedish citizens aged 35 years were attributed to OA and possibly its accompanying

comorbidity. Morphine medication prescriptions for OA in the United States were steady between 2007 and 2014, despite the lack of clear evidence for the advantages of analgesics for arthritides and the growing awareness of the hazards [2]. Several joints may be affected by arthritis, which may be either acute or chronic. Musculoskeletal bruising, abnormalities discomfort, and rigidity may be in the diagnostic range. Chronic Diseases such as OA, crystal deposition, such as in Gout and Pseudogout, unusual metabolism, such as in Hemochromatosis, immune-mediated processes. The review summarizes the literature on the connections between arthritic pain, mental anguish, bodily inflammation, and immunity [3]. Patients who satisfy the recovery criteria have an overall incidence of 11.9% for physically severe pain. Patients do not show an increased risk of severe pain due to chronic disease progression. Non-inflammatory mechanisms may now be the primary source of RA discomfort. As well as perhaps being unsuccessful, aggressive therapy can expose patients to the possibility of adverse effects and lead to needless treatment adjustments in those whose pain is not primarily caused by inflammation [4]. Induced inflammatory reactions and suffering in the joint and periarticular tissues can be triggered differently. Mainly neutrophils release anti-inflammatory cytokines and stimulation of distal pathways. Gout arthritic pain and inflammation are both mediated by the inflammasome, which is activated in reaction to uric acid crystals. Currently, colchicine, nonsteroidal anti-inflammatory medications, and corticosteroids are the mainstays of treatment for gout irritation and discomfort [5]. Chronic pain, inflammation, and loss of mobility are symptoms of OA, defined by the gradual degeneration of articular cartilage and changes in the peri-articular bone. No therapy is currently demonstrated to slow or stop the development of joint structural decline in OA patients, nor has it been shown to encourage healing [6].

Related Work.

Reducing risk factors via focused therapies is an important part of optimal therapy for knee osteoarthritis (KOA). The purpose of a review is to catalog all of the risk variables for KOA and to assess how amenable they are to modification by individual, clinical, and public-level action. The osteoarthritis possibility factors and enhancement were used to conduct the searches in PubMed and Scopus. Managing the impact of immediate and persistent risk factors is necessary for this era and obesity-related disorders. Holistically treating a patient with KOA may include dietary changes, weight reduction, occupational rehabilitation, medication management, and bio-mechanical assistance, such as thigh exercises that strengthen muscles [7].

Due to global rises in life expectancy and obesity, the incidence of knee OA has skyrocketed in the past decade. The first line of defense when treating knee OA is education, exercise, and weight reduction. The least risky treatments for KOA outline the frequently utilized evaluation metrics in clinical research studies [8]. Pain reduction enhanced physical performance, and enhanced quality of life are all possible outcomes of physical therapy, exercise, weight loss, and other lifestyle adjustments. Still, not one of them can regenerate damaged articular cartilage. Improved knowledge of osteoarthritis has led to the creation of cutting-edge novel therapies. Intra-articular human serum albumin, conventional disease-modifying anti-rheumatic drugs, metformin, lipid-lowering agents, antagonists of nerve growth factors, bone morphogenetic protein, fibroblast growth factors, Platelet-Rich Plasma, Mesenchymal Stem Cells, exosomes, interleukin-1 blockers, gene-based therapy, and bisphosphamide are all discussed in this narrative review of emerging treatments for osteoarthritis of the knee [9]. Rheumatoid arthritis patients often experience extreme tiredness. It is more strongly associated with pain, mood, personality traits, lack of sleep, obesity, and complications, but only moderately with the activity of diseases. Numerous standard surveys exist to gauge fatigue levels, but a Visual Analogue Scale simplifies things. Most patients report feeling tired, and at least one in six report feeling very tired. Patients with RA often experience substantial tiredness and other symptoms, such as chronic pain and depression. It harms females' ability to do daily tasks and overall quality of life. The best treatments for tiredness go to the root of the problem, such as cognitive behavioral counseling, meditation, and encouragement in a monitored managing one's emotions approach. There is a lack of uniformity in the fitness and behavioral intervention programs. Medications like methotrexate might make you feel tired. Fatigue is a frequent, complicated symptom, and for some individuals, it may be the most severe symptom they experience [10]. One to two percent of the human race aged 20 to 50 suffers from rheumatoid arthritis, a debilitating illness of the joints. In both the global South and the global North, RA is the leading cause of illness. Inflammation and discomfort in the synovial joints are symptoms of this autoimmune illness. Disease-modifying anti-rheumatic pharmaceuticals including cyclophosphamide, sulfasalazine, methotrexate, as well as nonsteroidal anti-inflammatory drugs and intravenous gold, are among the synthetic medications used to cure RA. These chemicals have harmful effects on the liver and kidneys, as well as hypertension and stomach ulcers. The joint function may be improved, and pain alleviated with a multidisciplinary approach to treating rheumatoid arthritis [11]. Rheumatoid arthritis symptoms include pain, which may be caused by inflammation and non-inflammation processes. Patients with RA treated with an inhibitor had a greater reduction in suffering than those handled with a tumor necrosis measure blocker, according to recent clinical trial results; however, typical clinical indicators and indicators of swelling were unaffected by either treatment [12]. Interventions to increase medication adherence may be easier to develop if major drivers of adherence can be isolated. The purpose of this research was to evaluate the frequency and determinants of expressed adherence to drugs in patients with rheumatoid arthritis (RA)

throughout a 12-month follow-up period. The Conformance Assessment for Rheumatology assessed patients' self-reported medication adherence at baseline, six months, and 12 months. The association among commitment and possible variables was studied using mixed-effects modeling [13]. To determine medication adherence across rheumatoid arthritis patients was related to disease coping mechanisms, demographics, medical variables, and Approaches. Patients with RA were recruited from an outpatient rheumatology clinic in Vienna for this cross-sectional investigation. The Medication Adherence Assessment was used to analyze medication compliance. The Assessment for Coping with Illness evaluated patients' coping methods. Multivariate regression models, however, found no statistically significant relationship between coping methods and persistence [14]. Outcomes for children with juvenile idiopathic arthritis (JIA) have been greatly enhanced because of advances in early detection and therapy with conventional and biological disease-modifying anti-rheumatic medications. The majority of kids with JIA nowadays have clinically inactive illnesses or remission. Important concerns have emerged from this accomplishment, including whether it is safe to quit drugs and how to weigh the advantages of maintaining medication against the danger of a flare if treatment is suddenly discontinued [15]. Osteoarthritis (OA) is a degenerative joint condition that mostly damages the cartilage and results in pain, stiffness, and decreased mobility. Although there is no known treatment for OA, managing symptoms frequently includes a mix of prescription drugs and dietary adjustments. It's crucial to speak with a healthcare expert for individualized guidance and to go through the best drugs and lifestyle modifications for your particular circumstance.

Materials and methods.

The frequency of KOA has roughly doubled in the last several decades, making it a significant cause of disability and health care burden in the United States. The rising prevalence of knee arthroplasties, in particular, has led to a dramatic increase in both immediate and subsequent expenditures associated with KOA. Numerous medical groups have issued scientific-proof healthcare recommendations to standardize treatment and improve knee osteoarthritis management. The methods are helpful; most individuals with KOA may use them without risk.

Datasets.

The information in the National Ambulatory Medical Care Survey (NAMCS) database was analyzed for several years of data. Direct-patient-care doctors not employed by the federal government are the focus of the nationwide Ambulatory Medical Care study, a nationwide statistical sample study. Each year, the National Center for Health Statistics at the Centers for Disease Control and Prevention investigates to collect data on how often people in the United States use outpatient medical services. Demographic auditors visit the office of a chosen group of doctors once every week for an entire month to gather data on patient visits. Patients' demographic data and see features, the primary evidence for a visit, the physician's diagnosis, and diagnostic/therapeutic services ordered/provided during the visit are collected using a standardized survey form. The NAMCS office visit serves as the primary sampling mechanism. The central sampling units (PSUs) are selected at the first step

of the NAMCS's multistage probability sampling scheme. Each PSU comprises a county or cluster of counties, towns, or cities stratified according to socioeconomic and demographic factors and then randomly chosen. Stage two of the sampling process entails selecting individual doctors from each PSU. These doctors are then divided up into their respective specialties. The final step in the sample process involves choosing which patients to interview at the participating doctors' offices. The first stage entailed stratifying the doctors according to their specialty, while the second stage utilized random selection. Every time the NAMCS is carried out, a new structured data collection is compiled. The data sets, dictionary, and accompanying documentation are freely accessible via the Centers for Disease Control and Prevention.

Methods for Identifying groups and Selecting Measures.

Through the use of the International Classification of Diseases, Ninth Revision codes, health files of patients who were diagnosed with knee OA are located. We next determined if the doctor prescribed painkillers, PT, or offered advice on exercise and weight loss. Lexicon Plus, used by the NAMCS, classifies medications according to therapeutic class and active components. Salicylates, nonsteroidal anti-inflammatory drugs, narcotic analgesics, and others were the categories used to describe pain treatments. Patient demographics were collected, including age, sex, race/ethnicity, insurance status, primary diagnosis, co-morbidities, and the nature of the visit (e.g., acute, chronic, surgical, or preventive). Additional information gleaned from the records comprised the type of medical professional who treated the patient (e.g., an orthopedist, general physician, or other medical specialist), the patient's primary care physician (PCP) status, and whether or not the patient was treated by an advanced practice provider. The detailed comparison is represented in Table 1.

Table 1. Knee osteoarthritis patient visits: demographics broken down by specialist treatment preferences.

Factors	Behavior (%)	Drugs (%)	Generalized average (%)	PT (%)
Primary motivation for attending				
Surgical	4.7	13	10.3	19.4
Precautionary	4.2	3.2	3.8	4.3
Absent	3.4	4.4	2.5	0.9
Hypersensitivity	13	12.3	18.7	11.8
Recurring	77	70	65.3	65
Sub-Division of Medicine				
Clinic for Communities	9.3	14.2	12.6	4.7
Other	37	22.5	18.9	18.3
Practice of Internal Medicine	18	12.7	8.1	16
Orthopedic surgeon	37	51	60.8	61.3

Quantitative research.

Prescriptions for NSAIDs, referrals to physical therapy, and lifestyle recommendations have been developed as potential

outcomes. To improve the accuracy of the estimations, we computed the triennial prevalence rates of PT referrals, lifestyle advice, and pharmaceutical orders throughout the intervals. We assessed triennial rates for orthopedic surgeons and primary care specialists individually since the treatment of KOA might vary depending on the practitioner. Patient gender, age, racial or ethnic background, coverage status, and the leading cause for appointment were all considered during the incidence estimates to allow for anticipated shifts in these demographics as time passed, in addition to the complicated sample methodology. Corrected triennial levels of prevalence were calculated using edge statements; predict queries were used to assess for linear patterns across time. Every dependent variable physician referral to PT, diet guidance, NSAID, and the opioid prescription was the subject of its logistic regression study. The doctors' specialties were used to divide the regression models even more. Clinical features, patient profiles, doctor features, clinic features, and physical location were all considered distinct factors across all models. We also double-checked that no statistical presumptions would be broken by conducting the regression analysis beforehand.

When doing evaluations, we used the NAMCS-recommended weighting schemes and estimate methodologies. Each dependent variable physician referral to PT, lifestyle counseling, NSAID prescription, and opioid prescription was the subject of its logistic regression analysis. The doctors' specialties were used to divide the regression models even more. Clinical features, patient demographics, physician characteristics, practice characteristics, and geographic location were independent variables across models.

We also double-checked that no statistical hypotheses would be broken by conducting the regression analysis beforehand.

For each analysis, we used the NAMCS-recommended weighting schemes and estimate processes.

Results.

The expected results of this research are that those participating in the intervention would be better able to work with their medical professionals to develop a personalized medical strategy, include their values in decision-making about their assistance, and boost their autonomy. The findings, which revealed significant enhancements in the standard of treatment patients measured by the OAQI, partly validated our theory. Notably, we saw a dramatic increase in the quality of advice given for conservative alternatives, including self-management, lifestyle, and physical exercise, in addition to weight loss. These advances in traditional care understanding could assist in filling the void left by conventional medical practice, which focuses on painkillers and surgery as the initial lines of defense. In addition, the rise in these results may have resulted from participants' increased self-assurance in conservative areas that did not need the involvement of a medical professional. This research offers a number of results from individuals with hip and/or knee OA who used the publicly accessible Web-based tool My Joint Pain during a 12-month period. The goal of My Joint Pain was to provide as a free clearinghouse for materials supporting self-management and evidence-based knowledge. The website seeks to enhance and empower well-informed

treatment decision making in the medical environment. As a result, the objective of this study was to assess the effectiveness of care and self-management among My Joint Pain users who had hip or knee OA.

Prescription drugs, lifestyle changes, and physiotherapy prescription tendencies.

It shows the evolving patterns in the frequency with which doctors prescribe NSAIDs, opioids, and physical therapy (PT). Orthopedic surgeons' referrals to physical therapists (PTs) have dropped dramatically during the last three years. The triennial rates of lifestyle advice by orthopedic experts also went down. On the other hand, prescriptions for narcotics and nonsteroidal anti-inflammatory drugs (NSAIDs) rise dramatically every three years represented in Fig 1A.

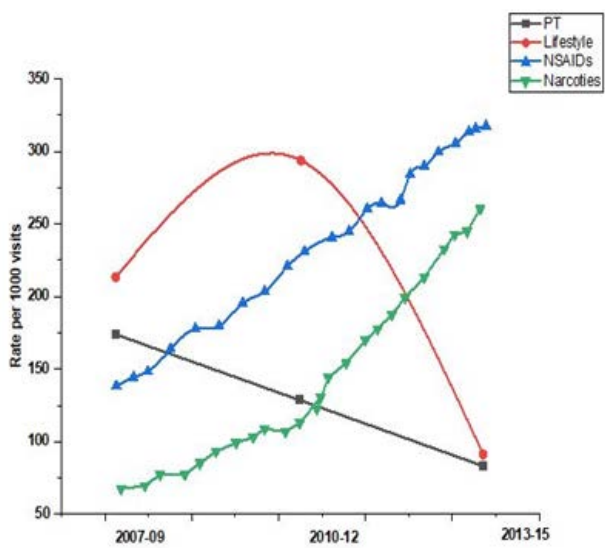


Figure 1A. Triennially modified rates of therapy for patients diagnosed with arthritis in medical centers and orthopedic clinics.

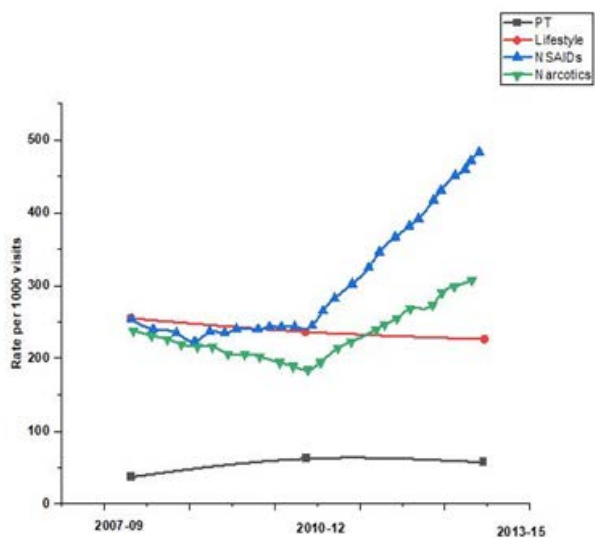


Figure 1B. Orthopedist consultations for arthritis, and the reported therapies received.

Primary care physicians' referral rates for physical therapy were low and stable for three years. Lifestyle counseling

by PCPs was more common during the last three years than physical therapy referrals, but the difference was not statistically significant. Figure 1B represents that whereas the triennial rate of narcotic prescriptions has not changed much, the rate of NSAID prescriptions has increased significantly.

Influence Survey on the Appraisal of Wellness

There was no correlation between musculoskeletal doctors' suggestions for therapy and patients' demographics is depicted in table 2. It's important to note that Hispanic people have a higher rate of receiving prescriptions for pain relievers and opioids. Recommendations for physical therapy are more frequent among People of color who are not African descent. In terms of clinical features, surgically-related visits were associated with increased referrals for physical therapy (PT) and decreased prescriptions for nonsteroidal anti-inflammatory drugs. Medications for NSAIDs were also less common during preventative visits. In terms of the type of doctor and practice, patients who saw advanced practice doctors were more inclined to be prescribed nonsteroidal anti-inflammatory drugs and opioids. Physical therapy recommendations and lifestyle counseling were less common during consultations with remote orthopedic doctors.

Table 2. Treatment options for knee osteoarthritis while seeing an arthritis specialist: interactions among patient, doctor, and organization characteristics.

	Lifestyle	NSAIDs	Narcotics	PT
Manifestations in the Medicine				
Radiograph	1.42	1.32	0.82	1.24
Other imaging (CT/MRI)	1.77	0.92	1.79	1.60
Opioids by prescription	1.11	NA	NA	1.69
Prescribed NSAIDs	1.43	NA	NA	1.24
persistent	0.85	0.91	1.39	0.76
Surgical	0.87	0.50	3.13	4.60
Visit type				
Reference	1.01	1.01	1.01	1.01
Preventative	3.03	0.05	2	0.59
Absence	1.21	0.26	0.19	0.79
PT referral	-	1.05	1.48	NA
Provided lifestyle counselling	NA	1.37	1.02	NA

Influence Survey on the Assessment of Wellness

The heiQ demonstrated substantial gains from the beginning to subsequent assessments across the intervention category in all areas studied, except emotional distress, constructive attitudes and methods, and wellness system mobility. A considerable worsening in mental health was detected in the non-users during the 12 months, even though there was barely any variation in starting mean ratings between the two groups is depicted in Table 3. Additionally, treatment category summary change ratings were obtained. There were negligible changes in core treatments between the intervention group and nonusers but none that were statistically significant.

Table 3. 12-month monitoring and baseline for each dimension of the Health Evaluation Impact Questionnaire.

heiQ	Users Baseline score, mean	Mean difference	P	Nonusers Baseline score, mean	Mean difference	P
Distressed feelings	2.59	0.09	.17	2.61	0.17	.009
Acquiring Knowledge and Competence	2.70	0.19	.002	2.80	0.08	.27
Assistance and socialization	2.67	0.11	.007	2.65	0.09	.26
Medical care navigation	2.85	0.10	.08	2.99	0.10	.08
Physical exercise for health	2.79	0.14	.03	2.94	0.03	.75
Encouragement and participation	2.98	0.12	.04	3.11	0.05	.45
Independent and observant	3.07	0.11	.02	3.13	0.08	.20
mental and behavioral methods	3.00	0.09	.13	3.07	0.04	.59

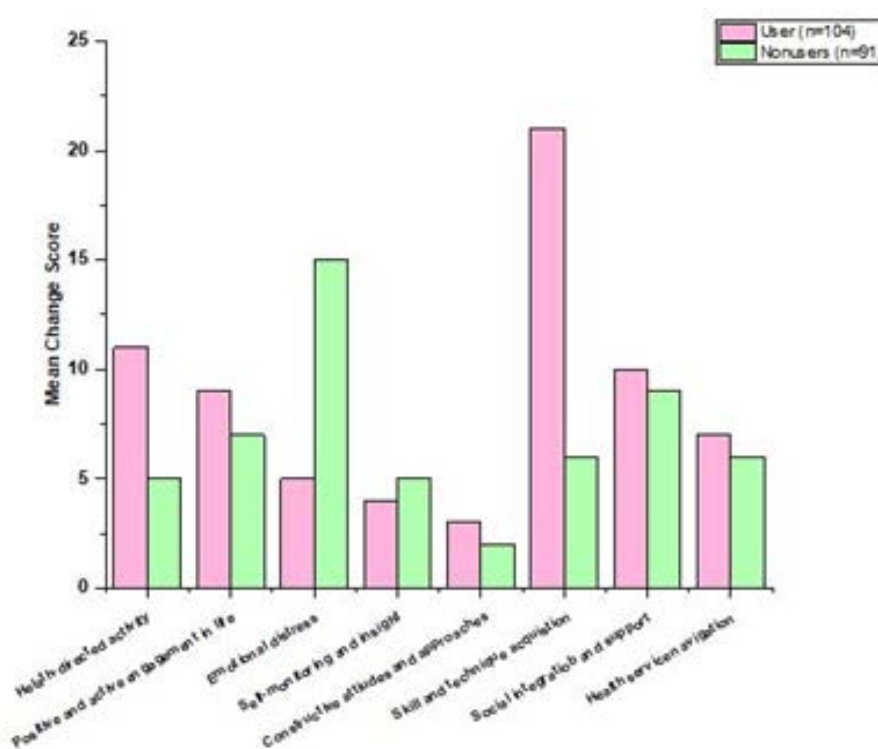


Figure 2. 12-month monitoring and baseline for each dimension of the Health Evaluation Impact Questionnaire.

Despite there wasn't a significantly different in improvement ratings comparing the treatment and nonuser groups, there was an apparent upward trend in all categories, excluding medical facility routing is represented in Figure 2. The average modifications were determined by subtracting every group's monitoring value from their initial value. A rising percentage of alteration signified progress. Unpaired t-tests were utilized to compare the evolution of every category to itself, yielding the corresponding P values. With an exemption of inquiries designed to gauge levels of mental anguish, all of the evaluation's queries were phrased in the affirmative.

Predictive Variables for PCP therapy suggestions

PCP suggestions for therapy did not correlate with the demographics of patients. African American ethnicity and female were two characteristics that came close to statistically significant in predicting increased risk of obtaining drugs.

Prescriptions for NSAIDs became less common among sessions paid for by workers' compensation. Prescriptions for drugs were more common during office visits, including computerized tomography or magnetic resonance imaging. A greater frequency of prescribing NSAIDs was connected with visits supervised by a patient's primary healthcare provider. In contrast, a more negligible probability of lifestyle counseling was associated with consultations in a research center. The patient's symptoms and complaints may help determine if PCP treatment is necessary. Variables like pain, weariness, cognitive decline, respiratory problems, or other particular symptoms might be taken into account. The recommendation for PCP therapy may be guided by determining the patient's risk factors for certain illnesses. For instance, it could be wise to think about PCP medication as a prophylactic strategy if the patient has a family history of cancer, diabetes, or cardiovascular disease.

Discussion.

This research summarizes the rates at which doctors suggest physical therapy, lifestyle counseling, NSAID medication, and opioid therapy for knee OA. The results of this study reveal that patients with knee OA had a poor likelihood of receiving the recommended nonpharmacologic, nonsurgical treatments, such as physical therapy, exercise, or weight reduction. On the other hand, there was a 30-50% rise in the number of prescriptions written for NSAIDs and a 10-15% increase for opioids. Since more people are becoming aware of the risks associated with long-term drug use and since standards of care for knee OA either have ambiguous suggestions for opioid painkillers, providing them only with caution and, in particular instances, the rise in drug prescriptions seems counterintuitive.

Because most clinical practice recommendations recommend physical therapy and lifestyle advice as first-line treatments for knee OA, the recent decline in its utilization is unexpected. Our findings are consistent with those from other studies on OA, which have shown rising rates of opioid prescriptions and decreasing rates of lifestyle or PT therapies in hospitals and clinics. Current data highlights the need for more research to understand why compliance with guidelines based on evidence is poor and to identify approaches that effectively encourage pattern-informed treatment.

The aging of the population and the rise in the number of persons with chronic illnesses are leading to an increased reliance on an already overburdened healthcare system. This pressure on the A need for self-management techniques and resources for patients with OA is highlighted by the health care system's shortcomings and the medical context's inadequate attention to OA. Since programs for self-management are unsuccessful and current clinical intervention for OA is inadequate, it's critical to find alternative self-management tools.

Conclusion.

The expected results of this research are that those participating in the intervention would be better able to work with their medical professionals to develop a personalized treatment strategy, include their values in decision-making about their assistance, and boost their autonomy. The findings, which revealed significant enhancements in the standard of treatment patients measured by the OAQI, partly validated our hypothesis. Notably, we saw a dramatic increase in the quality of advice given for conservative alternatives, including self-management, lifestyle, and physical exercise, as well as weight loss. These advances in traditional care understanding may help fill the void left by conventional medical practice, which focuses on painkillers and surgery as the initial lines of defense. In addition, the rise in these results may have resulted from participants' increased self-assurance in conservative areas that did not need the involvement of a medical professional.

The medical sector's strain, a growing elderly population, and rising penetration all provide fertile ground for the growth of online healthcare services. Users of My Joint Pain reported gains in various areas of care quality, and this information may guide future development to remedy deficiencies in the site's structure

and communication. The online resource should be continually reconsidered to ensure it continues to suit the demands of the OA community. Further studies should be conducted to assess its efficacy in these areas.

REFERENCES

1. Bobos P, Nazari G, Szekeres M, et al. The effectiveness of joint-protection programs on pain, hand function, and grip strength levels in patients with hand arthritis: a systematic review and meta-analysis. *Journal of Hand Therapy*. 2019;32:194-211.
2. Hong JI, Park IY, Kim HA. Understanding the molecular mechanisms underlying the pathogenesis of arthritis pain using animal models. *International Journal of Molecular Sciences*. 2020;21:533.
3. Harth M, Nielson WR. Pain and affective distress in arthritis: relationship to immunity and inflammation. *Expert review of clinical immunology*. 2019;15:541-552.
4. Simon LS, Taylor PC, Choy EH, et al. The Jak/STAT pathway: A focus on pain in rheumatoid arthritis. In *Seminars in arthritis and rheumatism*. 2021;51:278-284.
5. Yin C, Liu B, Wang P, et al. Eucalyptol alleviates inflammation and pain responses in a mouse model of gout arthritis. *British Journal of Pharmacology*. 2020;177:2042-2057.
6. Zhao G, Ren R, Wei X, et al. Thermoresponsive polymeric dexamethasone prodrug for arthritis pain. *Journal of Controlled Release*. 2021;339:484-497.
7. Georgiev T, Angelov AK. Modifiable risk factors in knee osteoarthritis: treatment implications. *Rheumatology international*. 2019;39:1145-1157.
8. Pope JE. Management of fatigue in rheumatoid arthritis. *RMD open*. 2020;6:p.e001084.
9. Chehade L, Jaafar ZA, El Masri D, et al. Lifestyle modification in rheumatoid arthritis: dietary and physical activity recommendations based on evidence. *Current rheumatology reviews*. 2019;15:209-214.
10. Akram M, Daniyal M, Sultana S, et al. Traditional and modern management strategies for rheumatoid arthritis. *Clinica Chimica Acta*. 2021;512:142-155.
11. Cao Y, Fan D, Yin Y. Pain mechanism in rheumatoid arthritis: from cytokines to central sensitization. *Mediators of Inflammation*. 2020.
12. Dantas LO, de Fátima Salvini T, McAlindon TE. Knee osteoarthritis: key treatments and implications for physical therapy. *Brazilian journal of physical therapy*. 2021;25:135-146.
13. Charlesworth J, Fitzpatrick J, Perera N.K.P, et al. Osteoarthritis-a systematic review of long-term safety implications for osteoarthritis of the knee. *BMC musculoskeletal disorders*. 2019;20:1-12.
14. De Luca K, Wong A, Eklund A, et al. Multisite joint pain in older Australian women is associated with poorer psychosocial health and greater medication use. *Chiropractic & Manual Therapies*. 2019;27:1-9.
15. Aeschlimann FA, Chong SL, Lyons TW, et al. Risk of serious infections associated with biologic agents in juvenile idiopathic arthritis: a systematic review and meta-analyses. *The Journal of Pediatrics*. 2019;204:162-171.