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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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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 ბაზებში.

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 საყურადღებო!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ 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, შემავჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების 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.

Babry I. Oren, Marina I. Devdariani, Gela V. Beselia, Nino N. Sikharulidze, Manana G. Dashniani, Maia A. Burjanadze, Ia R. Kvachakidze, Marina I. Nebieridze, Lena Sh. Davlianidze, Lali M. Gumberidze, Nodar P. Mitagvaria. ROLE OF ANTIOXIDANT FOLIUM EXPOSURE ON OXIDATIVE STRESS IN A VALPROIC ACID-INDUCED ANIMAL MODEL OF AUTISM.....	6-15
Hajdi Gorica, Pavlo Djamandi, Gentian Vyshka. DELAYED ONSET OF MYASTHENIA GRAVIS FOLLOWING COLECTOMY FOR ULCERATIVE COLITIS: A CASE STUDY.....	16-17
Zhadyra Yersariyeva, Bagdad Suleyeva, Botagoz Turdaliyeva, Yeldos Tussipbayev. HEMOSTASIS GENE POLYMORPHISM IN RETINAL VASCULAR OCCLUSION: A SYSTEMATIC REVIEW.....	18-28
Ilia Nakashidze, Nameera Parveen Shaikh, Shota Nakashidze, Aleena Parveen Shaikh, Sarfraz Ahmad, Irina Nakashidze. EVALUATION OF TNF- α LEVELS IN MALE PATIENTS WITH STROKE: PROGNOSTIC IMPLICATIONS.....	29-32
Yerbolat Iztileuov, Marat Iztileuov, Altynbek Dushmanov, Gulmira Iztileuova. PREVENTION IN THE PARENTAL GENERATION OF EXPOSED RATS: CONSEQUENCES OF TOXIC EXPOSURE TO CHROMIUM AND GAMMA IRRADIATION IN AN EXPERIMENTAL MODEL.....	33-45
Rashid Nassar, Nadine Khayyat, Michele Halasa, Fahad Hussain. TRAUMATIC ANTERIOR SHOULDER INSTABILITY (TUBS): A NARRATIVE REVIEW OF CURRENT LITERATURE.....	46-50
Albadawi Abdelbagi Talha, Mawaheip A. Abdo Jeweser, Abubakr Ali Elamin Mohamed Ahmed, Abdelrahman Eldaw Mohammed, Elhadi Abdalla Ahmed, GadAllah Modawe, Sanaa Elfatih Hussein. THE HBV AND HCV SEROPREVALENCE AMONG BLOOD DONORS IN AI-DAMAZIN STATE, SUDAN: A THREE-YEAR RETROSPECTIVE STUDY.....	51-54
Hiba Salah Hasan, Teeb Ali, Kadhim Adnan Ali, Al Hassan Ali, Hany A. Al-hussaniy. MODELING DRUG-ORGAN INTERACTIONS AND OPTIMIZING IMMUNOTHERAPY: A QUANTITATIVE SYSTEMS PHARMACOLOGY AND ODRONEXTAMAB DYNAMICS.....	55-60
Zilola Mavlyanova, Davron Ravshanov, Malika Ibragimova, Lola Irbutaeva, Khalimova Fariza, May K. Ismail, Shawgi A. Elsiddig, Marwan Ismail, Salma E R Mohamed, Sara Mohammed Ali. PROGNOSTIC SIGNIFICANCE OF PROLIFERATION (KI-67) AND ANGIOGENESIS (CD34) MARKERS IN MENINGIOMAS FOR THE DEVELOPMENT OF REHABILITATION STRATEGIES.....	61-65
A.R. Abzaliyeva, K.K. Kurakbayev, A.R. Ryskulova, Z.R. Abzaliyev, E. Tasmagambet, D.Zh. Saussanova. TURNOVER INTENTIONS AMONG PHYSICIANS AND NURSES IN KAZAKHSTAN DURING THE COVID-19 PANDEMIC: A CROSS-SECTIONAL STUDY OF PSYCHOLOGICAL AND PROFESSIONAL CHALLENGES.....	66-72
A.A. Mammadov, A.N. Mustafayev, A.H. Aliyev. RADIOLOGICAL IMAGING METHODS FOR ACCURATE DIAGNOSIS OF ABDOMINAL POSTOPERATIVE COMPLICATIONS.....	73-76
I.A. Lebedev, E.V. Zakharchuk, Yu.V. Boldyreva, I.A. Aptekar, E.I. Malinina. OSSIFICATION OF THE POSTERIOR LONGITUDINAL LIGAMENT: A CASE REPORT AND LITERATURE REVIEW.....	77-79
Zhanar Balmukhamedova, Gulmira Derbissalina, Aliya Dzholdasbekova, Dariga Blyalova, Luiza Murzakhalova. SPECKLE-TRACKING ECHOCARDIOGRAPHY FOR EARLY DETECTION OF SUBCLINICAL SYSTOLIC DYSFUNCTION IN PERIMENOPAUSAL WOMEN WITHOUT APPARENT DIASTOLIC DYSFUNCTION.....	80-86
Arkam Thabit Al Neama, Musab Mohammed Khalaf, Ahmed A.J. Mahmood. PATTERNS OF ACETYLCHOLINESTERASE AND BUTYRYLCHOLINESTERASE ACTIVITY IN COMMON CARDIOVASCULAR PHENOTYPES.....	87-94
Argjira Veseli, Shefqet Mrasori, Ivana Čuković-Bagić, Lul Raka, Kaltrina Veseli, Enis Veseli. PARENTAL QUALITY OF LIFE WHEN RAISING CHILDREN WITH AUTISM SPECTRUM DISORDER: A NARRATIVE REVIEW.....	95-100
Anas Ali Alhur, Daliya T. Sendi, Miad M. AlZahrani, Layla T. Abusharha, Rahaf Y. Abudaak, Rahmah Alsinan, Rama R. Alharbi, Lamia Almadhi, Laila M. Alotaibi, Mona A. Hadadi, Shaima H. Alattas, Fatimah Almisbah, Fathi Almisbah, Abdulrahman Alrashed, Kawkab Alharbi. EVALUATING THE TRUSTWORTHINESS OF CHATGPT-GENERATED HEALTH INFORMATION AMONG FUTURE HEALTH CARE PROFESSIONALS.....	101-106
Ting-Ting Wang, Yan Wang. HUMANISTIC CARE NURSING FOR PATIENTS IN THE OPERATING ROOM DURING THE PERIOPERATIVE PERIOD: FULL-CYCLE CARE FROM PHYSIOLOGY TO PSYCHOLOGY.....	107-109
Zauresh Barmanasheva, Mariya Laktionova, Anna Onglas, Ayaulym Kossetova, Ivan Melnikov. PREVALENCE AND RISK FACTORS OF UTERINE FIBROIDS IN WOMEN OF REPRODUCTIVE AGE: A FACILITY-BASED STUDY IN AMEGACITY.....	110-120
Bolat Ashirov, Assel Kassymova, Jamilya Mansurova, Andrey Orekhov, Meiramgul Tokbulatova, Mirgul Kapakova, Zhanar Toktarova, Aisulu Zhunuspekova. PROGNOSTIC MARKERS OF ISCHEMIC AND HEMORRHAGIC COMPLICATIONS IN PATIENTS WITH ATRIAL FIBRILLATION AFTER PERCUTANEOUS CORONARY INTERVENTION.....	121-128

Khalilov Sh. Dzh. ELECTROCARDIOGRAPHY CHARACTERISTICS OF THE PATIENTS WITH NON-ST-ELEVATION MYOCARDIAL INFARCTION (NS TEMI).....	129-132
Salome Kordzaia, Elene Dolmazashvili, Khatuna Tsiklauri, Lasha Khmaladze, Nana Chikhladze. FROM INFUSION REACTION TO IMMUNE CASCADE: A CASE OF SEQUENTIAL TAXANE AND CAPECITABINE TOXICITIES IN TRIPLE-NEGATIVE BREAST CANCER.....	133-136
Yu Zhu, Fandong Zeng, Weiwei Chang, Liying Wen, Lijun Zhu, Yuelong Jin. AN EMPIRICAL STUDY ON THE ASSOCIATION BETWEEN ASPIRATION INDEX AND ACADEMIC PERFORMANCE AMONG PREVENTIVE MEDICINE STUDENTS.....	137-142
Alaa O Ahmed, Mubarak S Karsany, Mohamed Elfatih Abdelwadoud, Mutaz Ali, Osama Mohamed, Amged Gaffer Mostafa, Hussam Ali Osman, Elryah I Ali, Elyasa Elfaki, Tagwa Yousif Elsayed Yousif, Ayman H. Alfeel, Mohammed Ibrahim Saeed. MOLECULAR DETECTION OF HIGH RISK HUMAN PAPILLOMA VIRUS SUBTYPES IN CERVICAL SMEARS AMONG SUDANESE WOMEN.....	143-149
Tchernev G, Tchernev KG Jr, Krastev DS, Krastev NS, Kordeva S. DERMATOLOGIC SURGERY ROUNDS: RECONSTRUCTIVE SURGERY EMPLOYING THE SHARK ISLAND FLAP FOR BASAL CELL CARCINOMA AFFECTING THE NASAL ALA.....	150-153
Saltanat Imanalieva, Bayan Sagindykova, Rabiga Anarbayaeva, Murat Omirali, Gulnara Ospanova, Murat Ashirov. CURRENT STATUS AND PROSPECTS FOR THE DEVELOPMENT OF PEDIATRIC DOSAGE FORMS BY THE EXAMPLE OF COMBINED MELOXICAM AND VITAMIN B12 TABLETS.....	154-167
Ahmed Miri Saadoon. INCIDENCE OF PRESSURE SORE IN THE INTENSIVE CARE UNIT AT AL-DIWANYIA TEACHING HOSPITAL.....	168-171
Isoyan A.S, Danielyan M.H, Antonyan I.V, Azizyan N.H, Mkrtchyan A.A, Karapetyan K.V, Nebogova K.A. MORPHOHISTOCHEMICAL ANALYSIS OF CORTICAL STRUCTURES IN AN EXPERIMENTAL MODEL OF PROLONGED COMPRESSION SYNDROME OF THE HIND LIMB IN RATS.....	172-179
Abdulaziz Alroshodi, Faisal A. Al-Harbi, Rasil Sulaiman Alayed, Fahad M. Alharbi, Khalid A Alkhalifah, Mayadah Assaf Alawajji, Ibrahim S. Alsabhawi. FACTORS IMPACTING HEMODIALYSIS TREATMENT ADHERENCE IN END-STAGE RENAL DISEASE PATIENTS RECEIVING IN- CENTER HEMODIALYSIS IN QASSIM REGION.....	180-187
Gulshat Alimkhanova, Marat Syzdykbayev, Rinat Ashzhanov, Kulsara Rustemova, Maksut Kazymov, Rustem Kazangapov, Asem Kazangapova, Saule Imangazinova, Yernar Kairkhanov, Bazar Tuleuov, Sanzhar Khalelov, Roman Khripunov, Samatbek Abdrakhmanov, Abay Mijatov. THE TRANSVERSUS ABDOMINIS PLANE BLOCK AS A METHOD OF MULTIMODAL OPIOID-SPARING POSTOPERATIVE ANALGESIA: A NARRATIVE REVIEW.....	188-194
Zhengmei Fang, Xiaoling Ran, Lijun Zhu, Yingshui Yao, Yuelong Jin. THE IMPACT OF BMAL1 GENE POLYMORPHISM ON SLEEP QUALITY IN HEALTHY CHINESE YOUTH: A GENDER-SPECIFIC ANALYSIS.....	195-201
Muwafaq H. Zaya, Ahmed A. J. Mahmood, Musab M. Khalaf. CROSS SECTIONAL EVIDENCE FOR OPPOSING EFFECTS OF HYPERGLYCAEMIA AND HYPERLIPIDAEMIA ON CHOLINESTERASE ACTIVITIES.....	202-210
Erleta Muçaj, Erëza Durmishi, Serbeze Kabashi Muçaj, Leart Kuçi, Elza Muçaj, Gerta Durmishi. CHALLENGES IN RADIOLOGICAL DIAGNOSIS: CRANIOPHARYNGIOMA VS ASTROCYTOMA.....	211-214
Uday Mahajan, Imran Khan, Ria Gupta, Meraj Akhtar, Vibhore Gupta, Edward Spurrier, Mohamed Kabary, Adnan Asif, Salman Shoukat Ali Parpia. NAMING CONVENTIONS FOR UNIDENTIFIED PATIENTS IN EMERGENCY AND TRAUMA SETTINGS: A NARRATIVE REVIEW.....	215-218
Xuexue Li, Wenjie Wen, Dandan Ren. MOLECULAR MECHANISMS OF DIABETIC PERIODONTITIS: IDENTIFICATION OF KEY OXIDATIVE STRESS-RELATED GENES AND POTENTIAL THERAPEUTIC ROLE OF METFORMIN THROUGH MMP14 AND PXDN.....	219-231
Davron Ravshanov, Zilola Mavlyanova, Kholmirezayev Bakhtiyor, Malika Tursunovna, Khalimova Fariza. HISTOPATHOLOGICAL PREDICTORS AND FUNCTIONAL RECOVERY IN PATIENTS WITH INTRACRANIAL MENINGIOMAS.....	232-240
Aymuhambetov Y, Khismetova Z A, Iskakova N, Akhmetova K, Serikova-Esengeldina D, Shalgumbayeva G.M. ASSESSMENT OF QUALITY OF LIFE IN BREAST CANCER PATIENTS BY USING EORTC QLQ-C30 QUESTIONNAIRE IN EAST KAZAKHSTAN REGION.....	241-248
Yujing Tao, Long Hua, Liu Zhang, Ying Feng, Liying Wen, Weiwei Chang. THE CORRELATION BETWEEN STRESS, ACADEMIC PERFORMANCE, AND SLEEP DISTURBANCES AMONG HIGH SCHOOL STUDENTS IN ANHUI PROVINCE: A CROSS-SECTIONAL STUDY.....	249-257
Fahad AlAmr, Muhannad Essa S. Alghamdi, Ahmed Saeed A. Alghamdi, Osama Khamis A. Alghamdi, Hassan Mahfouz B. Alghamdi, Osama Mesfer S. Alghamdi, Abdullah Ali A. Almimoni, Abdulmalik Ahmed S. Al-Zahrani. PREVALENCE AND ASSOCIATED RISK FACTORS OF NOCTURNAL ENURESIS AMONG CHILDREN AGED 5-18 YEARS IN ALBAHA REGION, SAUDI ARABIA.....	258-263

Aya Saad Aldewachi, Mohammed I Aladul. APPETITIVE TRAITS AND QUALITY OF LIFE IN WOMEN WITH OBESITY USING GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS: INSIGHTS FROM A PCOS-ENRICHED SAMPLE.....	264-269
George Shaburishvili, Nikoloz Shaburishvili, Georg Becker, Solomon Zeikidze, Bacho Tsiklauri. INCIDENCE OF ADVERSE EVENTS RESULTING FROM BETA-BLOCKER TITRATION IN PATIENTS WITH HEART FAILURE.....	270-279
Blushinova A.N, Orazalina A.S, Shalgumbayeva G.M. INDUCED ABORTION IN KAZAKHSTAN: WOMEN'S PERCEPTIONS AND EXPERIENCES BASED ON CROSS-SECTIONAL STUDY.....	280-288
Qunru Hu, Liying Wen, Jingqi Zhang, Weiwei Chang, Yuelong Jin, Anshi Wang, Lijun Zhu. IS CORE SELF-EVALUATION A PROTECTIVE FACTOR FOR COLLEGE STUDENTS' MARITAL ATTITUDES? THE MODERATING ROLE OF PSYCHOLOGICAL STATUS.....	289-294
Gulfariza Gani, Ubaidilla Datkhayev, Kairat Zhakipbekov, Serzhan Mombekov, Murat Ashirov, Nurgali Rakhymbayev, Zhanerke Seitova. STUDY OF THE CHEMICAL COMPOSITION AND ANTIMICROBIAL ACTIVITY OF SUBCRITICAL CO ₂ EXTRACT FROM <i>EUPHORBIA HUMIFUSA</i> WILLD.....	295-302
Maysoon Mohammed Hassan, Mohammed Abdulwahab Ati Al-askeri, Naseer Kadhim Jawad. PROGNOSTIC IMPACT OF EGFR2 AND KI-67 OVEREXPRESSION WITH DOWNREGULATION OF <i>miR-17</i> AND <i>miR-1307</i> IN FEMALE BREAST CANCER PATIENTS.....	303-313
Imzharov Talgat Abatovich, Zhakiev Bazylbek Sagidolievich, Sarkulov Marat Nukinovich, Pavlov Valentin Nikolaevich, Kurmangaliev Oleg Maratovich. THE EFFECTIVENESS OF METAPHYLAXIS OF NEPHROLITHIASIS DURING PERCUTANEOUS NEPHROLITHOTRIPSY: A SYSTEMATIC REVIEW AND META-ANALYSIS.....	314-322
Yan Wang, Ting-Ting Wang, Chang-Sheng He. PROGRESS IN T-CELL IMMUNE RESEARCH ON HYPERLIPIDEMIC PANCREATITIS.....	323-326
Marwan I Abdullah. MINING THE CELLMINER DATABASE TO IDENTIFY SHARED BIOMARKERS OF 5-FU AND OXALIPLATIN RESPONSE.....	327-341
Shyngys Adilgazyuly, Tolkyun Bulegenov, Akmaral Mussakhanova, Tasbolat Adylkhanov, Kanat Abdilov, Zhannur Altybayeva, Gulmira Bazarova, Malike Kudaibergenova, Makpal Alchimbayeva, Aigul Utegenova, Gulnara Otepova. ASSESSING THE INFLUENCE OF MEDICAL EDUCATION REFORMS ON ONCOLOGIST WORKFORCE AND LUNG CANCER MORTALITY IN KAZAKH-STAN: AN INTERRUPTED TIME SERIES ANALYSIS WITH PREDICTIVE MODELING OF NATIONWIDE DATA FROM 1998 TO 2023.....	342-351
Wen-Wen Liu, Zhi-Juan Xu, Fang Xu. NEW INSIGHTS INTO THE PATHOGENESIS AND TREATMENT ADVANCES OF AGE - RELATED MACULAR DEGENERATION.....	352-354
Zhamilya Zholdybay, Zhanar Zhakenova, Madina Gabdullina, Yevgeniya Filippenko, Suria Yessentayeva, Galymzhan Alisherov, Aigerim Mustapaeva, Jandos Amankulov, Ildar Fakhradiyev. ⁶⁸ GA-FAPI PET/CT IN DIAGNOSIS OF THE BREAST CANCER DEPENDING ON THE MOLECULAR SUBTYPES AND EXPRESSION STATUS OF HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 (HER2/NEU).....	355-363
A.I. Rybin, V.E. Maksymovskiy, O.V. Kuznetsova, V.V. Osyk, A.S. Bohdan. THE RESULTS OF LIFE QUALITY ASSESSMENT IN PATIENTS WITH PRIMARY OVARIAN CANCER DURING TREATMENT: EFFECT OF DIFFERENT TACTICS AND HIPEC.....	364-368
Miranda Sejdiu Abazi, Arbër Prokshaj, Shpëtim Prokshaj, Fitim Alidema, Nora Leci, Linda Abazi Morina. ASSESSMENT OF PRACTICAL PERFORMANCE IN ORTHODONTIC CLASP FABRICATION AMONG DENTAL TECHNICIAN STUDENTS AT UBT: A REAL-TIME ANALYSIS OF WORKING TIME AND PERCEIVED STRESS.....	369-377
Abylay Baimakhanov, Ainash Oshibayeva, Temirkhan Kozhakhmetov, Nazarbek Omarov, Dinara Akhmetzhanova, Berikuly Duman. RESULTS OF MEDICAL CARE FOR PERSONS WITH POLYTRAUMA IN ALMATY AND CORRECTION OF THE ORGANIZATIONAL APPROACH.....	378-382
Khatia Mikeladze, Nino Chikadze, Nino Gachechiladze, Marina Tediashvili, Irina Datikashvili-David, Peter Lydyard, Nina Porakishvili. SERUM IL-6, IL-12, AND IL-10 LEVELS IN EARLY-STAGE, UNTREATED CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS: INSIGHTS FROM GEORGIA.....	383-387
Musayeva H.H. FREQUENCY OF COMPLICATIONS IN PATIENTS WITH ADENTIA (BASED ON ARCHIVAL DATA).....	388-393
Hong-Xia Wang, Xiao-Xia Hou, Jie Xu. NURSING RESEARCH ON EMERGENCY GASTROSCOPIC TREATMENT OF UPPER GASTROINTESTINAL FOREIGN BODIES.....	394-396
Tolegenova Z.Zh, Tokanova Sh.E, Baibussinova A.Zh, Kalikhanova K, Iskakova A.M, Shalgumbayeva G.M. ASSESSMENT OF INFECTIOUS DISEASE RISK FACTORS, INCLUDING COVID-19, AMONG HEALTHCARE WORKERS IN EAST KAZAKHSTAN REGION.....	397-405

Bassam A. Al- jabery, Majid R. Al-bahrani.

ENVIRONMENTALLY SAFE CsPbBr₃/MXene/MWCNTs HYBRID NANOCOMPOSITES: OPTOELECTRONIC AND STRUCTURAL CHARACTERISTICS FOR POSSIBLE BIOMEDICAL AND HEALTH APPLICATIONS.....406-414

Hasan AlAidarous.

PIGMENTED VILLONODULAR SYNOVITIS IN THE ANKLE OF A PEDIATRIC PATIENT: A CASE REPORT.....415-419

Kuat Zhussupov, Nazarbek Omarov, Sagit Imangazinov, Saule Imangazinova, Yernar Kairkhanov, Olga Tashtemirova, Rustem Kazangapov, Aldiyar Masalov, Darkhan Otkenov.

ENDOSCOPIC INJECTION HEMOSTASIS AND LOCAL TREATMENT OF GASTRODUODENAL BLEEDING. LITERATURE REVIEW AND OWN DEVELOPMENTS.....420-424

THE IMPACT OF BMAL1 GENE POLYMORPHISM ON SLEEP QUALITY IN HEALTHY CHINESE YOUTH: A GENDER-SPECIFIC ANALYSIS

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Abstract.

Objective: Epidemiological studies suggest that brain and muscle Arnt-like protein-1 (*BMAL1*) gene may impact sleep quality. However, research on this relationship among Chinese youth is limited. This study aimed to explore the relationship between *BMAL1* gene polymorphism and sleep quality among Chinese youth.

Methods: We employed a cross-sectional design to genotype four single-nucleotide polymorphisms (SNPs) in the *BMAL1* gene using peripheral blood samples from 2715 college students. Questionnaires were used to collect demographic information about the participants, and sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). Logistic regression was employed for association analysis, considering interactions between genes and the environment.

Results: Overall, no significant correlation was found between *BMAL1* polymorphism and sleep quality. However, quantitative trait analysis showed higher sleep latency scores in rs9633835 AA and AG genotype carriers, in the PSQI. Gender stratification analysis linked rs7107287 to sleep quality, particularly in men (OR 0.747, 95% CI, 0.5740-0.973, P=0.030, dominant model). Among men, rs7107287 AA mutant homozygous carriers had higher sleep efficiency and daytime dysfunction scores, while among women; rs9633835 AG heterozygous carriers had higher sleep latency scores. Further interaction analyses showed that sleep quality was significantly influenced by the multiplicative interaction between rs7107287 and physical exercise in men, whereas it was significantly influenced by the multiplicative interaction between rs7107287 and mental condition in women.

Conclusions: These findings suggest an association between *BMAL1* gene polymorphisms and sleep quality in Chinese youth, with notable gender differences. Moreover, sleep quality appears to be affected by multiple interactions between genes and the environment.

Key words. BMAL1, sleep quality, gender difference, youth, interactions, PSQI.

Introduction.

Sleep is an important physiological requirement for the human body and is essential for maintaining both physical and mental health [1]. In recent years, the pace of life has accelerated, accompanied by an increased reliance on technological products. This has exacerbated issues related to sleep quality disorders, and research indicates that one-fifth of the global population currently suffers from insomnia [2]. A survey conducted among 17,335 individuals worldwide showed some concerning trends. For example, the sleep duration among young people gradually decreases as they age. Interestingly, young people in Asia have the shortest average daily sleep duration globally, clocking in at just 6.5 hours [3]. These data demonstrate the severity of sleep disorders among the younger population.

Research shows that poor sleep quality is generally the result of a combination of factors, such as genetic predisposition, exercise, dietary habits, environmental factors, lifestyle habits, etc [4,5]. A strong link between genetic predispositions and sleep quality has been increasingly reported. Single nucleotide mutations in *ADRB1* and *DEC2* have been found in individuals known as “short sleepers,” who can function well even if they sleep 4–6 hours a night. Interestingly, the sleep quality

in these individuals is influenced by genetic mutations rather than the sleep duration [6]. Studies exploring heritability have confirmed that variations in circadian rhythm genes are involved in many physiological and metabolic processes, including the sleep-wake cycle [7]. Recent genome-wide association studies (GWAS) further support these findings. Three large-scale GWAS studies involving individuals of European ancestry have found that circadian rhythm genes like *Period2* and *Period3* are associated with genetic susceptibility to sleep quality [8-10].

The transcriptional translation feedback loop (TTFL) is the foundation of daily circadian rhythms. The basic elements of TTFL are *CLOCK*, brain and muscle Arnt-like protein-1 (*BMAL1*), *Period* (*PER1*, *PER2*, and *PER3*), and *Cryptochrome* (*CRY1* and *CRY2*). *CLOCK* and *BMAL1* form heterodimeric transcription factors that regularly activate the expression of *PER* and *CRY* genes [11]. Several studies have revealed a close relationship between variations in rhythmic gene loci and sleep quality. For example, in a Spanish study of 102 adults, sleep duration showed association with rs238666 in *PER3* and rs4580704 in *CLOCK* but did not with *BMAL1* single nucleotide polymorphisms (SNPs) [12]. Sakurada et al. [13] investigated SNPs in circadian regulation genes in Japanese individuals over 40 years of age. This study identified *CRY1*-rs11113179, *BMAL1*-rs1026071, and *BMAL1*-rs1562438 as risk factors for inherited sleep disorders, with polymorphisms in the *CRY1* and *BMAL1* genes linked to sleep-onset issues. In a U.S. community-based study, rs3816358 in *BMAL1* was associated with later sleep and wake onset time [14]. Additionally, evidence from a Chinese heritability study suggested that the *CLOCK* rs11932595 polymorphism correlates with sleep latency and sleep disturbance scores [15]. These findings suggest an association between rhythm gene polymorphisms and sleep quality. However, understanding of the relationship between *BMAL1* and sleep quality in the Chinese population remains limited. Furthermore, age, nationality, and regional factors, have been identified [16], as positive predictors of sleep status, suggesting these environmental factors may have an impact on genetics. In light of these evidences, our study aimed to evaluate the relationship between *BMAL1* mutations, sleep quality, and related components in young Chinese individuals.

Materials and Methods.

Participants: This study adopted a cross-sectional design and recruited 3450 freshmen for routine physical examinations in 2018; detailed information was reported in a previous study [17]. The inclusion criteria for this study were as follows: willingness to participate in this study; completion of the Pittsburgh Sleep Quality Index (PSQI), including each component, and verification that no logical errors were present in the data; blood samples collected successfully; and successful DNA genotyping. Ultimately, 2715 participants were included in the study.

This study was approved by the Ethics Committee of Wannan Medical College, Yijishan Hospital and informed consent was obtained from all participants.

Blood sample collection:

At approximately 7 am on the day of the physical examination, 5 ml of fasting peripheral venous blood was collected from the participants and stored in EDTA anticoagulant tubes for DNA extraction. Other blood biochemical indicators such as blood lipids, uric acid, blood

cells, and liver and kidney indicators were measured by the daily physical examination centre.

Anthropometric measurements:

After blood sample collection, the anthropometric indices of the participants were measured by trained and qualified medical personnel. The indices measured included height, weight, waist circumference, hip circumference, and blood pressure, in two sitting positions with a 5-min interval according to standard measurement methods [17].

Questionnaire:

The questionnaire was completed under the guidance of the research team members on the day of the physical examination. The questionnaire included questions related to general demographic information, lifestyle habits, such as smoking and drinking, dietary habits, exercise habits, medical history, and medication history. Physical exercise was defined as continuous physical activity lasting more than 30 min per day, accompanied by substantial sweating and a significant increase in heart rate or breathing.

Pittsburgh Sleep Quality Index (PSQI) score:

Sleep quality was evaluated using the PSQI. This scale was developed by Buysse et al. [18] in 1989 and subsequently translated into Chinese by Liu et al. [19], who also tested its reliability and validity. The study found that the internal consistency coefficient of the PSQI was 0.842 and the test-retest reliability was 0.809, indicating that the PSQI is suitable for sleep quality evaluation research in China. The PSQI consists of seven components: subjective sleep quality, sleep latency, effective sleep time, sleep efficiency, sleep disorders, hypnotic drug use, and daytime dysfunction. Each component is scored from 0 to 3 points, with a total score of 21 points. A score greater than 7 points indicates poor sleep quality, whereas a score less than or equal to 7 points indicates normal sleep quality [20].

Genotyping:

DNA was extracted from the peripheral blood of participants using the protein precipitation method and the concentration and purity were measured using an ultra trace spectrophotometer K5800 (Kaiao Beijing China) to determine the quality of the sample. The *BMAL1* polymorphism was detected using the qPCR-TaqMan MGB probe array method. DNA amplification was performed using a QuantStudio 7 Flex Real-Time PCR System (Applied Biosystems, city, state, USA). The qPCR reaction conditions were 50°C for 2 min, 95°C for 10 min, 95°C for 15 s and 60°C for 1 min with 40 cycles. The SNPs sequences of the amplification primers and probes are listed in Supplementary Table 1.

Statistical analysis:

SPSS version 26.0 (Company name, city, state, country) was used for data organisation and analysis. Continuous variables that follow a normal distribution are presented as mean \pm standard deviation (SD) and t-tests and one-way analyses of variance (ANOVAs) were used to compare intergroup differences, categorical variables are presented as frequency and composition ratio, and chi square (χ^2) tests were used to compare intergroup distribution differences. Logistic regression was performed to evaluate the association between *BMAL1* gene polymorphisms and sleep quality and the multiplicative interaction between the environment and genes. All analyses were adjusted for age, smoking, drinking, physical exercise, and mental health. Statistical significance was defined as a two-tailed *P* value of <0.05 .

Results.

Characteristics of the participants between normal sleep quality and poor sleep quality:

The characteristics of the participants according to sleep quality component data are presented in Table 1. Considering a PSQI score

of 7 as the threshold, 1703 (62.7%) participants in this study had normal sleep quality, while 1012 (37.3%) participants had poor sleep quality. No statistically significant differences were detected in age, BMI, gender, and distribution frequency between the normal and poor sleep quality groups ($P > 0.05$). In contrast, no physical exercise, poor mental condition, smoking, and drinking distribution frequency and the scores of the seven components in the poor sleep quality group were higher than those in the normal sleep quality group ($P < 0.05$).

Associations between the *BMAL1* gene polymorphisms and sleep quality:

The genotypic frequency results of the four polymorphisms in the normal and poor sleep quality groups are provided in Table 2. The genotype results of the four SNPs did not show significant differences in frequency between the normal and poor sleep quality groups (all SNPs: $P > 0.05$). In the total population, the genotype frequencies of all four SNPs were consistent with Hardy-Weinberg equilibrium ($P > 0.05$).

The effects of *BMAL1* polymorphism on the seven component scores of the PSQI:

The results showed that the sleep latency scores of carriers of rs9633835 AA and AG genotypes were higher than those of carriers of the GG genotype, with scores of 0.61 ± 0.75 , 0.63 ± 0.74 , and 0.52 ± 0.69 , respectively. The other component scores showed no significant differences among the different genotypes at other SNP sites. The results are summarised in Table 3.

Stratified analysis by gender:

In the subgroup analysis stratified by gender, no difference was found between the *BMAL1* polymorphism and sleep quality in different genetic models in women. In men, the results showed that rs7107287 was associated with sleep quality, and the odds ratio (OR; 95%) of the dominant model was 0.747 (0.574–0.973), $P=0.030$. After adjusting for age, smoking, drinking, physical exercise, and mental condition, the association remained statistically significant, with an OR (95%) of 0.758 (0.578–0.995), $P=0.046$. Detailed data are shown in Table 4.

The effects of *BMAL1* polymorphisms on the seven components scores by gender:

For men, the results indicated that rs7107287 AA mutant homozygous carriers had slightly higher scores in sleep efficiency and daytime dysfunction than GG wild-type homozygous carriers. For women, the results suggested that AG heterozygous carriers had higher scores for sleep latency than GG homozygous carriers. Detailed data are presented in Figure 1.

The interactions between environmental factors and the *BMAL1* rs7107287 polymorphism on sleep quality:

In men, sleep quality was significantly influenced by the multiplicative interaction between rs7107287 and physical exercise, whereas in women, sleep quality was significantly influenced by the multiplicative interaction between rs7107287 and mental health. Table 5 shows the interactive effects.

Discussion.

Epidemiological studies have indicated that sleep quality issues are prevalent among college students, with rates ranging from 70% to 80%, emphasizing the significance of investigating sleep quality as a significant health concern [21,22]. While environmental factors have traditionally been studied as the primary factors influencing sleep quality, there is growing evidence suggesting that genetic factors may also play a role in regulating sleep [23]. Twin studies have shown a high heritability of sleep quality, ranging from 0.3 to 0.5 [24]. Therefore, early identification and intervention for those genetically predisposed

Table 1. Demographic and clinical characteristics of subjects with and without poor sleep quality.

Item	Normal sleep quality(n=1703)	Poor sleep quality(n=1012)	t/ χ^2	P
Age (year)	18.52±0.99	18.45±0.91	1.859	0.063
Gender				
Male, n(%)	668(39.2)	408(40.3)	0.316	0.574
Female, n(%)	1035(60.8)	604(59.7)		
BMI (kg/m ²)	22.29±3.44	22.34±3.63	0.386	0.700
Physical exercise				
No	1149(69.8)	759(77.1)	16.793	<0.001
Yes	498(30.2)	225(22.9)		
Mental condition				
Normal	1691(99.4)	991(98.0)	11.205	0.001
Poor	10(0.6)	20(2.0)		
Smoking				
No	1616(98.1)	949(96.4)	6.479	0.011
Yes	32(1.9)	35(3.6)		
Drinking				
No	1448(87.9)	815(82.8)	12.978	<0.001
Yes	200(12.1)	169(17.2)		
Subjective sleep quality	0.51±0.56	1.23±0.66	29.138	<0.001
Sleep latency	0.38±0.56	0.96±0.84	19.273	<0.001
Effective sleep time	1.45±0.65	2.10±0.46	30.45	<0.001
Sleep efficiency	0.80±1.29	2.31±1.14	31.714	<0.001
Sleep disorders	0.49±0.52	0.91±0.49	21.47	<0.001
Using hypnotic drugs	0.02±0.17	0.05±0.30	2.864	0.004
Daytime dysfunction	1.04±0.81	2.00±0.70	32.753	<0.001

BMI, Body mass index.

Table 2. The association of BMAL1 polymorphism and sleep quality.

SNPs	Normal sleep quality(n=1703)	Poor sleep quality(n=1012)	Genotypic P	HWE P
rs9633835				
AA	498(29.2)	311(30.7)	0.573	0.273
AG	841(49.4)	479(47.3)		
GG	364(21.4)	222(21.9)		
AA vs AG+GG			0.412	
AA+AG vs GG			0.730	
rs6486121				
CC	1188(69.8)	718(70.9)	0.574	0.435
CT	462(27.1)	269(26.6)		
TT	53(3.1)	25(2.5)		
CC vs CT+TT			0.512	
CC + CT vs TT			0.333	
rs7107287				
GG	506(29.7)	307(30.3)	0.153	0.946
GA	866(50.9)	481(47.5)		
AA	331(19.4)	224(22.1)		
GG vs GA+AA			0.732	
GG +GA vs AA			0.092	
rs12364562				
AA	1217(71.5)	715(70.7)	0.444	0.424
AG	436(25.6)	274(27.1)		
GG	50(2.9)	23(2.3)		
AA vs AG+GG			0.652	
AA+AG vs GG			0.382	

HWE: Hardy-Weinberg equilibrium

Table 3. The effects of *BMAL1* polymorphism on the seven components scores of *PSQI*.

SNPs	N	Subjective sleep quality	Sleep latency	Effective sleep time	Sleep efficiency	Sleep disorders	Using hypnotic drugs	Daytime dysfunction
rs9633835	□	□	□	□	□	□	□	□
AA	809	0.78±0.70	0.61±0.75	1.71±0.70	1.37±1.43	0.65±0.55	0.04±0.28	1.38±0.91
AG	1320	0.78±0.71	0.63±0.74	1.69±0.64	1.32±1.44	0.65±0.55	0.03±0.22	1.41±0.90
GG	586	0.76±0.65	0.52±0.69	1.68±0.67	1.43±1.45	0.63±0.55	0.02±0.14	1.4±0.90
<i>F</i>		0.229	4.686	0.365	1.005	0.388	1.163	0.490
<i>P</i>		0.795	0.009	0.695	0.366	0.678	0.313	0.613
rs6486121								
CC	1906	0.78±0.69	0.61±0.74	1.69±0.67	1.34±1.44	0.64±0.56	0.03±0.25	1.41±0.90
CT	731	0.77±0.70	0.58±0.71	1.69±0.66	1.40±1.44	0.65±0.53	0.02±0.17	1.38±0.90
TT	78	0.67±0.62	0.51±0.70	1.63±0.63	1.35±1.45	0.64±0.53	0.03±0.16	1.37±0.91
<i>F</i>		1.087	0.927	0.341	0.406	0.113	0.562	0.198
<i>P</i>		0.337	0.396	0.711	0.667	0.893	0.570	0.820
rs7107287								
GG	813	0.77±0.69	0.60±0.74	1.70±0.64	1.39±1.44	0.65±0.56	0.03±0.23	1.42±0.90
GA	1347	0.76±0.68	0.58±0.71	1.68±0.67	1.32±1.43	0.65±0.55	0.02±0.21	1.38±0.91
AA	555	0.83±0.72	0.64±0.77	1.69±0.69	1.40±1.44	0.64±0.54	0.04±0.26	1.41±0.88
<i>F</i>		1.853	1.248	0.064	0.788	0.047	0.601	0.447
<i>P</i>		0.157	0.287	0.938	0.455	0.954	0.548	0.639
rs12364562								
AA	1932	0.78±0.69	0.59±0.73	1.69±0.65	1.36±1.44	0.65±0.54	0.03±0.23	1.39±0.91
AG	710	0.77±0.70	0.61±0.74	1.69±0.69	1.34±1.43	0.63±0.56	0.03±0.22	1.42±0.90
GG	73	0.75±0.72	0.63±0.81	1.60±0.72	1.40±1.45	0.75±0.57	0.00±0.00	1.38±0.86
<i>F</i>		0.076	0.260	0.641	0.111	1.857	0.617	0.351
<i>P</i>	□	0.927	0.771	0.527	0.895	0.156	0.540	0.704

Table 4. Association analyses of four SNPs in *BMAL1* with sleep quality by gender.

□	□	Normal sleep quality(n=1703)	Poor sleep quality(n=1012)	OR (95%CI)		
				<i>Additive model</i>	<i>Dominant model</i>	<i>Recessive model</i>
Males		668	408			
rs9633835	AA	197(29.5)	135(33.1)	0.968(0.816-1.149) <i>P</i> =0.713	0.846(0.649-1.102) <i>P</i> =0.215	1.119(0.832-1.504) <i>P</i> =0.457
	AG	330(49.4)	179(43.9)			
	GG	141(21.1)	94(23.0)			
rs6486121	CC	456(68.3)	287(70.3)	0.905(0.716-1.144) <i>P</i> =0.406	0.907(0.694-1.185) <i>P</i> =0.474	0.774(0.361-1.661) <i>P</i> =0.511
	CT	191(28.6)	111(27.2)			
	TT	21(3.1)	10(2.5)			
rs7107287	GG	192(28.7)	143(35.0)	0.901(0.756-1.074) <i>P</i> =0.246	0.747(0.574-0.973) <i>P</i>=0.030*	1.077(0.791-1.467) <i>P</i> =0.636
	GA	348(52.1)	182(44.6)			
	AA	128(19.2)	83(20.3)			
rs12364562	AA	485(72.6)	289(70.8)	1.096(0.861-1.394) <i>P</i> =0.458	1.091(0.831-1.434) <i>P</i> =0.53	1.416(0.648-3.091) <i>P</i> =0.383
	AG	169(25.3)	108(26.5)			
	GG	14(2.1)	11(2.7)			
Females		1035	604			
rs9633835	AA	301(29.1)	176(29.1)	0.992(0.860-1.143) <i>P</i> =0.91	0.997(0.800-1.244) <i>P</i> =0.98	0.979(0.766-1.251) <i>P</i> =0.866
	AG	511(49.4)	300(49.7)			
	GG	223(21.5)	128(21.2)			
rs6486121	CC	732(70.7)	431(71.4)	0.956(0.788-1.158) <i>P</i> =0.644	0.970(0.777-1.210) <i>P</i> =0.785	0.798(0.429-1.486) <i>P</i> =0.477
	CT	271(26.2)	158(26.2)			
	TT	32(3.1)	15(2.5)			
rs7107287	GG	314(30.3)	164(27.2)	1.150(0.997-1.327) <i>P</i> =0.055	1.168(0.935-1.460) <i>P</i> =0.171	1.248(0.979-1.592) <i>P</i> =0.074
	GA	518(50.0)	299(49.5)			
	AA	203(19.6)	141(23.3)			
rs12364562	AA	732(70.7)	426(70.5)	0.954(0.788-1.155) <i>P</i> =0.631	1.009(0.810-1.258) <i>P</i> =0.933	0.563(0.290-1.090) <i>P</i> =0.088
	AG	267(25.8)	166(27.5)			
	GG	36(3.5)	12(2.0)			

* Adjustments for age, smoking, drinking, physical exercise, and mental condition, the adjusted OR (95%CI) for the dominant model of rs7107287 in males was OR=0.758(0.578-0.995) with *P*=0.046.

Table 5. The interactions between environmental factors and rs7107287 on sleep quality.

<input type="checkbox"/>	Interaction	Genetic model	OR (95%CI)*	P
Males				
	rs7107287*Physical exercise	Additive model	0.761(0.645-0.899)	0.001
		Dominant model	0.885(0.789-0.992)	0.036
Females				
	rs7107287*Mental health	Additive model	3.216(1.272-8.134)	0.014
<input type="checkbox"/>	<input type="checkbox"/>	Dominant model	4.460(1.531-12.994)	0.006

* Adjustments for age, smoking, drinking, physical exercise, and mental condition

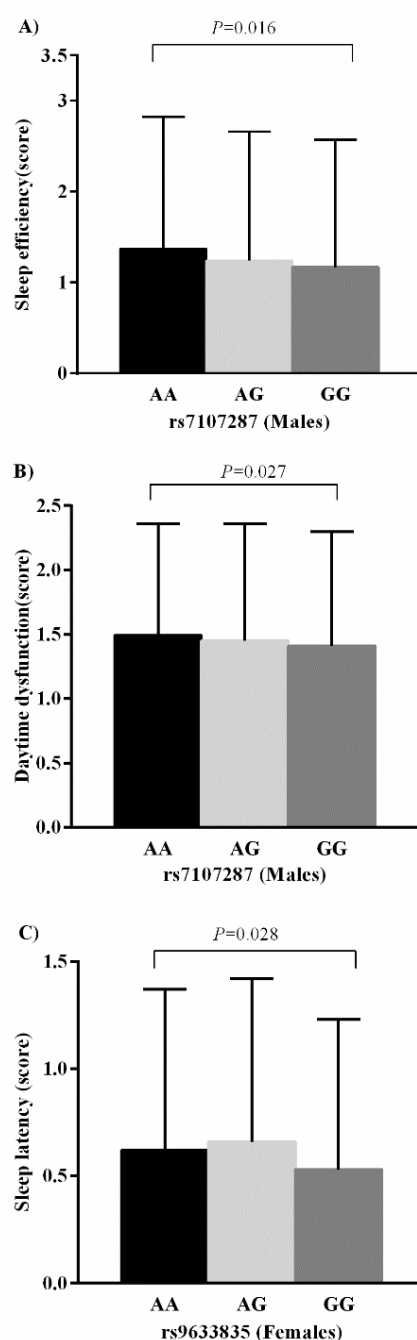


Figure 1. The effects of BMAL1 polymorphism on the components scores of PSQI by gender. A) rs7107287 AA carriers had higher scores in sleep efficiency; B) rs7107287 AA carriers had higher scores in dysfunction; C) rs9633835 AG heterozygous carriers had higher scores in sleep latency. The data was presented in mean with standard deviation (SD).

to sleep disorders are crucial for effectively improving sleep quality and overall quality of life.

In this study, we evaluated the relationship between polymorphisms at four *BMAL1* loci and sleep quality, including its components, among Chinese youth. Our results showed no significant association between *BMAL1* polymorphisms and overall sleep quality. However, rs9633835 was correlated with the sleep latency score of the PSQI component. *BMAL1* is a key gene that regulates circadian rhythms in living organisms. Animal sleep research has revealed that mice with the *BMAL1* gene knocked out display fragmented sleep [25]. Similarly, *BMAL1* gene-knockout cynomolgus monkeys also demonstrate reduced nocturnal sleep and heightened nocturnal activity [26]. In an adult human study, Sakurada et al. [13] reported that variant rs1026071 in *BMAL1* was weakly associated with increased difficulty falling asleep in Japanese individuals aged over 40 years, although the association was no longer significant after Bonferroni correction. Unfortunately, due to prioritising loci with strong linkages to multiple SNPs to gather more data, we did not genotype this locus. In specific populations, such as patients with emotional disorders, the *BMAL1* rs11022778TT and rs1982350AA genotypes are linked to greater difficulty falling asleep [27]. Similarly, in women with breast cancer, genetic variations in *BMAL1* are associated with self-reported deterioration in sleep quality [28]. However, these results were not replicated in the general population aged 18 and above [12]. Positive predictors of sleep status, including age, nationality, and regional factors, have been identified [16], suggesting these environmental factors may have had an impact on genetics, leading to inconsistent findings. In our study, we employed seven dimensions of the PQSI to assess sleep quality, which differs slightly from previous sleep assessment methods. Our results indicate that, among general participants in early adulthood, the relationship between *BMAL1* variation and overall sleep quality is not significant. However, when we analysed the seven components that evaluated sleep quality, we found that carriers of the rs9633835 AA genotype experienced longer sleep latency than those with other genotypes. These findings, along with previous reports, support the hypothesis that *BMAL1* is likely associated with the time it takes to fall asleep.

Previous reports indicate significant differences in the sleep patterns of females and males throughout adolescence and young adulthood [29]. Therefore, we conducted a sex-stratified analysis despite the lack of sex differences in the prevalence of sleep quality. Our results showed that rs7107287 variation is linked to sleep quality in men, while no such association was observed in women. Analysis of the correlation between PQSI component scores and genes uncovered sex-specific differences. Among men, rs7107287 AA was associated with higher sleep efficacy and daytime dysfunction scores, whereas among women, rs9633835 AG genotype was associated with higher sleep latency scores. Research has shown that sex differences in the expression of androgen and oestrogen receptors have direct and indirect effects on the circadian rhythm, thus affecting sleep [30]. Boivin et al. [31] observed that the stages of the menstrual cycle can affect the biological rhythm of body temperature and sleep status, and by controlling the menstrual cycle and using hormonal contraceptives, sleep quality can be improved. Given these sex differences in sex hormones, we hypothesised that sex moderates the relationship between genetic variation and sleep quality.

This study provides new insights into the effects of genetic and environmental interactions on sleep quality. It is likely that physical exercise may moderate sleep quality in males, whereas females are more susceptible to regulation by their mental state in current work. A possible explanation for this interaction is that females are more likely to be trapped by mental problems. In recent years, numerous scientific studies have supported the occurrence of poorer mental health disorders in females compared to males (18.4% vs 8.9%) [32]. In addition, a study involving multiple universities indicated that mental

health symptoms play an important role in predicting poor sleep states among college students [33]. Given these findings, it is plausible that mental conditions influence the impact of genetics on sleep quality in females more than in males. Previous studies have highlighted that regular physical exercise is an effective strategy to improve sleep quality, with participants often experiencing improvements in their sleep disorders through exercise intervention [34]. In our study, the proportion of males engaging in exercise was over three times that of females, potentially leading to more pronounced interactions among males due to larger sample size.

In addition to the valuable information provided on the gender differences in sleep quality among Chinese youth, this study has some limitations. First, owing to the lack of detection of the mRNA expression level of *BMAL1*, it was not possible to analyse whether site variations affected the gene expression level, as they were all located in the non-coding region. Second, the study design was based on a cross-sectional, single-centre approach, meaning the results could not establish a causal relationship between gene polymorphisms and sleep quality. Drawing such conclusions would require further validation and support from additional samples. Finally, although this study suggests an interaction between environmental factors and genes in sleep quality, the specific mode of action remains unclear. Despite these limitations, our study has several strengths. To the best of our knowledge, this is the first study to investigate the relationship between genetic variation in *BMAL1* and sleep quality in a relatively large sample of youths. Moreover, compared with previous studies, our results provide further confirmation of the interaction between environmental factors and genes, as well as the influence of gender on this relationship.

Conclusion.

In summary, the AA genotype of rs7107287 appears to be a risk factor for poor sleep quality in males, and the *BMAL1* polymorphism shows association with the two PQSI component scores. Interestingly, we found a multiplicative interaction between physical exercise and rs7107287 variation in sleep quality in males, whereas in females, the interaction between mental condition and genes was more significant. Our findings underscore the importance of considering genetic factors alongside environmental influences in addressing sleep disorders. More functional research is needed in the future to explore the mechanisms of gene environmental interaction in sleep.

Conflict of interest.

Authors declare that there is no conflict of interest

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