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Safety Assessment of Proton-Pump Inhibitors: Study of Cardiovascular Adverse Events Using Global Pharmacovigilance Data

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Abstract
Proton-pump inhibitors (PPIs) have been associated with adverse cardiovascular events, underscoring the need for comprehensive safety evaluation, yet systematic consolidation of data on PPI-related adverse drug reactions (ADRs) leading to cardiovascular events remains lacking. This study aims to descriptively analyze cardiovascular events related to PPI use to summarize their safety profile. A quantitative descriptive analysis was performed on cardiovascular ADRs associated with PPIs using global pharmacovigilance data. The top 25 reported cardiovascular ADRs for each PPI were identified from VigiAccess launched by World Health Organization (WHO) global database. We selected the same 20 set potential ADRs using Venny 2.1.0 to enhance the comparability of data and we summarized by frequency and percentage. A total of 15,263 cardiovascular ADR cases were identified. Omeprazole showed the highest reports, mainly palpitations (1,675 cases; 28.5%), cardiac flutter (759 cases; 12.91%), tachycardia (549 cases; 9.34%), and myocardial infarction (498 cases; 8.47%). Pantoprazole reported palpitations (893 cases; 27.43%), tachycardia (332 cases; 10.20%), and cardiac flutter (326 cases; 10.01%), while lansoprazole (1,782 cases; 11.7%) reported palpitations (451 cases; 25.3%), tachycardia (166 cases; 9.3%), and cardiac flutter (153 cases; 8.6%). Esomeprazole was most associated with myocardial infarction (951 cases; 21.88%), palpitations (621 cases; 14.29%), and cardiac failure congestive (380 cases; 8.74%). PPIs are associated with cardiovascular ADRs such as palpitations and myocardial infarction, emphasizing the importance of careful risk assessment during therapy.

Keywords: Proton-pump inhibitors; Adverse drug reaction; Cardiovascular.

1. INTRODUCTION

Proton-pump inhibitors (PPIs) are widely used globally for acid-related disorders and include omeprazole, pantoprazole, lansoprazole, esomeprazole, dexlansoprazole, and rabeprazole, approved by United States Food and Drug Administration (FDA) (Ahmed & Clarke, 2025). Omeprazole was the most common prescribed PPI drug followed by esomeprazole, pantoprazole, and lansoprazole (Shanika et al., 2023). Inappropriate PPI prescribing is a key issue in Southeast Asia (SEA) with regional studies consistently reporting

rates of 40% to 60% (Fah et al., 2019; Wenedy et al., 2019). In Indonesia, self-medication is frequently practiced since omeprazole is in the list of drugs that pharmacies must stock and can be dispensed by pharmacists without prescription for short-term use called pharmacist-only medicines (POMs). This can cause great risks for unmonitored adverse drug reactions (ADRs). Adequate pharmacovigilance of this drug worldwide is a critical priority, which needs more attention, considering its widespread use globally.

The adverse cardiovascular effects associated with PPI use have become a subject of major interest, given previous findings that the PPI drug omeprazole may be associated with increased blood pressure. Omeprazole have been linked to 1,043 reported cases of hypertension in different countries with a median onset of 2 days (Bahta et al., 2024). In another cohort study involving 459,207 individuals without a history of cardiovascular disease, regular PPI use was associated with increased risks of multiple cardiovascular events, including coronary heart disease, stroke, heart failure, atrial fibrillation, and venous thromboembolism (Li et al., 2024). There is a lack of studies that systematically consolidate data on PPI use and its association with ADRs leading to cardiovascular events. This study provides an evidence-based synthesis of clinical research data and highlights the detailed characterization of PPI-related ADRs to inform and improve clinical decision-making.

The World Health Organization (WHO) maintains a pharmacovigilance database known as VigiAccess which facilitates the retrieval of information regarding the number of reported potential cardiovascular ADRs associated with the use of PPIs. VigiAccess serves as an open-source platform containing spontaneous reports of potential ADRs categorized by the active compounds of pharmaceutical products (World Health Organization, 2025). This study utilizes the WHO VigiAccess database to descriptively analyze the incidence of cardiovascular ADR cases related to PPI use with the aim of summarizing the safety profile of widely used PPIs.

2. MATERIAL AND METHODS

2.1. Study design and data source

A quantitative descriptive method was conducted in this study to analyze cardiovascular ADR cases due to PPIs reported to the WHO global open access database, VigiAccess. VigiAccess provides information on potential ADRs of pharmaceutical product in VigiBase, the largest worldwide pharmacovigilance database established by WHO.

2.2. Data-mining approach

The potential ADR reports were collected from 1984 until August 2025 based on VigiAccess availability data. The data set of ADRs were retrieved from VigiAccess (www.vigiaccess.org) on each PPIs drug as an active compound, regardless the dose, frequency, route, and duration of the treatment. We extracted data by querying each PPI individually, specifically "omeprazole," "pantoprazole," "lansoprazole," and "esomeprazole." Subsequently, we retrieved detailed information on the number of reported potential ADR cases associated with each active compound as documented within the database. The VigiAccess database includes a dedicated section on cardiac disorders. The data we collected were limited to this

section and only to reports of cardiac disorder. These were then ranked to identify the 25 most reported cases, which were further analysed to be representative of cardiovascular events. The number of reported cardiovascular cases for each PPI was different. Omeprazole had 5,878 cases, pantoprazole 3,256 cases, lansoprazole 1,782 cases and esomeprazole 4,347 cases. Because of the large number of reports (often more than 1,000 cases per drug), the data were summarized by ranking all potential ADRs within the cardiac disorders section to identify the top 25 most frequently reported across the PPIs. This gave a balanced stratification, showing the most severe cardiovascular events for each drug, but restricting the detailed review to the 25 top of these. This approach enabled in-depth assessment of cardiovascular-related ADRs for these PPIs.

2.3 Data analysis

All potential ADRs for each of the proton pump inhibitors (PPIs) have been analyzed and studied to assess the likelihood of experiencing cardiovascular events. A total of 25 most frequent ADRs for each PPI have been listed based on their incidence rate. However, out of the 25 potential ADRs, only 20 have been kept because a Venn diagram analysis using the Venny 2.1.0 online tool (bioinfogp.cnb.csic.es/tools/venny/) showed that only 20 ADRs appeared in all four drugs (Figure 1). The 20 overlapping ADRs generated from the use of Venny were chosen to easily compare the frequencies of cases and to identify which PPI had the most reported ADRs. This analysis yielded a frequency table showing the number and percentage of cases in terms of the PPI associated with these ADRs.

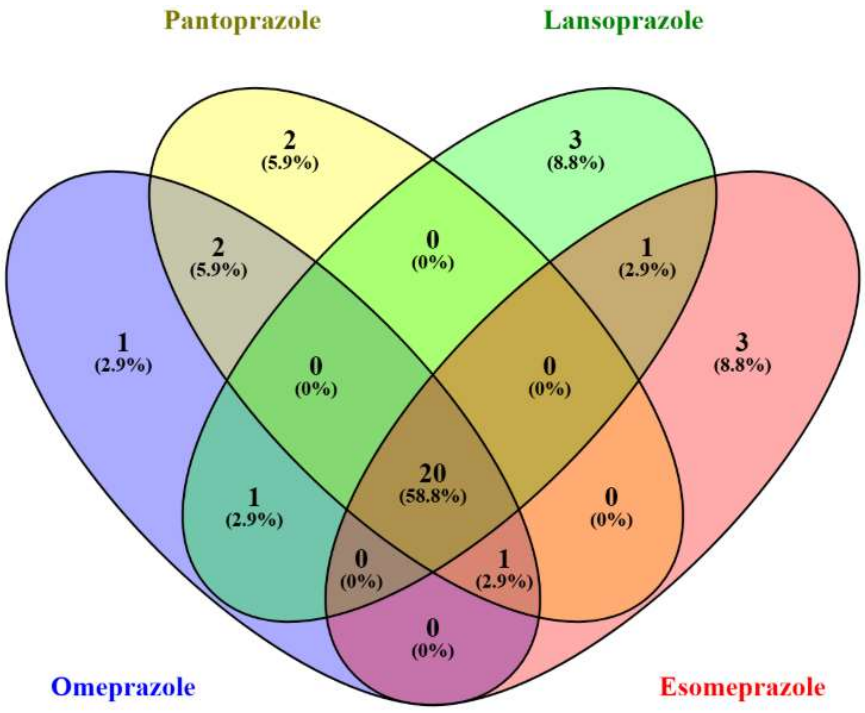

Figure 1. Venn Diagram showing 20 overlapping ADRs from initial top 25 across four PPIs using Venny 2.1.0.

3. RESULTS AND DISCUSSION

A total of 15,263 potential ADR cases related to cardiovascular events were retrieved from the VigiAccess database, comprising 5,878 cases for Omeprazole, 3,256 for Pantoprazole, 1,782 for Lansoprazole, and 4,347 for Esomeprazole. We selected four PPI drugs for analysis based on their high frequency of global use, with omeprazole being the most commonly used, followed by esomeprazole, pantoprazole, and lansoprazole (Shanika et al., 2023). According to the reported potential ADRs in VigiAccess, cardiac disorders represent the second most frequently reported risk after blood and lymphatic system disorders, in association with PPI use as shown in Table 1. The most frequently reported ADRs were palpitations, cardiac flutter, tachycardia, myocardial infarction, and congestive cardiac failure as presented in Figure 2.

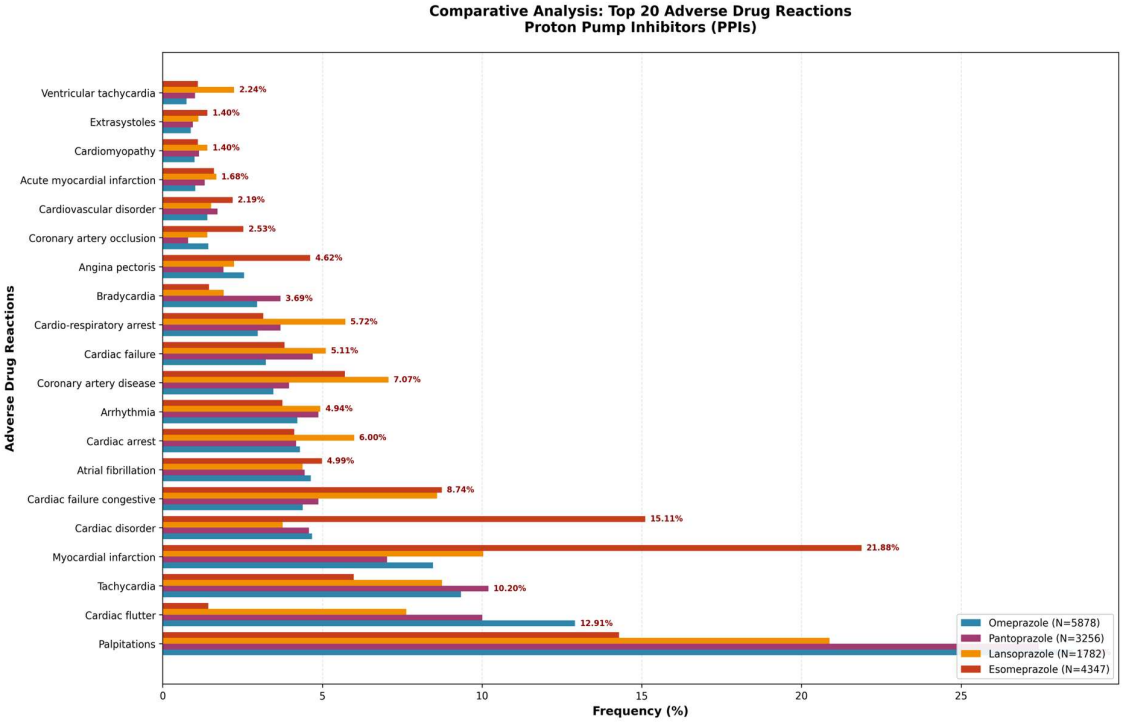

Figure 2. Comparative analysis of top 20 cardiovascular adverse drug reactions among proton pump inhibitors.

The PPI use elevates cardiovascular risk through multiple mechanisms, including hypomagnesemia-induced arrhythmias that typically emerge after about three months and worsen with diuretics or digoxin, reduced absorption of vitamin B12, calcium, and iron, and pharmacokinetic interactions that diminish clopidogrel efficacy, such as with esomeprazole. PPIs also inhibit dimethylarginine dimethylaminohydrolase (DDAH), raising asymmetric dimethylarginine (ADMA) levels that suppress nitric oxide (NO) production to promote thrombosis and atherosclerosis, while blocking V-ATPase proton pumps disrupts endothelial lysosomal acidification, akin to their action on gastric H+/K+-ATPases. This triggers proteostasis imbalance, oxidative stress, endothelial senescence with telomere shortening and reduced proliferation, and endothelial-to-mesenchymal transition (Ariel & Cooke, 2019). These

findings suggest a potential cardiovascular risk profile for PPIs, warranting a descriptive study on PPI-related cardiovascular events for careful clinical consideration.

Table 1. Top 20 potential adverse drug reaction of PPIs associated with cardiovascular events based on VigiAccess by WHO global database

Top 20 Adverse Drug Reactions (ADRs)	Omeprazole (N=5878)		Pantoprazole (N=3256)		Lansoprazole (N=1782)		Esomeprazole (N=4347)	
	Frequency							
	n	%	n	%	n	%	n	%
Palpitations	1675	28.50	893	27.43	372	20.88	621	14.29
Cardiac flutter	759	12.91	326	10.01	136	7.63	62	1.43
Tachycardia	549	9.34	332	10.20	156	8.75	260	5.98
Myocardial infarction	498	8.47	229	7.03	179	10.04	951	21.88
Cardiac disorder	275	4.68	149	4.58	67	3.76	657	15.11
Cardiac failure congestive	258	4.39	159	4.88	153	8.59	380	8.74
Atrial fibrillation	273	4.64	145	4.45	78	4.38	217	4.99
Cardiac arrest	253	4.30	136	4.18	107	6.00	179	4.12
Arrhythmia	248	4.22	159	4.88	88	4.94	163	3.75
Coronary artery disease	204	3.47	129	3.96	126	7.07	248	5.71
Cardiac failure	190	3.23	153	4.70	91	5.11	166	3.82
Cardio-respiratory arrest	175	2.98	120	3.69	102	5.72	137	3.15
Bradycardia	174	2.96	120	3.69	34	1.91	63	1.45
Angina pectoris	150	2.55	62	1.90	40	2.24	201	4.62
Coronary artery occlusion	84	1.43	26	0.80	25	1.40	110	2.53
Cardiovascular disorder	82	1.40	56	1.72	27	1.52	95	2.19
Acute myocardial infarction	60	1.02	43	1.32	30	1.68	70	1.61
Cardiomyopathy	59	1.00	37	1.14	25	1.40	48	1.10
Extrasystoles	52	0.88	31	0.95	20	1.12	61	1.40
Ventricular tachycardia	44	0.75	33	1.01	40	2.24	48	1.10

3.1. Omeprazole

Omeprazole continues to be the most widely used PPIs, which makes it a subject of great interest in safety studies. It appears that, according to data on recorded adverse drug reactions, omeprazole demonstrates the largest number of cardiovascular-related ADRs among other PPIs. In this case, the most frequent cardiovascular events associated with omeprazole were palpitations (1,675 incidents; 28.5%), cardiac flutter (759 incidents; 12.91%), tachycardia (549 incidents; 9.34%), and myocardial infarction (498 incidents; 8.47%). Cardiac flutter, with the percentage of 12.91%, is rather significant when compared to other PPIs and especially when compared to esomeprazole, which shows this percentage at only 1.43%. The almost nine times difference is interesting since esomeprazole is an S-isomer of omeprazole. Therefore, the R-isomer of omeprazole seems to cause the occurrence of arrhythmia.

3.2. Pantoprazole

As seen with omeprazole, pantoprazole is commonly used all over the world, which means that it is one of the major PPIs, whose safety should be considered when addressing the issue of cardiovascular adverse effects. The analysis of the ADRs reports showed that pantoprazole was associated with any cardiovascular events. In particular, the most common adverse effect was palpitations (893 incidents; 27.43%), after which came tachycardia (332 incidents; 10.20%), cardiac flutter (326 incidents; 10.01%), and myocardial infarction (229 incidents; 7.03%). In comparison with the other PPIs, pantoprazole demonstrates the lowest level of adverse effects; in addition, there were no prominent adverse effects in this drug, but rather a relatively balanced distribution. Frequencies mostly lay between omeprazole and the other agents; therefore, this drug may be assumed to have a safe adverse effect profile.

3.3. Lansoprazole

Like omeprazole, lansoprazole is extensively used around the world as a treatment for acid-based disorders, and therefore, an investigation into the cardiovascular safety profile of the medication is essential. The most reported ADRs were palpitations (372 incidents; 20.88%), followed by myocardial infarction (179 incidents; 10.04%), congestive heart failure (153 incidents; 8.59%), tachycardia (156 incidents; 8.75%), and cardiac arrest (107 incidents; 6.00%). In addition, cardio-respiratory arrest was identified to be much more common among lansoprazole patients than in any other PPIs (5.72%), making it the most frequent outcome among the investigated side effects. This side effect appeared to be twice as likely among patients using lansoprazole compared to the two most popular medications, such as esomeprazole (3.15%) and omeprazole (2.98%).

3.4. Esomeprazole

Esomeprazole, the isomer of omeprazole, has also been associated with cardiovascular-related ADRs. Despite the widespread use of this medication, there are some concerns regarding its potential cardiovascular safety. According to the data retrieved from VigiAccess regarding ADRs to esomeprazole, the most frequent cardiovascular ADRs include myocardial infarction (951 cases; 21.88%), cardiac disorders (657 cases; 15.11%), palpitations (621 cases; 14.29%), and cardiac failure congestive (380 cases; 8.74%). However, the most striking finding within this entire data set relates to esomeprazole and its rate of patients developing myocardial infarctions. The rate for patients taking esomeprazole who developed myocardial infarctions is 21.88%, which is more than twice the rate of any other PPI. Additionally, the rate for patients with general cardiac disorders is 15.11%, which is again a notably high rate. Thus, these findings suggest that esomeprazole is associated with a potentially serious cardiovascular risk for patients, indicating the need for further investigation regarding the relationship between the two.

Long-term use of PPIs can lead to hypokalemia, which may progressively increase the risk of cardiovascular events. A case-control study showed that PPI users had a reduced potassium level compared to non-PPI users, with a mean potassium level of 3.92 ± 0.64 mmol/L

in the case group, which was lower than 4.20 ± 0.43 mmol/L observed in the control group (Arj et al., 2022). According to data from the American Heart Association (AHA) and other observational studies, potassium is the primary electrolyte influencing arrhythmias due to its key role in cardiac conduction and automaticity with potassium levels below 3.0 mmol/L significantly increasing the risk of new-onset atrial fibrillation (OR 1.93; 95% CI, 1.00–3.76) and cardiac arrest (OR 2.72; 95% CI, 1.56–4.74), both of which are critical arrhythmia-related events (Faxén et al., 2019; Fisch, 1973). The clinical data reported in previous studies are consistent with the high cases percentage of potential ADRs related to cardiac flutter, tachycardia, and palpitations observed in this study.

Palpitations, cardiac flutter, tachycardia, myocardial infarction, and congestive cardiac failure represent interrelated cardiovascular conditions that often occur sequentially as part of a pathological continuum of cardiac dysfunction. Cardiac flutter, a supraventricular arrhythmia caused by a macro-reentrant circuit in the atria, often manifests as rapid, irregular heartbeats perceived as palpitations due to accelerated atrial and ventricular rates (Ziccardi et al., 2025). Untreated cardiac flutter and tachycardia can lead to cardiac failure and create a substrate for arrhythmias with overlapping symptoms including palpitations, dizziness, and syncope, reflecting a continuum of rhythm disturbances that progressively impair cardiac function and increase the risk of fatal outcomes (Foth et al., 2025). Overlapping clinical symptoms of palpitations accounted for the highest reported percentage of potential ADRs on VigiAccess.

PPIs may contribute to the development or progression of heart failure (HF) through their effects on endothelial cells and nitric oxide (NO) signaling pathways. Endothelial dysfunction plays a key role in heart failure pathophysiology where the imbalance between oxidative stress and NO production impairs endothelium-dependent vasodilation particularly within the coronary circulation and leading to reduced myocardial perfusion and ventricular dysfunction (Drera et al., 2024). PPIs have also been reported to downregulate the expression of endothelial nitric oxide synthase (eNOS) and decrease the availability of NO (Nolde et al., 2021; Tayal et al., 2023). Endothelial dysfunction induced by decreased NO can contribute to vascular stiffness and myocardial infarction. Furthermore, all of these effects can contribute to the development of HF, especially in those with pre-existing conditions of the heart (Drera et al., 2024). Thus, HF can be directly related to PPI use because of NO reduction.

Following the findings of a meta-analysis study showed that the risk of myocardial infarction associated with PPI use demonstrated an odds ratio (OR) of 1.30 (95% CI, 1.19–1.41) (Shi et al., 2021). Another meta-analysis study reported an increased risk of myocardial infarction associated with PPI use, with an OR of 0.98 (95% CI, 0.88–1.09), indicating no statistically significant association (Jeridi et al., 2022). However, the high percentage of reported cases still warrants caution. Cardiac failure, as one of the most critical ADR associated with cardiovascular disease, has been demonstrated in a cohort study to have a 40% increase in the risk of developing cardiovascular diseases in patients who use PPI medications as compared to those who do not use these classes of drugs (HR 1.38 for cardiovascular diseases; 95% CI: 1.11-1.71) (Bell et al., 2021). Furthermore, in relation to the increased risk of cardiac failure

specifically, patients who use PPI medications were demonstrated to have an increased risk of developing cardiac failure relative to those who do not use these classes of drugs (HR 1.37 for cardiac failure; 95% CI: 1.03-1.82) (Bell et al., 2021). Related to these findings of the increased risk of adverse cardiovascular events in patients who use PPI medications is the fact that medications like esomeprazole can interfere with the enzyme CYP2C19, which is present in the liver. Clopidogrel must be metabolized into its active form in order for the medication to exhibit its therapeutic effect in the body, and the enzyme CYP2C19 is responsible for transforming the inactive drug into the active compound that helps to prevent blood platelets from clotting. As a result of taking drugs like esomeprazole in addition to clopidogrel, there is a reduction in the amount of active clopidogrel that is created by the body, leading to weakened antiplatelet activity. For patients who rely upon antiplatelet drugs to prevent the formation of blood clots, such as those patients who have coronary artery stents, this decrease in the antiplatelet effect can lead to adverse events; patients are at an increased risk of blood clot formation that can lead to heart attacks and other forms of cardiovascular complications. Patients with coronary artery disease who also take antiplatelet therapies like clopidogrel have been shown to have a 27% increased risk of cardiovascular complications if they are also treated with esomeprazole as compared to patients who do not use this PPI medication (Sherwood et al., 2015). The significant risk of cardiac failure associated with PPI use is consistent with the findings of this study.

Although the VigiAccess database contains valuable information regarding potential ADRs of various drugs, there are some limitations to the database that must be considered before the database is utilized. The database is based upon reported potential ADRs rather than confirmed ADRs, as there is no available information regarding the patients who developed those ADRs. Furthermore, the database groups medications according to their active ingredient rather than the brand names of the drugs, and it collects information regarding regions of the world rather than individual countries. Additionally, the potential for the under-reporting of some ADRs relative to others may lead to potential biases in the data that is published by the database. To mitigate these issues, it is recommended to perform further assessments of causality of these ADRs, perform additional prospective studies on these drugs with detailed information regarding the patients who developed these ADRs. By performing these steps, the conclusions that are drawn from the information in the VigiAccess database will be more reliable and applicable to the study of ADRs of these drugs.

4. CONCLUSION

The PPIs drug class includes several medications, such as omeprazole, pantoprazole, lansoprazole and esomeprazole. Each of these drugs has been associated with various cardiovascular ADRs. Omeprazole and esomeprazole have been found to have the highest number of ADRs, followed by pantoprazole and lansoprazole. Additionally, the ADRs that are most common with patients taking these drugs include palpitations and myocardial infarction.

Thus, these findings indicate that there is a need for cardiovascular patients to be assessed for the risks of taking these drugs.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest regarding this research, writing or publication.

DECLARATION OF GENERATIVE AI IN SCIENTIFIC WRITING

The authors declare that generative AI and AI-assisted technologies were used only to improve language, grammar, and readability. The authors have reviewed and approved the final manuscript and take responsibility for its content.

REFERENCES

Ahmed, A., & Clarke, J. O. (2025). Proton Pump Inhibitors (PPI). In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK557385/

Ariel, H., & Cooke, J. (2019). *Cardiovascular Risk of Proton Pump Inhibitors*. Methodist Debakey Cardiovasc J. DOI: 10.14797/mdcj-15-3-214.

Arj, A., ghaleh Takizadeh, Z., Gilassi, H., & Razavizadeh, M. (2022). Relationship between long-term use of proton pump inhibitor (PPI) and hypomagnesemia in patients with gastroesophageal reflux disease. *Caspian Journal of Internal Medicine*, *13*(1), 107–112. DOI: 10.22088/cjim.13.1.107.

Bahta, M., Russom, N., Ghebrenegus, A. S., Okubamichael, Y. T., & Russom, M. (2024). Omeprazole and Risk of Hypertension: Analysis of Existing Literature and the WHO Global Pharmacovigilance Database. *Drugs - Real World Outcomes*, *11*(4), 735–744. DOI: 10.1007/s40801-024-00441-2

Bell, E. J., Bielinski, S. J., Sauver, J. L., Chen, L. Y., Rooney, M. R., Larson, N. B., Takahashi, P. Y., & Folsom, A. R. (2021). Proton Pump Inhibitors Are Associated With Higher Risk of Cardiovascular Disease and Heart Failure. *Mayo Clinic Proceedings*, *96*(10), 2540–2549. DOI: 10.1016/j.mayocp.2021.02.025

Drera, A., Rodella, L., Brangi, E., Riccardi, M., & Vizzardi, E. (2024). Endothelial Dysfunction in Heart Failure: What Is Its Role? *Journal of Clinical Medicine*, *13*(9), 2534. DOI: 10.3390/jcm13092534

Fah, T. R., Jun, T. Y., Yan, P., & Yu, C. J. (2019). Appropriateness Of Proton Pump Inhibitors Prescription In Patients Admitted To A Malaysian Tertiary Hospital. *International Journal of Public Health Research*, *9*(1), 1043–1050.

Faxén, J., Xu, H., Evans, M., Jernberg, T., Szummer, K., & Carrero, J.-J. (2019). Potassium levels and risk of in-hospital arrhythmias and mortality in patients admitted with suspected acute coronary syndrome. *International Journal of Cardiology*, *274*, 52–58. DOI: 10.1016/j.ijcard.2018.09.099

Fisch, C. (1973). *Relation of Electrolyte Disturbances to Cardiac Arrhythmias | Circulation*. DOI: 10.1161/01.CIR.47.2.408

Foth, C., Gangwani, M. K., Ahmed, I., & Alvey, H. (2025). Ventricular Tachycardia. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK532954/

Jeridi, D., Pellat, A., Ginestet, C., Assaf, A., Hallit, R., Corre, F., & Coriat, R. (2022). The Safety of Long-Term Proton Pump Inhibitor Use on Cardiovascular Health: A Meta-Analysis. *Journal of Clinical Medicine*, *11*(14), 4096. DOI: 10.3390/jcm11144096

Li, Z.-H., Zhong, W.-F., Qiu, C.-S., Yang, P., Song, W.-Q., Shen, D., Zhang, X.-R., Liu, D., Chen, Y.-J., Chen, P.-L., Huang, Q.-M., Chen, Q., Wang, X.-M., Chung, V. C. H., Gao, X., Kraus, V. B., Liu, S.-D., & Mao, C. (2024). Association between regular proton pump inhibitors use and cardiovascular outcomes: A large prospective cohort study. *International Journal of Cardiology*, *395*, 131567. DOI: 10.1016/j.ijcard.2023.131567

Nolde, M., Bahls, M., Friedrich, N., Dörr, M., Dreischulte, T., Felix, S. B., Rückert-Eheberg, I.-M., Ahn, N., Amann, U., Schwedhelm, E., Völzke, H., Lerch, M. M., Linseisen, J., Meisinger, C., & Baumeister, S. E. (2021). Association of proton pump inhibitor use with endothelial function and metabolites of the nitric oxide pathway: A cross-sectional study. *Pharmacotherapy*, *41*(2), 198–204. DOI: 10.1002/phar.2504

Shanika, L. G. T., Reynolds, A., Pattison, S., & Braund, R. (2023). Proton pump inhibitor use: Systematic review of global trends and practices. *European Journal of Clinical Pharmacology*, *79*(9), 1159.

Sherwood, M. W., Melloni, C., Jones, W. S., Washam, J. B., Hasselblad, V., & Dolor, R. J. (2015). Individual Proton Pump Inhibitors and Outcomes in Patients With Coronary Artery Disease on Dual Antiplatelet Therapy: A Systematic Review. *Journal of the American Heart Association*, *4*(11), e002245. DOI: 10.1161/JAHA.115.002245

Shi, W., Yan, L., Yang, J., & Yu, M. (2021). Ethnic variance on long term clinical outcomes of concomitant use of proton pump inhibitors and clopidogrel in patients with stent implantation. *Medicine*, *100*(6), e24366.

Tayal, R., Yasmin, S., Chauhan, S., Singh, T. G., Saini, M., Shorog, E., Althubyani, M. M., Alsaadi, B. H., Aljohani, F., Alenazi, M. A., Abutaily, S. A., & Ansari, M. Y. (2023). Are Proton Pump Inhibitors Contributing in Emerging New Hypertensive Population? *Pharmaceuticals*, *16*(10), 1387. DOI: 10.3390/ph16101387

Wenedy, A., Lim, Y. Q., Lin Ronggui, C. K., Koh, G. C. H., Chong, P. H., & Chew, L. S. T. (2019). A Study of Medication Use of Cancer and Non-Cancer Patients in Home Hospice Care in Singapore: A Retrospective Study from 2011 to 2015. *Journal of Palliative Medicine*, *22*(10), 1243–1251.

World Health Organization. (2025). *VigiAccess*. https://www.vigiaccess.org/

Ziccardi, M., Goyal, A., & Maani, C. V. (2025). Atrial Flutter. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK540985/