GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 5 (374) Май 2026

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 ВИНИТИ 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 ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

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. Корректура авторам не высылается, 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 compu-ter-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 საყურადღებოდ!

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, 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 შეღებვის 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 ფჩხილებში 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.

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Содержание:

GEORGIAN MEDICAL NEWS
No 5 (374) 2026

HOMOCYSTEINE TESTING IN PREVENTIVE HEALTHCARE: COMPARATIVE INSIGHTS AND POLICY IMPLICATIONS FOR ALBANIA

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Abstract.

Background/Objectives: There is evidence that suggests a mechanistic link between elevated Homocysteine (Hcy) and Insulin Resistance (IR) through cysteine-homocysteinylation of insulin receptors, impairing receptor maturation and signaling. While testing is available in Albania, it is not reimbursed by the national health insurance scheme, creating inequities in access. The objective of this study was to evaluate the potential of Hcy testing as a preventive biomarker for IR and explore its integration into Albania's health insurance system by comparing it to some of inter-national practices. **Methods:** A mixed-methods approach was applied, combining a narrative literature review on the association between Hcy and IR with a comparative policy analysis of testing and reimbursement models in selected European countries (Germany, France, the United Kingdom, Sweden, Greece, and North Macedonia). Data sources included PubMed, Google Scholar, official health insurance documents, WHO country reports, and European Observatory profiles. Clinical thresholds and patient cost estimates were extracted and synthesized. **Results:** In Albania, routine and preventive laboratory panels are covered by insurance, but specialized tests such as Hcy are excluded, with patients paying privately. In comparison, Germany and Greece provide partial reimbursement under restricted indications, France largely classify testing as self-pay, and the UK covers testing for defined diagnostic contexts but not for screening. Costs varied significantly among countries. **Conclusions:** Across Eu-rope, Hcy testing is generally reimbursed only in targeted clinical scenarios rather than for routine screening. Introducing selective reimbursement for high-risk groups in Albania—through a coverage-with-evidence pilot—could enhance preventive strategies against IR, reduce health inequities, and align national practice with European models.

Key words. Homocysteine, insulin resistance, biomarker, preventive testing, health insurance, Albania, diabetes prevention.

Introduction.

Since 2015 Homocysteine testing is available in Albania but still it remains uncovered by the national health insurance scheme [1] and no studies have assessed its feasibility, cost-effectiveness, or integration into preventive health strategies, payers generally do not reimburse routine population screening. This is the common practice across insurers and national policies.

Homocysteine (Hcy) is a non-proteinogenic α-amino acid, structurally analogous to cysteine but distinguished by an extra methylene group in its side chain, with the chemical formula $C_4H_9NO_2S$ [2]. Biosynthetically, Hcy originates from methionine through a multi-step metabolic cycle [3]. Perturbations in Hcy metabolism can lead to hyperhomocysteinemia, which have been implicated in cardiovascular, neuro-degenerative and metabolic disorders [4-6] as well as evidence suggests a link even with Insulin Resistance (IR) [7]. Homocysteine has a plausible mechanistic link to insulin resistance (protein cysteine-homocysteinylation impairs insulin receptor maturation in animal and cellular models) by giving biological plausibility for testing in metabolic risk groups [8,9]. Clinically, homocysteine is currently used mostly for diagnostic/targeted indications (vitamin B12/folate deficiency, thrombosis/homocystinuria, selected high-risk CVD cases);

Insulin resistance is a metabolic condition characterized by impaired insulin-mediated regulation of glucose uptake and utilization in key tis-sues—particularly skeletal muscle, adipose tissue, and the liver—and represents one of the earliest pathological changes underlying a spectrum of disorders, including type 2 diabetes and cardiovascular disease [10]. In obese, hyperinsulinemic subjects, fasting homocysteine levels seems to be significantly elevated and correlated with fasting insulin implying a potential biomarker role [11]. Mechanistic animal and cellular studies have revealed that elevated homocysteine can induce IR via cysteine-homocysteinylation of the insulin receptor, impairing its maturation and down-stream signaling [12]. Hcy is a biomarker measured in blood sample of the patient and can be used to early detect some health condition.

The objective of this study is to evaluate the potential role of homocysteine as an accessible biomarker for the early detection of insulin resistance (IR), with particular attention to its integration into national health insurance schemes. By comparing current reimbursement practices and patient costs across selected European countries (Germany, France, the United Kingdom, Sweden, Greece, and North Macedonia), the study aims to identify best practices and policy models that could inform the Albanian healthcare system.

Materials and Methods.

Study design:

This research employed a mixed-methods approach combining a narrative literature review on the relationship between plasma homocysteine (tHcy) and insulin resistance (IR) and a comparative policy analysis of homocysteine testing practices and reimbursement models across selected European countries.

Literature Search and Selection:

A search of PubMed, and Google Scholar was conducted from inception to April 2025. Search terms included keywords relevant to the respective research: "homocysteine" AND "insulin resistance", "homocysteine" AND "prediabetes", "homocysteine testing" AND "reimbursement", "homocysteine screening" AND "national health systems".

Inclusion criteria: peer-reviewed articles in English reporting original research, re-views, or policy documents on (a) biochemical and clinical associations between tHcy and IR, (b) population-based tHcy screening, and (c) health system reimbursement policies. Exclusion criteria: animal-only studies (unless providing mechanistic in-sight), case reports without population-level relevance, and non-English papers without translation. References were screened by title and abstract, with full-text re-view for eligible articles. Data were extracted on study design, population characteristics, laboratory thresholds, associations with IR, and intervention effects.

Policy Review:

A targeted policy review was conducted by searching the official health ministry, national health insurance, and clinical laboratory association websites for Germany, France, the UK, Sweden, Greece, and North Macedonia.

Countries were selected for comparison based on three criteria: (i) geographic and economic relevance (neighboring Balkan states such as Greece and North Macedonia); (ii) availability of documented reimbursement practices for homocysteine testing (e.g., Germany, France, United Kingdom); and (iii) diversity of health financing models in Europe, allowing for the contrast of self-pay systems with insurance-based models.

Key documents included reimbursement lists, national testing guidelines, and tariff schedules. Supplementary data were collected from WHO Health Systems in Transition (HiT) country reports and the European Observatory on Health Systems and Policies database.

Where official reimbursement tariffs were unavailable, approximate patient costs were derived from publicly accessible private laboratory price lists and institutional laboratory service information. These values were interpreted as illustrative estimates intended to support comparative analysis rather than definitive national reimbursement data.

Comparative model:

Albania and six other countries were compared across three domains:

1. Clinical practice (how homocysteine is used, screening vs. targeted indications),
2. Coverage (is plasma total homocysteine reimbursed, and under what conditions), and
3. Policy context (gatekeeping, referral rules, copayments/ out-of-pocket patterns).

Data sources:

National insurer/gov sites, WHO/European Observatory profiles, and NHS/academic hospital laboratory handbooks (for clinical indications and practical availability).

Data Synthesis:

Findings from the literature review were synthesized narratively, focusing on the clinical validity and potential utility of tHcy as an IR biomarker. Policy data were organized into comparative tables to identify patterns in coverage models. Best practices were selected based on evidence of clinical utility, cost-effectiveness, and feasibility for adaptation in Albania.

Results.

Insurance Coverage of Lab Tests in Albania.

In Albania, the Health Insurance Institute (FDSKSH) covers a wide range of basic diagnostic tests when ordered by a physician, particularly in public facilities at the primary, secondary, and tertiary levels. Since 2015, a national preventive check-up program for adults aged 35–70 has also been in place, offering services such as blood pressure measurement, glucose testing, and lipid profiling at no direct cost to patients. However, coverage remains limited: many laboratory services still require out-of-pocket payments, and highly specialized diagnostics, including advanced metabolic or genetic tests, are generally not reimbursed and must be paid privately [13,14].

Currently, homocysteine measurement is not included among the routine or preventive laboratory services covered by the Health Insurance Institute in Albania. As a result, patients who require the test must pay for it privately, which introduces both financial barriers and inequities in access. Expanding insurance coverage to include homocysteine testing, at least for clearly defined high-risk groups such as individuals with prediabetes, would represent an important step forward in preventive care.

Such an inclusion would not only align Albania with selective European practices but also promote more equitable access to early risk detection and targeted preventive strategies.

International practices.

Across European health systems, homocysteine testing is generally applied in targeted clinical contexts rather than as part of routine screening programs. In the United Kingdom, National Health Service (NHS) laboratories offer homocysteine testing primarily for specific indications such as suspected vitamin B_{12} or folate deficiency, thrombotic disorders, and inherited methylation defects, with coverage determined by clinical need rather than general population screening (Table 2) [15].

In Germany, statutory health insurance (GKV) reimburses the test in patients with established cardiovascular disease or elevated cardiovascular risk, but not for asymptomatic low-risk individuals [16]. In Sweden, testing is available in both public and private laboratories, with reimbursement dependent on indication and regional practice [17]. In France, the national health insurance generally does not reimburse routine testing, which is often paid out-of-pocket by patients, although coverage is provided in rare inherited disorders or specific clinical scenarios [18].

Comparative Policy Model.

Across Western and neighboring systems, homocysteine is rarely reimbursed for general screening; it is used selectively for B-vitamin deficiency workup, thrombotic risk, and rare metabolic disorders (e.g., homocystinuria) (Table 3). The UK provides it within NHS laboratories when clinically indicated [15]. Germany generally treats cardiovascular-risk homocysteine measurement as an IndividuelleGesundheitsleistung (IGeL) (self-pay) out-side rare-disease indications [16], while France

shows heterogeneous reimbursement: some hospital catalogs map the test to NABM codes (notably for non-blood fluids), but many private lists flag plasma homocysteine as hors nomenclature (self-pay). Greece reimburses diagnostics via EOPYY with regulated co-payments and has acted to reduce overuse; North Macedonia's HIF finances a broad benefits package, though test-level listings are not publicly granular. Albania covers basic labs and runs a national check-up, but specialized tests (including homocysteine) are typically out-of-pocket unless part of specific pro-grams, highlighting a clear policy gap if Albania aims to introduce targeted reimbursement for high-risk groups [23].

Marked variation in patient costs was observed (Table 3). In Germany, private laboratories typically charge €20–30 per test. Similar pricing is observed in Greece, where accredited laboratories charge €20 plus a 15% co-payment under the EOPYY system. In Sweden, homocysteine testing is available in both public and private laboratories, although reimbursement and patient costs vary according to regional healthcare policies and clinical indication [17]. In Albania, private laboratory pricing suggests costs in the range of €40–50, while in North Macedonia estimated prices are approximately €20–30. In contrast, France shows higher pricing, with private laboratories listing tHcy between €40–60, reflecting its frequent classification as a non-reimbursed test. The highest costs were reported in the United Kingdom, where private clinics charge £111.55, plus a phlebotomy fee of £50, bringing the total to nearly £160 per test (ap-proximately €185).

These findings highlight substantial inequities: while patients in Germany, Greece, Albania, and North Macedonia face relatively modest costs, those in France and particularly the UK encounter far greater financial barriers to accessing tHcy testing in the absence of public reimbursement.

Clinical Cut-offs and Interpretation.

In clinical practice, plasma homocysteine levels can be interpreted along a spectrum of cardiovascular and metabolic risk. Values below 10 µmol/L are considered optimal and are associated with the lowest risk for adverse outcomes. When concentrations fall within the 10 to 14.9 µmol/L range, they are regarded as borderline elevated, prompting further evaluation of B-vitamin status—particularly vitamins B12, folate, and B6—as well as renal function and lifestyle factors that may influence homocysteine metabolism. Levels at or above 15 µmol/L define hyperhomocysteinemia, a threshold at which targeted interventions should be initiated, including nutritional correction and comprehensive management of coexisting cardiometabolic risk factors. Marked elevations, exceeding 30µmol/L, require a more in-depth investigation for underlying rare metabolic disorders, such as homocystinuria, and warrant referral to specialist care for definitive diagnosis and management (Table 4).

Discussion.

Based on the analysis of European health system practices and available scientific evidence, the integration of plasma homocysteine (tHcy) testing into Albania's health insurance framework should follow a targeted and phased approach rather than universal screening.

Priority Testing Groups.

Potential priority groups for future pilot evaluation of homocysteine testing in Albania may include individuals with prediabetes and metabolic syndrome [10], women with polycystic ovary syndrome [27], patients experiencing early-onset or unexplained cardiovascular or thrombotic events [28,29], and those with suspected vitamin B12 or folate

Table 1. *Insurance Coverage of Lab Tests in Albania (source: www.eurohealthobservatory.who, Primary health care in Albania: rapid assessment WHO 2018).*

Type of Test	Coverage Status
Routine blood tests (e.g., glucose, lipids)	Covered with physician referral within public facilities
Preventive screening (check-up panel)	Covered for adults aged 35–70 via national program
Specialized tests (e.g., metabolic, genetic)	Largely not covered; often paid out-of-pocket or private

Table 2. *Homocysteine Testing in Different European Countries.*

Country	Availability	Reimbursement Status	Typical Indications Covered	Notes
UK	Widely available in NHS pathology labs	Covered for specific indications; not for general screening	Vitamin B_{12}/folate deficiency, thrombotic disorders, inherited methylation defects	Guidance varies by NHS Trust [19]
Germany	Available in clinical labs	Covered for high cardiovascular risk or manifest CHD; not for low-risk screening	Cardiovascular disease, high-risk patients	Clinical guidelines recommend selective testing [16]
Sweden	Available in public and private labs	Conditional; depends on indication/local policy	B-vitamin deficiency, kidney disease	Private testing widely accessible [20]
France	Available in clinical labs	Generally not reimbursed for routine use; self-pay common (~€50–€70)	Rare inherited disorders, certain clinical conditions	Public coverage limited [18]
Greece	Available in public and contracted private labs	Co-pay 0–15%, depending on facility and referral	Depends on clinical indication and lab status	Homocysteine reimbursement unclear; likely limited coverage [21]
North Macedonia	Available in public system/ private options	Most basic services covered; diagnostics may require co-pay	Likely selective diagnostics under referral authority	No specific homocysteine policy found; cost may fall to patient [22]

Table 3. *Homocysteine Testing and Insurance Coverage by Country.*

Country	Clinical use in practice	Coverage /reimbursement signal	Policy notes & sources	Estimated Out-of-Pocket Cost per Test
Albania	Routine basic labs via PHC and the national preventive check-up (35–70 yrso); specialized tests often outside core package.	Out-of-pocket;	WHO PHC rapid assessment; WHO affordability review; gov/ITA notes on ISKSH roles. World Health OrganizationIrisTrade.gov)	≈ €40–€50 (private lab estimation: *Genius Lab., Intermedica Laboratories*)
Germany	Homocysteine used for specific indications (e.g., suspected homocystinuria, rare metabolic disorders), not for general cardiovascular screening.	Tests outside guideline indications are typically billed as **IGeL** (self-pay). Related statutory codes exist for *MTHFR mutation* testing when Hcy is very high, showing reimbursement in rare-disease contexts.	G-BA press on newborn screening (homocystinuria); EBM materials; IGeL concept and clinic statements that Hcy is not a GKV benefit for routine risk assessment.	€20–€30 (IGeL/private testing) * *G-BA+1kvb.de GKV-Spitzenverbanddr-thudium.de*
United Kingdom (NHS)	Hospital lab handbooks list homocysteine for B-vitamin deficiency workup, thrombotic risk evaluation, and suspected homocystinuria; not for population screening.	Tests requested by NHS clinicians are provided within NHS pathology services (no patient billing), but use is indication-driven.	NHS trust pathology pages (by South Tees; North Bristol; University Hospitals Sussex). South Tees NHS TrustNorth Bristol NHS Trustpathology. uhsussex.nhs.uk	£111.55 + £50 phlebotomy (~€160 total) Evidence review for diagnostic tests: Vitamin B12 deficiency in over 16s: diagnosis and management: Evidence review C. NICE Guideline, No. 239. London: National Institute for Health and Care Excellence (NICE); 2024 Mar.
Sweden	Homocysteine testing available in public and private laboratories, mainly for B-vitamin deficiency, renal disease, and selected metabolic conditions	Conditional reimbursement depending on regional policy and clinical indication	Karolinska University Hospital laboratory services; regional clinical practice variation	Variable; testing available in public and private laboratories.
France	Clinical use mainly in targeted contexts (deficiency workup, rare disorders, some CVD contexts).	Mixed signals: some hospital labs list NABM identifier K012 (homocystéinetotale—liquidesbiologiques), whereas many private price lists mark homocystéine as HN (hors nomenclature)—often self-pay for routine blood testing.	CHU Lille catalog (NABM K012); Assurance Maladie pages on NABM/TNB;	≈ €40–€60 (estimation via private labs: private tariff sheets showing HN for homocysteine. biologiepathologie.chu-lille. fr, Amelicodage.ext.cnamts.fr, Laboratoire SYNLAB Barla
Greece	Test widely available in private and hospital labs; ordering and access governed by EOPYY contracting and EKPY rules.	Co-payments vary by provider and service; Greece has recently tightened diagnostic volumes to curb abuse.	EOPYY NCP pages on cost-sharing; national media report on reductions in reimbursed diagnostics; example Greek lab listing for availability. NCPeKathimeriniAthens Lab	€20 + 15% co-pay (~€23)
North Macedonia	Compulsory insurance system with HIF as single purchaser; access to diagnostics via referral within a comprehensive benefits package, but capacity constraints exist.	WHO country profiles describe comprehensive coverage but do not specify homocysteine; practical access depends on contracted providers and referral pathways.	WHO/European Observatory country profile; 2024 system review (HIF purchaser role); WHO HBP profile. Euro Health Observatory	≈ €20–€30 (estimation via private labs)

Table 4. *Recommended laboratory thresholds and possible actions.*

Plasma total Hcy (µmol/L)	Interpretation	Suggested clinical action
< 10	Desirable/optimal (target per DACH consensus)	No action, routine care [24]
10–14.9	Borderline / mildly elevated	Check B-vitamin status (B_{12}, folate, B_6), renal function; repeat fasting Hcy; lifestyle advice [25].
≥ 15	Hyperhomocysteinemia (classic cutoff)	Investigate nutritional causes, medication, renal disease; treat deficiencies; consider cardiometabolic risk management and follow-up [26].
≥ 30	Moderate to severe elevation	Specialist referral (genetics/metabolic or hematology) [34]

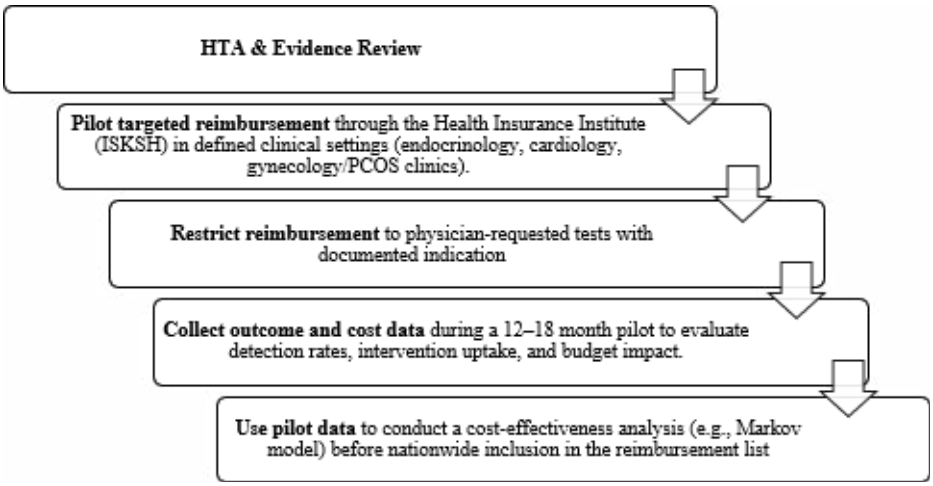

Figure 1. *Policy Pathway for Introducing Homocysteine Testing in Albania.*

deficiency, chronic kidney disease, or a strong family history of premature cardiovascular disease [30].

Although mechanistic and epidemiological studies suggest a plausible relationship between elevated homocysteine levels and insulin resistance, current evidence re-mains insufficient to support routine population-based screening [8,9]. Most available data derive from observational studies and experimental models, while randomized controlled trials evaluating whether homocysteine-guided interventions improve metabolic outcomes or prevent progression to type 2 diabetes are still limited. Therefore, the present study does not advocate universal reimbursement of homo-cysteine testing, but rather proposes cautious pilot evaluation in selected high-risk groups within a coverage-with-evidence framework.

Practical Policy Pathway for Introducing Homocysteine Testing in Albania.

The introduction of homocysteine (Hcy) testing into Albania's public health insurance scheme should follow a structured, evidence-based pathway to ensure both clinical value and financial sustainability. The first step is to commission a concise Health Technology Assessment (HTA) that evaluates clinical effectiveness and budget im-pact, focusing specifically on targeted testing in well-defined high-risk groups such as individuals with prediabetes. This assessment should follow WHO and EU HTA methodological guidance to ensure robustness and comparability [31,32].

Based on HTA findings, Coverage with Evidence Development (CED) pilot should be launched under the Health Insurance Institute (FDSKSH). This pilot would reimburse Hcy testing only in select high-risk clinics (e.g., endocrinology, cardiology, gynecology/PCOS services) while systematically collecting outcome data — such as changes in homocysteine levels, detection of B-vitamin deficiencies, prevention of diabetes progression, and associated costs. Such CED schemes have been applied in European health systems for novel diagnostics.

To optimize cost efficiency, laboratory processing should be centralized in accredited regional facilities. This allows bulk purchasing of reagents, automation of assays, and accurate collection of Albanian-specific cost data. Negotiating favorable tariffs with suppliers during the pilot phase will further reduce per-test costs. Clear reimbursement rules should be established from the outset: Hcy testing would only be covered with documented physician justification and restricted to defined clinical indications, avoiding inappropriate population-wide screening.

The process should involve all key stakeholders — including the Ministry of Health, FDSKSH, the Institute of Public Health, central reference laboratories, and relevant specialty societies — to ensure clinical alignment, financial stability, and equitable access.

Conclusion.

This study highlights the potential of homocysteine testing as a preventive biomarker for the early detection of insulin resistance. While some routine laboratory services are reimbursed in Albania, specialized metabolic markers such as homocysteine re-main excluded from health insurance coverage, limiting accessibility and equity. Comparative analysis shows that most European countries also restrict reimbursement to specific diagnostic indications, with routine screening rarely supported. However, targeted testing in high-risk groups—such as patients with prediabetes, PCOS, or unexplained cardiovascular events—offers a feasible pathway to integrate homocysteine into preventive health strategies. During the Health-policy route: countries typically require an HTA/economic evaluation and often use coverage with evidence development for new diagnostic tests before broad reimbursement — a recommended pathway for Albania as well. For Albania, a national pilot reimbursement model, linked with evidence collection and cost-effectiveness evaluation, would provide an informed approach to policy adoption. Such an initiative could strengthen early prevention of type 2 diabetes, align national practice with European models, and reduce long-term healthcare costs.

Abbreviations.

The following abbreviations are used in this manuscript:
Hcy: Homocysteine
IR: Insulin Resistance
HTA: Health Technology Assessment
FDSKSH: Health Insurance Institute
CED: Coverage with Evidence Development
PCOS: Polycystic Ovary Syndrome

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