GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 9 (366) Сентябрь 2025

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 9 (366) 2025

GUIDELINE-DIRECTED MEDICAL THERAPY (GDMT) FOR HEART FAILURE MANAGEMENT: ADDRESSING APPLICATIONS, BARRIERS AND OPTIMIZING IMPLEMENTATION

Ahmed Alaa Al-Temimi[1,2], Raja Ezman Raja Sharif[3,6], Mohd Shahezwan Abd Wahab[4,6], Hanis Hanum Zulkifly[5,6]*.

[1]Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Selangor Branch, Puncak Alam Campus, 42300, Selangor, Malaysia.

[2]Clinical Pharmacy Department, College of Pharmacy, Al-Bayan University, Baghdad, Iraq.

[3]Department of Medicine, Universiti Teknologi MARA (UiTM), Faculty of Medicine Sungai Buloh, Sungai Buloh, Malaysia.

[4]Department of Pharmacy Practice and Clinical Pharmacy, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Selangor Branch, Puncak Alam, Selangor, Malaysia.

[5]Department of Pharmacy Practice and Clinical Pharmacy, Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Selangor Branch, Puncak Alam Campus, 42300, Selangor, Malaysia.

[6]Cardiology Therapeutics Research Group, Universiti Teknologi MARA, Selangor Branch, Bandar Puncak Alam, Malaysia.

**Corresponding Author: Hanis Hanum Zulkifly, Email: hanish2984@uitm.edu.my*

Abstract.

Heart failure (HF) remains a major public health issue globally, characterized by high morbidity and mortality rates. The complexity of HF management requires continuous evolution of treatment paradigms to ensure optimal patient outcomes. This comprehensive review focuses on the fundamental role of Guideline-Directed Medical Therapy (GDMT) in enhancing the management of heart failure across various dimensions, and to identify effective strategies and areas for improvement in the management of heart failure. The ultimate goal is to underscore the critical importance of GDMT in elevating the standard of care and improving patient outcomes in heart failure. GDMT, endorsed by leading cardiology societies, provides a comprehensive framework for HF treatment, based on the latest evidence and expert consensus.

Key words. Heart failure (HF), Guideline-Directed Medical Therapy (GDMT), Quadruple therapy, HF with reduced ejection fraction (HFrEF), implementation science, multidisciplinary team, evidence-practice gap.

Pharmacological Treatment of Heart Failure.

The largest cardiovascular societies, such as: European Society of Cardiology (ESC), Canadian Cardiovascular Society (CCS), Canadian Heart Failure Society (CHFS), and the American Heart Association (AHA), American College of Cardiology (ACC), and Heart Failure Society of America (HFSA), endorse quadruple therapy for HF with reduced ejection fraction (HFrEF), intravenous iron for HFrEF with iron deficiency, and sodium restriction for all HF patients.

Controversies persist in the management of heart failure with preserved ejection fraction (HFpEF) and heart failure with mildly reduced ejection fractions (HFmrEF) due to lower quality evidence [1-4]. The latest guidelines for managing heart failure with reduced ejection fraction (HFrEF) have shifted focus towards initiating the four critical life-saving therapies as soon as possible, rather than the guidelines highly recommend that HF patients with (HFrEF) have medical therapy titrated to target doses, as tolerated [5,6].

In a systemic clinical illness like heart failure (HF), numerous pathways typically interact, impacting several organ systems such as the myocardium, kidney, and endocrine system. Current therapeutics such as Inotropic drugs, Beta blockers, Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARB), Angiotensin receptor-neprilysin inhibitor (ARNIs), Mineralocorticoid receptor antagonists (MRA), SGLT2 inhibitors, Ivabradine, Hydralazine–isosorbide dinitrate, Soluble guanylate cyclase stimulators and Omecamtiv mecarbil which have produced the greatest advantages. The practical use GDMT for some therapeutic groups such as SGLT-2 inhibitors, ARNi, beta blockers, and MRAs have multiple pathways of action that target multiple pathophysiological pathways simultaneously. When used together, these medications offer additional advantages by significantly reducing the risk of death, worsening the disease, repeated hospitalization, organ damage, and improving the overall quality of life [7,8].

Polypharmacy has been observed as a significant cause of increased hospital readmission rates among heart failure (HF) patients. Nonetheless, there is limited information on the impact of pharmacist-led interventions on reducing inappropriate medicine usage in patients. A comprehensive evaluation of randomized trials in which pharmacists assessed the appropriateness of treatment based on particular HF guidelines revealed significant variations in patients' clinical outcomes. The development and validation of a specialized method for evaluating drug appropriateness in patients with HF might be beneficial to improve patient health [9,10].

HF prevention and treatment approved options have been developed during the last two decades. Patients who have risk factors for cardiovascular disease, such as high blood pressure, diabetes, ischaemic heart disease, BMI over 30, are thought to be at risk of developing heart failure. These patients would benefit from undergoing screening for heart failure.

The initial treatment for HFrEF involves starting and optimising foundational therapy with ARNIs, ACEIs/ARBs, BBs, MRAs, and SGLT2 inhibitors [11,12]. Commencing GDMT quadruple treatment in HFrEF might enhance the symptoms, quality of life, and clinical conditions. This includes a significant decrease in cardiovascular mortality by up to 73% within a span of two years, as well as a reduction in hospitalisations due to heart failure [13,14].

Based on a study of a large group of patients in the USA who were hospitalised for new onset heart failure with reduced ejection fraction, it was shown that over 80% of the patients were considered suitable for quadruple medical therapy, However, only 15.3% of the HFrEF patients were managed quadruple therapy, whereas 41.5% were assigned triple therapy. Initiating quadruple therapy for newly diagnosed heart failure with reduced ejection fraction (HFrEF) in the hospital might result in significant reductions in rate of death, despite there are some circumstances shown not all patients eligible to quadruple therapy [15]. There are several well-known factors that contribute to the inability to accomplish GDMT what is required with adequate effort such as medical reasons, clinician reason, patient reason and overall system reason [16].

The pharmacological treatment of various co-existing medical conditions frequently poses challenges in therapy, including drug-disease interaction, drug-drug interactions, adverse drug events, and poor compliance. Thus, the widespread occurrence of polypharmacy arises from the utilisation of combination pharmacological treatments

to manage heart failure, treat co-morbidities, and the extensive usage of nonprescription medications such as herble or supplements. Commonly encountered in therapeutic practice are therapeutic difficulties, like drug-disease interactions and drug-drug interactions including both prescription and nonprescription drugs [17,18].

Elderly patients frequently have co-morbidities, many of which necessary the use of medications. Polypharmacy can decrease adherence to treatment in this population. Consequently, pharmacists have been actively involved in the development, supervision, and implementation of patient-centred strategies to optimise medication use. These strategies include pharmacist-led medication reviews, which facilitate the prompt [19].

GDMT is effective in improving the outcomes and quality of life of patients with acute heart failure AHF, for the patients they have poor adherence to the medications is a potential contributor to HF exacerbation [20].

Heart Failure Medications enhancement through GDMT.

GDMT forms the cornerstone of pharmacological management in heart failure. GDMT guidelines provide a structured approach to medication selection, dosing, and monitoring, which are key to mitigating HF symptoms and improving patient quality of life. In clinical practice highly encourage to the adherence of GDMT recommendations and implementation medication management strategies in HF, to come out with effectiveness results [21]. This section of the review will explore how expert knowledge and skill in HF management contribute to the precision and personalization of therapy, which are essential for tackling the diversity of heart failure.

The frequency of inadequate adherence to guideline directed medical therapy during hospitalisation for heart failure is determined by calculating the percentages of patients who get each of these three categories of medication at the recommended target doses, the study shows as follows the percentages for ACEI/ARB, ARNI, BB, and MRA are 17%, 14%, 28%, and 77% respectively. Furthermore, during the 12-month follow-up, a minority of patients experienced medication initiation or up-titration, with the following percentages ACEI/ARB, ARNI, BB, and MRA are 7%, 10%, 10%, and 6% respectively [22]. The suboptimal implementation of GDMT is linked to a worse prognosis [23,24].

The conventional methods of utilization GDMT frequently result in a delay in starting and adjusting treatments for patients with heart failure. The present research aims to analyse different care models involving nonphysician providers leading GDMT treatments. The focus is on understanding the relationship between these interventions, the utilisation of therapy, and the resulting clinical outcomes. Pharmacist-led interventions for initiating and/or increasing the dosage of GDMT have shown improvement in adhering to guidelines for managing heart failure [25,26].

The expertise of healthcare providers in heart failure management, particularly in the application of GDMT, is critical for achieving desired health outcomes. Research indicates that centres with specialized HF teams, including cardiologists, nurse practitioners, and clinical pharmacists with advanced training in heart failure care, are more effective in applying GDMT principles [27,28].

Some studies have shown that the most effective approach to managing heart failure with a reduced ejection fraction (HFrEF) involves adjusting the dosage of guideline-directed medical therapy (GDMT) to the highest dose that can be tolerated within the approved range and the most frequently utilised treatment was ACEIs/ARBs, particularly in non-cardiovascular hospitalisations, especially when accompanied by low blood pressure, impaired kidney function, hyperkalemia, and care supplied by a non-cardiologist. Reduction of ACEIs/ARB dose was associated with worse age-adjusted post-discharge survival [29].

The studies supporting the use of GDMT in HFrEF, the actual usage of these drugs in real-world settings is limited, and there is plenty of room for improvement [30].

Registry data in the US reveals that 33% of eligible patients do not receive prescriptions for ACEis, ARBs, and ARNIs, 25% do not receive prescriptions for BBs, and 55% do not receive prescriptions for MRAs [31].

The limited utilisation of GDMT in HFrEF severely reduces the potential positive effects of these drugs at a population level. The collective impact of applying BBs, ARNIs, MRAs, and SGLT2is is estimated to increase the lifespan of patient with HFrEF by more than 6 years when compared to using ACEi and beta-blockers alone [32].

Medication therapy management is crucial for optimising treatment by attaining target doses of GDMT for individuals with heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection (HFmrEF), and heart failure with preserved ejection fraction (HFpEF).

Recent large-scale clinical trials, including EMPEROR-Preserved and DELIVER, have demonstrated that SGLT2 inhibitors significantly reduce the risk of cardiovascular death and heart failure hospitalization in patients with HFmrEF and HFpEF [33,34]. These agents also attenuate the rate of eGFR decline and confer modest improvements in health-related quality of life at 52 weeks, with benefits observed irrespective of baseline diabetes status. Importantly, SGLT2 inhibitors represent the first class of pharmacological agents to provide consistent benefit across the full spectrum of ejection fractions, although subgroup analyses suggest a potential attenuation of effect at higher LVEF thresholds (>62.5%). While evidence for other GDMT agents in HFpEF remains inconclusive, SGLT2 inhibitors have established a pivotal role in contemporary management of this population [35,36].

Effectively managing heart failure symptoms involves administering medication and implementing required modifications the patient's lifestyle [17,37].

MTM clinics provide evaluation and assessment for patients who need to determine their level of adherence to medications for heart failure, and the reasons for nonadherence by investigating appropriateness selection medications, dosing, availability of dosage form in the market, and monitoring [38,39].

Kim and colleagues [40] investigates the role of diet modification in the progression of heart failure with (HFpEF) in Dahl Salt-Sensitive (DSS) rats. HFpEF was induced in male DSS rats by feeding them a high-salt (8% NaCl) diet, while a normal-salt (0.3% NaCl) diet was used as a control, the finding it was switching from a high-salt to a normal-salt diet in HFpEF rats improved several HFpEF phenotypes, including diastolic function, functional capacity, and survival, without affecting blood pressure or ventricular hypertrophy.

Various challenges and strategies at multiple levels, from patient and clinician barriers to system-level interventions and patient engagement, the barriers to Guideline-Directed Medical Therapy (GDMT) Implementation such as: The challenges in prescription guideline-directed medical therapy (GDMT) include some crucial points like patient barriers, physician and hospital system barriers, physician reminders, physician financial incentives, physician benchmark reporting and audits, furthermore involvement of nurses, pharmacists, and multidisciplinary teams, interventions, and patient engagement [32].

Currently, there is an important discrepancy between the guidelines and actual clinical practice in the management of heart failure patients. This problem arises from limitations connected to patients, barriers associated with healthcare professionals, and systemic limitations. Method to narrowing this discrepancy include addressing clinical inertia, enhancing patient and physician knowledge, ensuring well implementation of GDMT, improving affordability, and exist multidisciplinary team collaboration [24].

Eleven studies from the U.S., India, New Zealand, Australia, Germany, and Switzerland were included, with sample sizes ranging

from 52 to 2,211 patients. Among these, three studies were conducted prospectively, four were retrospective, and others were randomized controlled trials (RCTs) or interventional studies. The populations studied included both hospitalized and outpatient HF patients. The main outcomes of the studies in Table 2.8 regarding GDMT in HF management which include: improved medication titration and optimization, reduction in mortality and readmission rates, enhanced quality of life and symptom relief, effective remote management, and cost-effectiveness and feasibility of GDMT Integration. These outcomes indicate that GDMT can substantially improve HF patient care, reducing mortality, rehospitalization, and enabling practical, cost-effective management approaches. (Table 1) shown the Application of Guideline-Directed Medical Therapy globally.

Bridging Gaps in GDMT Implementation.

Addressing the gaps in GDMT implementation requires identifying and mitigating the barriers that hinder its consistent application

Table 1. *Application of Guideline-Directed Medical Therapy Globally.*

Country of study	Author / Year	Study Design / Data Source	Sample Size	Influences and Conclusion
US	(Mukhopadhyay et al., 2023) [41]	Cluster RT / Outpatient cardiology clinics, single site	2211 Patients	Broader adoption of selective and tailored clinical decision support tools, like those evaluated in this study, may result in more suitable prescription of GDMT and improved results for patients particularly with HFrEF patients.
14 Countries	(Mebazaa et al., 2022) [42]	randomized, open-label, parallel-group study / Outpatient, 87 hospitals	1078 Patients	The patient was highly accepting of the therapeutic approach involving titration of GDMT and close monitoring after hospital admission, as it effectively relieved symptoms, improved quality of life, and reduced the risk of all-cause mortality or readmission for heart failure when compared to standard therapy.
US	(Ghazi et al., 2022) [43]	RCT / Outpatient internal medicine and cardiology clinicians, single site	1310 Patients	Enabled cost-effective intervention that may be quickly included into clinical care and accelerate the implementation of valuable treatments in heart failure.
New Zealand	[44]	Outpatient, single site	52 Patients	Remote application of GDMT by telephone, particularly during the Covid-19 pandemic, was deemed satisfactory with reduced requirement for clinic evaluation, and titration rates similar to those reported in most real-world studies.
US	(McLachlan et al., 2021) [45]	Pilot study / Outpatient, single site	118 Patients	Virtual application by pharmacists and physicians for GDMT results in significant therapeutic titration and optimisation.
India	(Bhatt et al., 2021) [46]	prospective interventional / Inpatient, single site	716 Patients	Implementing GDMT primarily enhance and achieve a quality for routine clinical audits with HFrEF hospitalized patients
United States	(Desai et al., 2020) [47]	Case control study / Outpatients	1028 Patients	Bridging the gap between guidelines and clinical practice in patients with HFrEF can by using encoded algorithms and involving nonphysician to assist with clinic-based follow-up and support pharmacologic optimization.
US	(Blizzard et al., 2019) [48]	Retrospective / Inpatient, single site	400 Patients	The widespread application of GDMT due to active participation of pharmacists in the management of HF patients.
Australia	(Hickey et al., 2016) [49]	pre-intervention cohort and intervention cohort / Metro North Hospital and Health Service	335 Patients	Interprofessional communication system for coordinating GDMT titration between inpatient and outpatient to enable healthcare professionals for easy application of GDMT.
Germany	(Güder et al., 2015) [50]	RCT / Outpatient	1022 Patients	HF-specialist nurse led participate in implementation of GDMT algorithm to achieve optimal pharmacotherapy to the HF patients
US	(Martinez et al., 2013) [51]	Outpatients	144	The launch of GDMT in the pharmacist-managed HF medication titration clinic contributed to an increased percentage of patients achieving optimal treatment.
Switzerland	(Garin et al., 2012) [52]	Inpatients	363	Application of a critical pathway for HF patients admitted to the hospital led to a 28% decrease in the relative risk of mortality or re-hospitalisation and improved compliance with clinical practice guideline.

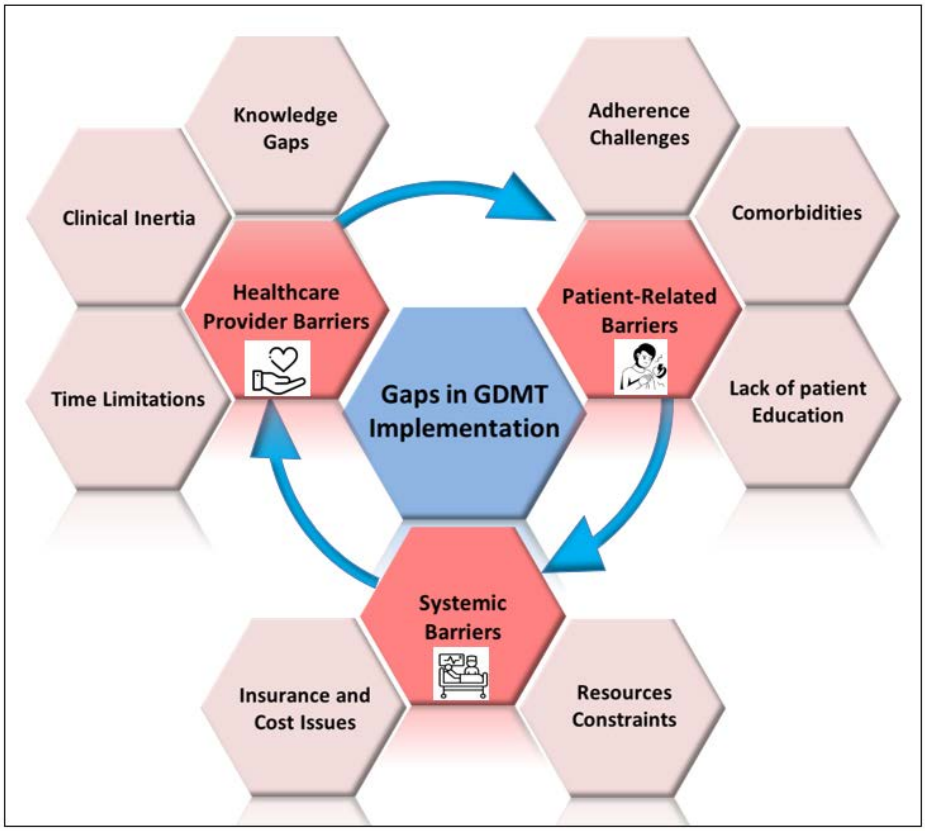

Figure 1. *Barriers to GDMT Implementation [53].*

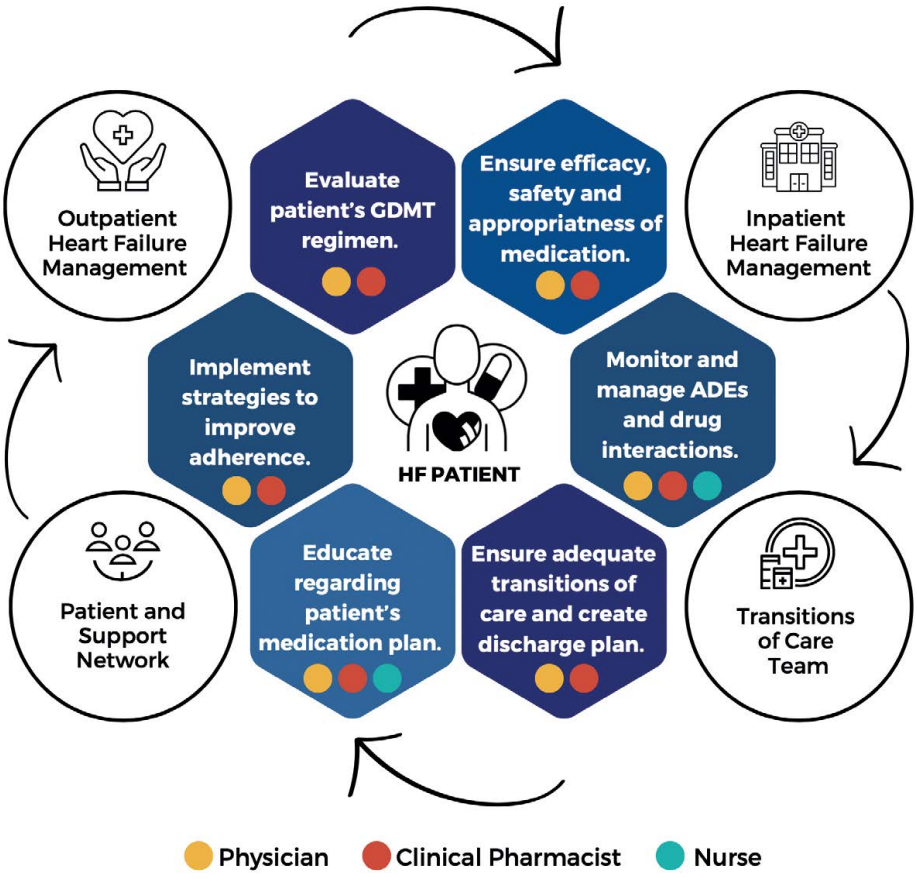

Figure 2. *Role of Multidisciplinary Team in Heart Failure Management.*

in clinical settings. These obstacles generally fall into three main categories as shown in in the Figure 1.

Better Management by Heart Failure Clinics.

HF clinics play a crucial role in the multidisciplinary management of heart failure [54]. These specialized clinics offer tailored patient care, leveraging GDMT to improve clinical outcomes [55]. Studies have shown that by implementing structured GDMT protocols in HF clinics, it significantly enhance patient adherence to treatment, reduce hospital readmission rates, and improve overall survival [56]. The literature highlights the benefits of integrated care models in HF clinics, which are designed to optimize therapy adjustment, patient education, and follow-up regimens [57].

Collaborative efforts between physicians and clinical pharmacists have been shown to enhance treatment efficacy and patient safety, mitigating risks associated with drug-related adverse events and prescription errors. Notably, the integration of clinical pharmacists facilitates individualized treatment approaches tailored to patients' needs. Furthermore, specialized transitional care programs have emerged as effective strategies to reduce post-discharge readmission rates, thereby improving patient outcomes [58].

Despite conducting extensive subgroup analysis that accounted for clinic visits, variations in GDMT dose remained, suggesting that rural patients encounter unexpected obstacles to receive care that cannot be exclusively attributed to costs or visits [59].

The pharmacist-led involvements included patient education, medication review, and medication adherence encouragement [60].

Telemonitoring is one approach technique which can be implemented to optimise guidelines using a remote patient management platform by applying the Guideline-Directed Medical Therapy for Heart Failure, according to the studies, it was feasible, effective, and safe for patients with reduced ejection fraction. Furthermore, it increased the percentage of patients who achieved their target doses within a shortened time frame, without any excessive adverse effects [61].

Optimizing GDMT Implementation.

Efforts to optimize GDMT implementation should focus on overcoming these barriers to ensure that heart failure patients consistently receive evidence-based treatments. Key strategies include:

Education and Training.

Improving Provider Knowledge: Regular training and updates for healthcare providers on heart failure guidelines can strengthen their ability to prescribe effective therapies while instilling confidence in their clinical decisions.

Enhancing Patient Understanding: Educating patients about their condition, the benefits of GDMT, and how to address potential side effects is essential for fostering adherence and engagement with treatment plans [62,63].

Clinical Decision Support Systems (CDSS).

Incorporating CDSS within electronic health records (EHRs) can serve as a practical tool for reminding providers to initiate or adjust GDMT during patient encounters. These systems can also offer tailored, evidence-based recommendations based on specific patient profiles [64].

Multidisciplinary Care Teams.

A collaborative, team-based approach that integrates the expertise of cardiologists, primary care providers, pharmacists, and other healthcare professionals is vital to addressing all dimensions of heart failure care. This strategy enhances the likelihood of optimal guideline-directed medical therapy (GDMT) implementation [65].

Telemedicine and remote monitoring present valuable solutions for overcoming logistical challenges in healthcare delivery. By enabling regular virtual consultations and real-time tracking of vital signs, these technologies support timely adjustments to treatment plans and early detection of potential complications.

Strategic Actions to Improve Acute Heart Failure Management and Patient Outcomes: Acute heart failure is a prevalent and life-threatening condition, responsible for about 5% of emergency hospital admissions in Europe and the USA. Admission rates are rising due to increasing prevalence, with patients over 75 years facing a nearly 50% one-year mortality rate, while approximately 20% of those under 75 dies within a year. In response, we propose the following actions:

Enhance Care Transitions.

Integrate hospital, community, and emergency services to improve patient outcomes and optimize resource use. Current discharge planning is inconsistent, highlighting the need for better coordination among care providers [66,67].

Strengthen Patient Education and Support.

Improve education and support for patients, families, and caregivers to enhance self-management and long-term adherence to health measures [68].

Ensure Equitable Access to Care.

Guarantee timely access to diagnostic procedures, therapeutic interventions, and follow-up care, addressing the current disparities in treatment quality across different regions [69].

Establish Multidisciplinary Leadership.

Appoint a heart failure expert to lead a multidisciplinary team responsible for developing clinical protocols, staff training, and regular audits to maintain high-quality care [70]. Through Develop and implement evidence-based performance indicators to monitor and improve care quality, reducing the variability and potential unintended consequences of current metrics [71].

Conclusion.

Heart failure (HF) continues to represent a major global health challenge, with prevalence rising due to aging populations and improved survival from cardiovascular disease. Guideline-Directed Medical Therapy (GDMT) remains the cornerstone of evidence-based management, particularly in heart failure with reduced ejection fraction (HFrEF), where early initiation and titration of quadruple therapy—ARNIs/ACEIs/ARBs, beta-blockers, MRAs, and SGLT2 inhibitors—substantially reduce morbidity, mortality, and hospitalizations. Despite this strong evidence base, real-world practice reveals significant underutilization and suboptimal dosing, creating persistent evidence–practice gap.

Barriers to implementation are multifactorial, encompassing patient-related factors (comorbidities, poor adherence, financial limitations), provider-related challenges (knowledge gaps, clinical inertia, limited time), and systemic obstacles (fragmented care, resource constraints, medication costs). The literature highlights the value of multidisciplinary care models—particularly pharmacist- and nurse-led optimization, structured titration protocols, and telehealth-enabled follow-up—in improving GDMT uptake, adherence, and outcomes. Clinical decision support systems embedded within electronic health records further demonstrate promise in bridging gaps between guideline recommendations and practice.

Although uncertainties persist regarding most GDMT in HFpEF, the consistent benefit of SGLT2 inhibitors highlights a major advancement and provides a new therapeutic cornerstone in this subgroup. Socioeconomic disparities continue to restrict access to newer, high-cost therapies, particularly in resource-limited or rural settings. Additionally, further work is required to evaluate digital health solutions, remote monitoring strategies, and performance-based incentive models for sustainable and equitable GDMT implementation.

Future directions should focus on scaling multidisciplinary, team-

based models, integrating advanced digital health tools into clinical workflows, and strengthening patient education to enhance adherence. At the policy level, strategies to improve affordability, ensure equitable access, and embed performance indicators into healthcare systems are critical. Expanding pragmatic trials and real-world evidence will also be essential to refine treatment strategies across diverse populations and HF phenotypes.

In summary, bridging the GDMT implementation gap requires a multifaceted, system-wide approach that integrates provider expertise, patient empowerment, and structural reforms. Closing this gap will not only reduce the global burden of HF but also extend survival and enhance quality of life for patients worldwide.

Acknowledgments.

I would like to express my gratitude to Al-Bayan University for their financial support, which significantly facilitated the successful completion of this research.

Conflict of Interest.

The authors declare no conflict of interest.

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