

Trend in Prescription Pattern in Heart Failure Medications

Septi Melisa¹; Christianus Heru Setiawan²; Daniel C.A. Nugroho^{3,4}; Muhammad Solihuddin Muhtar⁵; Dian Tri Wiyanti^{1,6}; Phan Thanh-Phuc¹; Nguyen Phung-Anh^{7,8,9}; Jason C. Hsu^{1,7,8,9*}

1. International Ph.D. program in Biotech and Healthcare Management, College of Management, Taipei Medical University, Taipei, Taiwan
 2. Ph.D. Program, School of Pharmacy, Taipei Medical University, Taipei, Taiwan
 3. Graduate Institute of Biomedical Informatics, Taipei Medical University
 4. Faculty of Medicine, Duta Wacana Christian University
 5. Graduate institute of Data Science, College of Management, Taipei Medical University, Taipei, Taiwan
 6. Faculty of Mathematics and Natural Sciences, Universitas Negeri Semarang, Indonesia
 7. Clinical Data Center, Office of Data Science, Taipei Medical University, Taipei, Taiwan
 8. Research Center of Health Care Industry Data Science, College of Management, Taipei Medical University, Taipei, Taiwan
 9. Clinical Big Data Research Center, Taipei Medical University Hospital, Taipei Medical University, Taipei, Taiwan;
- *Corresponding author

Background

The new 2022 AHA/ACC/HFSA Heart Failure Management Guidelines emphasize the goal of providing clinicians with patient-centered recommendations for preventing, diagnosing, and managing heart failure patients¹. Guideline-directed medical therapy (GDMT) for heart failure will be mostly determined by the clinical assessment from patient's history and physical examination. Our objective is to analyze the prescription patterns for heart failure among the Taiwanese population, aiming to gain a comprehensive understanding of the trends in prescription rates for individuals with heart failure in Taiwan.

Method

The data was collected from Taipei Medical University Clinical Research Database (TMUCRD) which consist of data from three hospitals in Taiwan (Taipei Medical University Hospital, Shuang Ho hospital, and Wanfang hospital). The data were mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM), and we used Observational Health Data Sciences and Informatics (OHDSI) ATLAS platform to create cohort definitions that included the first use of heart failure guideline directed medical therapy (GDMT) from 2008 to 2020.

The concept set for the cohort event was developed from class of medication for heart failure treatment, which are Angiotensin Receptor Blockers (ARB), Angiotensin Converting Enzyme Inhibitor (ACEi), Beta Blocker, mineralocorticoid receptor antagonist (MRA), Angiotensin Receptor/Neprilysin Inhibitor (ARNI), Sodium-glucose co-transporter 2 (SGLT2) inhibitors, and diuretics. We utilized cohort pathways to create sunburst plots to visualize the treatment pathway for three time period (2008-2012, 2013-2016, and 2017-2020) and used characterization to show patients' demographic. We created a table displaying the percentage of the initial five drug categories during each specific timeframe.

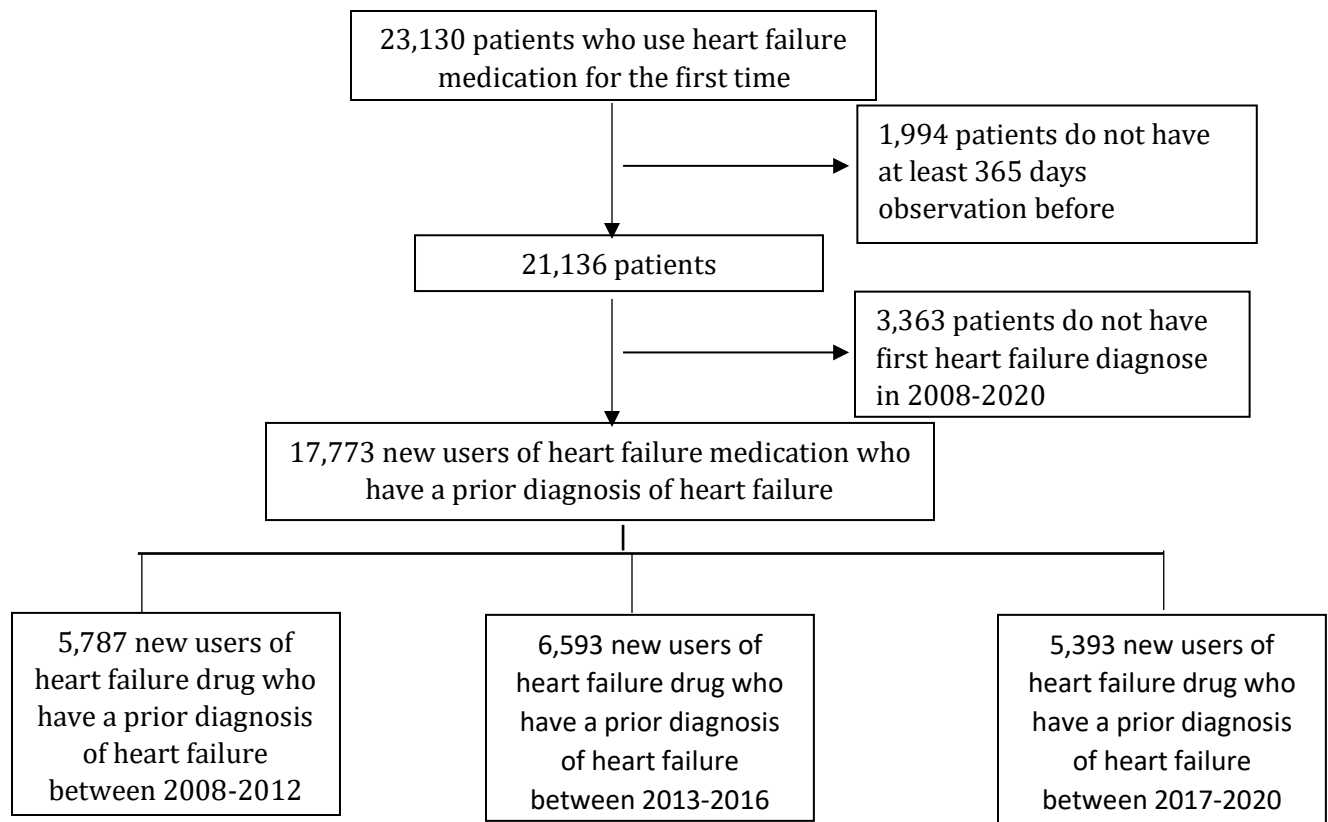


Figure 1. Study Cohort Flow Diagram

Result

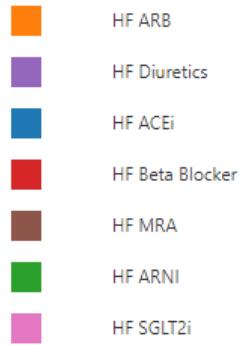
In our database, we identified 17,773 patients who had been diagnosed with heart failure and were prescribed at least one heart failure medication, following the 2022 guideline for heart failure treatment (see Figure 1.). The average age of individuals diagnosed with heart failure in our database was 66.49 years with a decrease in the mean age over time, indicating a shift towards a younger population being diagnosed with heart failure (see Table 1.). The Charlson Comorbidity Index (CCI) scores exhibited a consistent decline over time, potentially linked to the younger age distribution of the population and fewer comorbidities when diagnosed with heart failure.

Our analysis revealed a steady increase in the prescription of beta blockers over time, specifically between the time periods of 2008-2012 and 2013-2016. This finding aligns with the previous study in UK population that observed a rise in the use of beta blockers over a specific time frame ^{2,3}. A significant decline in the utilization of angiotensin receptor blockers has been observed from 2008-2012 to 2013-2016. This shift has resulted in beta blockers becoming the most frequently prescribed medication for heart failure (see Figure 2). However, the prescription rate for SGLT2 inhibitors remained lower compared to other drugs due to the fact that they were not recommended as the primary treatment for heart failure until 2022^{1,4}. Diuretics continue to be the third most frequently prescribed medication. Additionally, there has been a continued low utilization of mineralocorticoid receptor antagonists (MRAs) over the specified time period, which differs from a previous study that have reported higher utilization of MRAs ³. This probably because the prevalence of edema and chronic kidney disease in our population⁵.

Table 1. The characteristics of patient with heart failure

Covariates	Heart Failure patients			
	2008-2020 (N=17,773)	2008-2012 (N=5,787)	2013-2016 (N=6,593)	2017-2020 (N=5,393)
Age, years				
Mean (SD)	66.49 (16.43)	70.54 (14.44)	65.89 (16.85)	62.89 (16.96)
Gender, N (%)				
Male	8,467 (47.64)	2,542 (43.93)	3,414 (51.78)	2,746 (50.92)
Female	9,306 (52.36)	3,245 (56.07)	3,179 (48.22)	2,647 (49.08)
Charlson Comorbidity Index (CCI)				
Mean (SD)	2.96 (2.13)	3.22 (2.22)	2.93 (2.16)	2.71 (1.97)
Condition Era Start Long Term, N (%)				
Essential hypertension	9,590 (53.96)	1,856 (32.07)	1,724 (26.15)	683 (12.66)
Chest pain	3,035 (17.08)	901 (15.57)	1,214 (18.41)	920 (17.06)
Chronic ischemic heart disease	3,032 (17.06)	953 (16.47)	1,317 (19.98)	762 (14.13)
Cardiac arrhythmia	2,559 (14.40)	925 (15.98)	1,027 (15.58)	607 (11.26)
Type 2 diabetes mellitus without complication	2,300 (12.94)	988 (17.07)	915 (13.88)	656 (12.16)
Hyperlipidemia	2,018 (11.35)	843 (14.57)	723 (10.97)	452 (8.38)
Urinary tract infectious disease	1,642 (9.42)	694 (11.99)	585 (8.87)	363 (6.73)
Gastro-esophageal reflux disease with esophagitis	1,304 (7.34)	355 (6.13)	536 (8.13)	413 (7.66)
Atrial Fibrillation	1,253 (7.05)	439 (7.59)	512 (7.77)	302 (5.60)
Chronic Obstructive Lung Disease	1,098 (6.18)	546 (9.43)	404 (6.10)	204 (3.78)
Coronary atherosclerosis	933 (5.25)	612 (10.58)	304 (4.61)	17 (0.32)
Edema	1,241 (6.98)	466 (8.05)	538 (8.16)	237 (4.39)
Chronic Kidney Disease	818 (4.60)	353 (6.10)	350 (5.31)	115 (2.13)
Drug Era Start Long Term, N (%)				
Furosemide	7,171 (40.35)	2,667 (46.09)	2,712 (41.13)	1,792 (33.23)
Valsartan	6,315 (35.53)	2,288 (39.54)	2,103 (31.90)	1,924 (35.68)
Aspirin	6,270 (35.28)	2,006 (34.66)	2,447 (37.12)	1,817 (33.69)
Bisoprolol	5,304 (29.84)	1,443 (24.94)	1,930 (29.27)	1,950 (36.16)
Acetaminophen	4,854 (27.31)	1,236 (21.36)	1,975 (29.96)	1,643 (30.47)
Nitroglycerin	4,516 (25.41)	1,238 (21.39)	1,752 (26.57)	1,526 (28.30)
Amlodipine	4,080 (22.96)	1,632 (28.20)	1,413 (21.43)	1,035 (19.19)
Acetylcysteine	3,049 (17.16)	1,116 (19.38)	1,169 (17.73)	764 (14.17)
Famotidine	2,609 (14.68)	701 (12.11)	962 (14.59)	946 (17.54)
Atorvastatin	2,587 (14.56)	1,015 (17.54)	886 (13.44)	686 (12.72)
Diclofenac	2,551 (14.35)	964 (16.66)	919 (13.94)	668 (12.39)

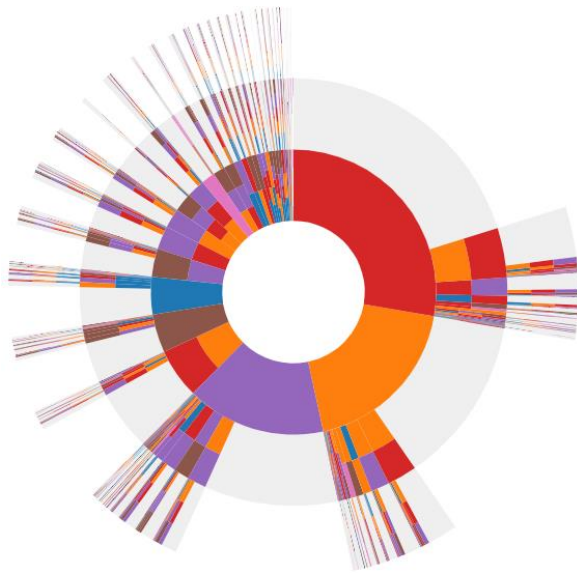
Event Cohorts



Target Cohort

New user of HF drug

- Target cohort count: 17,773
- Persons with pathways count: 17,773
- Persons with pathways portion: 100.0%

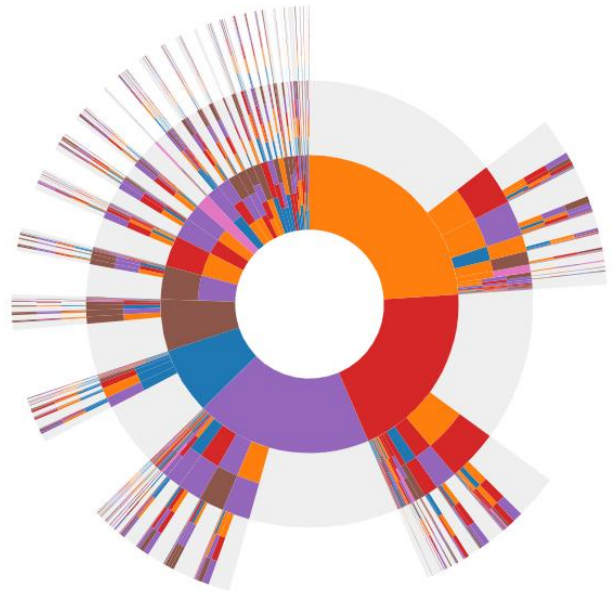


a. 2008-2020

Target Cohort

New user of HF drug (2008 - 2012)

- Target cohort count: 5,787
- Persons with pathways count: 5,787
- Persons with pathways portion: 100.0%

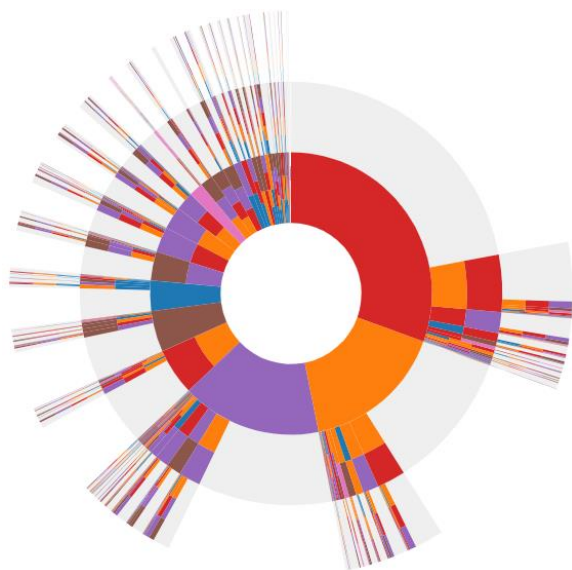


b. 2008-2012

Target Cohort

New user of HF drug (2013 - 2016)

- Target cohort count: 6,593
- Persons with pathways count: 6,593
- Persons with pathways portion: 100.0%



b. 2013-2016

Target Cohort

New user of HF drug (2017 - 2020)

- Target cohort count: 5,393
- Persons with pathways count: 5,393
- Persons with pathways portion: 100.0%



c. 2017-2020

Figure 2. Heart Failure Prescribing Patterns from 2008 to 2020

Table 2. Proportions of the primary drug class employed in the inner circle during each timeframe.

Overall		2008 - 2012		2013 - 2016		2017 - 2020	
Drug	N (%)	Drug	N (%)	Drug	N (%)	Drug	N (%)
Beta Blocker	3583 (20.16)	ARB	1386 (23.95)	Beta Blocker	2012 (30.52)	Beta Blocker	1780 (33.01)
ARB	2254 (12.68)	Beta Blocker	1134 (19.60)	ARB	1078 (16.35)	ARB	903 (16.74)
Diuretics	1796 (10.11)	Diuretics	1107 (19.13)	Diuretics	1059 (16.06)	Diuretics	638 (11.83)
ARB + Beta Blocker	810 (4.56)	ACEi	417 (7.21)	ARB + Beta Blocker	354 (5.37)	ARB + Beta Blocker	460 (8.53)
Beta Blocker	666 (3.75)	MRA	327 (5.65)	MRA	310 (4.70)	ARB + Diuretics + Beta Blocker + MRA	229 (4.25)

Conclusion

The findings of this study indicate that the prescription rate for beta blockers and angiotensin receptor blockers for patients with heart failure has changed. The prevalence of edema and chronic kidney disease within our population likely contributes to the continued prominence of diuretics as the third most prescribed medication for individuals suffering from heart failure. The limitation of our study is the absence of data on laboratory results and procedures, preventing us from distinguishing between patients with heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF).

References

1. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(18):e895-e1032.
2. Uijl A, Vaartjes I, Denaxas S, Hemingway H, Shah A, Cleland J, et al. Temporal trends in heart failure medication prescription in a population-based cohort study. *BMJ Open*. 2021;11(3):e043290.
3. Teng T-HK, Tromp J, Tay WT, Anand I, Ouwerkerk W, Chopra V, et al. Prescribing patterns of evidence-based heart failure pharmacotherapy and outcomes in the ASIAN-HF registry: a cohort study. *The Lancet Global Health*. 2018;6(9):e1008-e18.
4. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med*. 2015;373(22):2117-28.

5. Chiang CE, Hung CL, Wu YW, Lin TH, Ueng KC, Sung SH, et al. 2023 Consensus of Taiwan Society of Cardiology on the Pharmacological Treatment of Chronic Heart Failure. *Acta Cardiol Sin.* 2023;39(3):361-90.