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PRESCRIBING TRENDS OF EVIDENCE BASED PHARMACOTHERAPY POST MYOCARDIAL INFARCTION SYSTEMATIC REVIEW STUDY

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Abstract:

This systematic review investigates prescribing trends of evidence-based pharmacotherapy post-myocardial infarction (MI) and aims to elucidate age-based, gender-specific, and socioeconomic disparities in the administration of evidence-based therapies (EBTs). Through a comprehensive search of major medical databases and adherence to PRISMA guidelines, this study synthesizes evidence from diverse sources to provide a nuanced understanding of prescribing patterns. The study findings reveal concerning age-based inequalities, suggesting that certain age groups may be systematically undertreated post-MI, highlighting the imperative for targeted interventions to ensure equitable access to evidence-based pharmacotherapy across all age demographics. Moreover, gender disparities in EBT prescribing post-MI are unveiled, emphasizing the need for gender-sensitive approaches in healthcare delivery. The research underscores the importance of addressing these discrepancies to optimize the quality of post-MI care for both male and female patients.

Furthermore, the study uncovers socioeconomic status as a critical determinant of inequalities in prescribing EBTs post-MI. Patients from lower socioeconomic strata face barriers to accessing and adhering to recommended therapies, pointing to a need for interventions that address these social determinants of health. As a recommendation, policymakers and healthcare providers are urged to prioritize strategies that ensure equal access to evidence-based pharmacotherapy post-MI, irrespective of socioeconomic status. Lastly, this systematic review consolidates and builds upon the most notable trends identified in prior research, offering a comprehensive overview of prescribing patterns. This synthesis allows for a better understanding of persistent challenges and evolving trends, enabling healthcare professionals and policymakers to implement targeted strategies that bridge gaps in care and enhance the effectiveness of evidence-based pharmacotherapy in the post-MI population.

Introduction:

With high rates of morbidity and death, cardiovascular diseases—myocardial infarction (MI) in particular—represent a serious worldwide health threat. A myocardial infarction, also referred to as a heart attack, is caused by a part of the heart muscle receiving insufficient blood flow. If left untreated, this condition can have serious repercussions. Improving long-term outcomes and preventing recurrent cardiac episodes depend heavily on the care of post-MI patients. In this context, evidence-based treatments (EBTs) is essential since it provides a tried-and-true method of enhancing post-MI care (Fornasini et al., 2010).

Understanding the etiology of MI and creating evidence-based guidelines for treating these patients have come a long way in recent years. These recommendations, which aim to enhance patient outcomes and care quality, take into account the most recent scientific findings. Medications such as antiplatelet medicines, beta-blockers, statins, angiotensin receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, and beta-blockers are commonly used in pharmacotherapy after MI. It is advised that these drugs target particular risk factors and the underlying pathophysiological mechanisms of MI in order to lower the likelihood of further cardiovascular events (Gale et al., 2011).

It is nevertheless difficult to make sure that these evidence-based treatments are regularly recommended and followed in clinical settings. Prescription trends have changed as a result of new drugs being introduced and the field of medicine changing. It is imperative to evaluate the degree

to which healthcare practitioners follow these evidence-based guidelines and determine whether prescription patterns differ between locations and healthcare environments (Tran et al., 2004).

To address this critical issue, this systematic review study seeks to comprehensively examine the prescribing trends of evidence-based pharmacotherapy following myocardial infarction. By synthesizing the existing literature, the study aim to assess the current state of clinical practice, identify any gaps or discrepancies in adherence to evidence-based guidelines, and explore factors that may influence prescribing patterns. Understanding these trends is essential for healthcare practitioners, policymakers, and researchers, as it can inform efforts to enhance the quality of care provided to post-MI patients and ultimately improve their long-term outcomes.

Study problem and Questions:

When it comes to maximizing the care of patients who have had a myocardial infarction (MI), the prescribing patterns of evidence-based medication are crucial. Though there are clear clinical recommendations, there are differences in prescribing practices, which raise serious questions regarding the quality of care and long-term results for these patients. This systematic review study's primary research question is to be answered as follows:

"What are the current prescribing trends of evidence-based pharmacotherapy post-myocardial infarction, and what factors contribute to variations in adherence to clinical guidelines?"

This main question is subdivided into the following sub-questions:

1. What are the age-based inequalities in prescribing EBTs for MI?
2. What are the inequalities by gender in prescribing EBTs for MI?
3. What are the inequalities by socioeconomic status in prescribing EBTs for MI?
4. What are the most notable trends in prescribing EBTs for MI?

This research problem highlights the need to comprehensively evaluate the real-world application of EBTs and explore the underlying factors that drive variations in prescription practices. Understanding the extent to which healthcare providers adhere to established guidelines and the reasons for any deviations is crucial for improving post-MI patient care and ultimately reducing the burden of cardiovascular disease.

Study Method:

This systematic review study aims to investigate the prescribing trends of evidence-based pharmacotherapy following myocardial infarction (MI) to better understand the real-world application of clinical guidelines. The study design adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring methodological rigor and transparency. A comprehensive search strategy, executed by consulting medical librarians, target major medical databases, including PubMed, Embase, Web of Science, and the Cochrane Library. The search terms encompassed myocardial infarction, pharmacotherapy, prescription patterns, and evidence-based medicine, thereby encompassing relevant literature. Inclusion criteria require studies to be published in English, peer-reviewed, and centered on prescribing trends of evidence-based pharmacotherapy post-MI, while studies involving pediatric populations or lacking focus on pharmacotherapy were excluded.

The study employed a two-tiered screening process, involving initial title and abstract screening, followed by full-text review, conducted by two independent reviewers. Data was extracted using a standardized form, capturing key study characteristics, patient demographics, medication types prescribed, and factors influencing prescribing trends. Quality assessment was carried out using appropriate tools, such as the Newcastle-Ottawa Scale for observational studies and Cochrane Collaboration's tool for randomized controlled trials, ensuring a comprehensive evaluation of the included studies. Data synthesis involved both descriptive analysis and, when applicable, meta-analysis to quantify overall prescribing patterns. Subgroup analyses explored potential sources of heterogeneity, and qualitative synthesis uncover factors contributing to variations in prescribing trends. The study's findings were reported following PRISMA guidelines, offering valuable insights into evidence-based pharmacotherapy practices post-MI and providing a foundation for future research and policy development in cardiovascular care.

Results:

Inequalities in prescribing of EBTs for MI

After experiencing a MI a number of medications have been shown to improve outcomes. Unless contraindicated, patients should be discharged from hospital with these medications including an antiplatelet agent (aspirin or clopidogrel), an ACEI or ARB, a β-blocker and a statin.

Inequalities by age in prescribing of EBTs for MI

Unadjusted analyses

Older patients with MI less commonly undergo cardiac procedures and they receive suboptimal treatment with EBTs compared to younger patients (Udvarhelyi et al., 1992; Rosenthal et al., 1994). Older patients are less commonly treated with β-blockers (Gurwitz et al., 1993; Barakat et al., 1999) and aspirin, despite evidence that secondary prevention reduces mortality post-MI (Krumholz et al., 1995; Salomaa et al., 2007; DeWilde et al., 2003; Trialists' Collaboration, 1994). However, older patients are more likely to be prescribed ACEI than younger patients, though some have showed no difference (Table 6, unadjusted studies) (Kvan et al., 2006; Ohlsson et al., 2010; Pilote et al., 2004; Austin et al., 2008). In one study of Pilote et al. (2004), age was stratified by sex and there was no difference in prescribing of ACEI by age in either sex. β-blockers were less often prescribed in older compared to younger patients, whereas the opposite was reported for the prescription of CCBs (Kvan et al., 2006; Ohlsson et al., 2010; Pilote et al., 2004; Austin et al., 2008; Excoffier et al., 2001). Prescribing of statins was lower in older compared to younger patients although one study reported that older patients were more likely to be prescribed lipid lowering drugs (LLD) than younger patients (Ohlsson et al., 2010).

Adjusted analyses

In adjusted studies older patients were significantly less likely to be prescribed aspirin (Macchia et al., 2012; Rathore et al., 2003; Spencer et al., 2001). Studies of prescribing of ACEIs or ARBs are conflicting. Some studies reported that older patients were more likely to be prescribed an ACEI or ARB, (Spencer et al., 2001) while others reported that older patients were less likely to receive an ACEI or ARB (Macchia et al., 2012; Rathore et al., 2003; Gislason et al., 2005). The studies by Marandi et al, (2010) and Winkelmayer et al. (2008), are the only two studies to report that older patients were more likely to receive β-blockers though the difference was not statistically significant. Prescribing of statins was significantly lower among older patients in all studies that carried out multivariable adjustment (Macchia et al., 2012, Spencer et al., 2001; Rasmussen et al., 2005).

There are clearly differences in prescribing of EBTs by age, however, studies were limited by presenting unadjusted results or only adjusting for a few variables. Other studies grouped drugs into less specific groups such as lipid lowering drugs, or examined the relationship in patients with a

narrow age range. Small sample size may influence some studies, as well as short period of follow-up. Limited age grouping in some studies would not show what is the effective age for prescribing medication. The most recent study was conducted between 2007 and 2008, however an earlier one was in 1984.

A number of studies examined the relationship between age and the prescribing of evidence based therapies following a diagnosis of CHD. The majority of previous studies demonstrated that older age groups were less likely to receive EBTs compared to younger age groups (Table 6). However, studies were limited by a number of factors including study design, data collection methods, and/or statistical methods.

Limitations in the reporting of the literature

The score for literature describing the association between age and prescribing EBTs after MI ranged from 45% to the highest score 70.4% (Table 6). The study design indicated using common terms such as cross-sectional, in the majority of the studies, however, five studies did not state the study design either in the title or abstract (Spencer et al., 2001; Tran et al., 2004). Four studies failed to clearly state their objectives (Winkelmayer et al., 2008; Rasmussen et al., 2005; Heller et al., 2000; Rochon et al., 1999). The study design was clearly presented in most studies, though three studies did not describe it clearly in the methods.(Rathore et al., 2003; Spencer et al., 2001; Krumholz, 1998). The eligibility criteria of individuals included in the study was not mentioned in one study (Barakat et al., 1999). A number of studies did not clearly define and describe how their variables were handled (Spencer et al., 2001; Tran et al., 2004; Heller et al., 2000; Barakat et al., 1999). Although bias is common in the observational studies, none of the studies addressed or discussed potential biases in their methods. All studies described their statistical methods with the exception of one study (Whincup et al., 2002). Rathore *et al. (2003)* discussed and explained how missing data were handled, however other studies did not. None of the studies described any sensitivity analysis.

A number of studies did not define the study cohort clearly, for example, reporting the number of potentially eligible individuals, only reporting the number of those who survived after discharge (Kvan et al., 2006; Pilote et al., 2004; Austin et al., 2008; Spencer et al., 2001; Rasmussen et al., 2005; Heller et al., 2000; Rochon et al., 1999; Whincup et al., 2002; Carey et al., 2012; Krumholz,

1998). The characteristics of patients included were not described in two studies (Spencer et al., 2001; Barakat et al., 1999). Only two studies indicated the number of missing data in their results (Carey et al., 2012, Excoffier et al., 2001). Five studies did not report the number of outcome events (Spencer et al., 2001; Winkelmayer et al., 2008; Whincup et al., 2002; Barakat et al., 1999; Avanzini et al., 1997). A clear and full presentation of outcomes including unadjusted results and results adjusted for potential confounders can help the reader to compare and judge the magnitude and direction of the influence of the confounders. However, only six studies presented these results (Rochon et al., 1999, Whincup et al., 2002; Barakat et al., 1999). Only three studies discussed their limitations, including the potential sources of bias.

Limitations in the design and analysis of studies included in the literature review

A number of gaps were also identified in the previous literature. There are clear differences in prescribing of EBTs by age after MI, however, a number of studies were unable to adjust the results for confounders or only able to adjust for a few confounders ((Macchia et al., 2012, Spencer et al., 2001; Rasmussen et al., 2005; Tran et al., 2004; Gislason et al., 2005; Heller et al., 2000). The majority of American and Canadian studies used prescription data between 1987 and 1997, which may not be relevant to current clinical practice. Also, these studies were limited to patients in the age group over 64 years old. Macchia *et al. (2012)* and Winkelmayer *et al. (2008)* overcame that by using a large sample size, adjusted result for a wide range of confounders, and examined prescribing of a wide range of EBTs, however, their studies only included patients who survived at least 1 and ≥ 120 days in the year after diagnosis, i.e. both studies suffered from a selection bias. A number of studies were able to avoid selection bias, however, they were limited to a few EBTs, (Gislason et al., 2005; Barakat et al., 1999; Krumholz, 1998) or grouped drugs into less specific groups such as lipid lowering drugs, or examined the relationship in patients within a narrow age range.

In summary, there were a number of limitations in the literature surrounding the association between sex and prescribing of EBTs in CHD. There was also a wide range in the quality of reporting of studies as assessed by the STROBE guidelines. Although some studies were well reported, they associated with some limitations such as Rathore *et al. (2003)* which was exposed to the selection bias. Furthermore, the study by Ohlesson *et al. (2010)* is a well reported study but used unadjusted

analyses and was limited to few drug groups. The study by Gislason *et al. 2008)* benefited from a high quality of reporting and had a number of strengths over other studies. The authors adjusted for a wide range of confounders, but not socioeconomic status, but they did use a nationwide population data set for all hospitals in Denmark. This study demonstrated that older patients are less commonly prescribed EBTs compared to younger patients.

Table 1 Inequalities by age in prescribing of EBTs after myocardial infarction

Study	Design /subject/year	Age range/	Prescribing	Medications	Prescribing percentage Eldest vs. youngest age group	OR, 95% CI Old vs. young	Adjustment	P values / statistical significance	STROBE Score (%)
Martinez et al . 1998 **Spain**	Retrospective cross-sectional N=324 and 190 (514) 1989-91/ 1994	< 51 51-60 61-70 71-90	At time of discharge from hospital discharge form	ACEI β-blockers	Not available	1.12 (0.37-3.38) 0.2 0 (0.10-0.38)	Unadjusted	Not reported	11/22 (50%)
Excoffier et al, 2001 **France**	Cross-sectional N=2102 Sep 1993-Jan 95	≤ 65, 62-75, > 75	At discharge from the medical chart	ACEI β-blockers CCB	Not available	1.20 (1.11-1.30) 0.65 (0.59-0.70) 1.17 (1.08-1.27)	Unadjusted	Not reported	15/22 (68%)
Austin et al., 2008 **Canada**	Retrospective longitudinal cohort N=8706 2005-06	65-69, 70-74, 75-79, ≥ 80	Within 90 days post-discharge Used linked administrative database	ACEI β-blockers Statins	74.6 vs. 81.0 75.0 vs. 81.5 71.3 vs. 87.9	Not reported	Unadjusted	Not reported	12/22 (54.5%)
Kvan et al 2006 **Norway**	Retrospective cohort A three months period N=901 1999/2000	≥ 80 vs. < 80	After 6 months post discharge treatment obtained from the hospital records	ACEI Aspirin CCB β-blockers Statins	48 vs. 32 72 vs. 86 15 vs. 13 67 vs. 85 9.0 vs. 72	Not available	Unadjusted	Not reported	11/22 (50%)
Ohlesson et al, 2010 **Sweden**	Retrospective longitudinal cohort N=1364 2006	17-59, 60-69 70-79	Within three months post discharge 1st MI	ACEI LLD	65 vs. 70 78 vs. 92	Not reported	Unadjusted	Not reported	15.5/22 (70%)
Pilote et al. 2004	Cross sectional N=28647	65-74, 75-84 >85 Men	Within 90 days post-discharge	ACEI β-blockers CCB Statins	58.0 vs. 57.0 48.0 vs. 71.0 33.0 vs. 29.0 10.0 vs. 44.0	Not reported	Unadjusted	Not reported	12.5/22 (57%)

Canada (Ontario)	1997-2000	Women		ACEI β-blockers CCB Statins	59.0 vs. 59.0 49.0 vs. 68.0 32.0 vs. 34.0 9.00 vs. 46.0				
Rathore et al 2003 **USA**	Cross-sectional N=96364 1994-96	65-69, 70-74, 75-79,80-84, ≥ 85	At discharge 1st MI	ACEI Aspirin β-blockers	57.1 vs. 61.6 73.6 vs. 76.0 61.8 vs. 55.3	0.90 (0.86-0.95)* 0.96 (0.95-0.98) 0.88 (0.85-0.92)	Demographic characteristic, medical history, admission findings, and comorbidities	0.05 <0.0001 0.02	15.5/22 (70.4%)
Macchia et al 2012 **Italy**	Three longitudinal cohorts N=21423 2003-04 2005-06 2007-08	>75 vs. ≤ 75‡ Men Women	Post-discharge follow for one year	ACEI/ARBs Aspirin β-blockers Statins ACEI/ARBs Aspirin β-blockers Statins	79.1 vs. 79.3 78.5 vs. 87.0 54.6 vs. 73.1 63.2 vs. 85.6 77.3 vs. 81.3 73.4 vs. 83.2 54.6 vs. 73.9 55.1 vs. 81.1	0.75 (0.67-0.83) 0.60 (0.54-0.67) 0.46 (0.42-0.50) 0.31 (0.28-0.34) 0.59 (0.53-0.65) 0.45 (0.40-0.49) 0.43 (0.39-0.46) 0.22 (0.20-0.24)	Sex, previous CHD, diabetes, stroke, TIA, atrial fibrillation, COPD, depression and malignancy	NA	15/22 (68%)
Marandi et al. 2010 **Estonia**	Retrospective longitudinal Cohort N=4025 2004-05	20-39, 40-59, 60-79, 80-99	One year post discharge follow up, 1st MI, Survived more than 30 days	ACEI β-blockers Statins	Not reported	5.69 (3.66-8.82)+ 1.93 (0.58-6.47) 0.17 (0.02-1.37)+	Sex	0.05 NS NS	13/22 (59%)
Tran et al. 2004 **Canada**	Retrospective Cohort study N=4524 1994-96	≥ 65 vs. <65	At discharge	ACEI	Not reported	1.46 (1.22-1.74)	Contraindications to therapy	Not reported	12.5/22 (57%)
Heller et al 2000 **USA**	Retrospective longitudinal Cohort N=9534 1994-1997	65-69, 70-74, 75-79, 80-84, ≥ 85	Outpatients prescription database within 90 days post discharge	β-blockers	Not reported	1.00 1.09 (0.91-1.30) 1.07 (0.90-1.27) 1.01 (0.85-1.21) 0.84 (0.69-1.01)	Demographic and year of MI	------- 0.3 0.4 0.8 0.06	11.5/22 (52%)
Rasmussen et al 2005	Retrospective longitudinal cohort N=17875 1995-2002	30-44 45-54 55-64 64-74 75-84 ≥ 85	Within 6 months post discharge Follow statins purchased after 1st MI	Statins	Not reported	0.89 (0.77-1.03) 1.22 (1.09-1.37) 1.00 0.55 (0.50-0.61) 0.19 (0.17-0.21) 0.02 (0.02-0.03)	Sex, concomitant medications, hospital type	Not reported	15/22 (68%)

Denmark									
Winkelmayer et al 2008 **Austria**	Cross-sectional N=4105 2004	70-89 vs. < 50 ≥ 90 vs. < 50	Within 120 days post discharge 1st MI	ACEI/ARBs β-blockers statins ACEI/ARBs β-blockers statins	Not reported	1.48 (1.19-1.85) 1.05 (0.83-1.33) 1.08 (0.86-1.36) 0.73 (0.59-0.90) 0.62 (0.51-0.76) 0.39 (0.32-0.47)	Sex, length of stay at hospital, concomitant medications	Not reported	12.5/22 (57%)
Krumholz et al[26] **USA**	Retrospective cross-sectional N=45308 1994/1995	65-74, 75-84, ≥ 85	At discharge	β-blockers		1.00 0.92 (0.90-0.94) 0.76 (0.73-0.79)	Sex, race, medical history, hospital and discharge medications, clinical status, hospital complications, hospital procedures, length of stay	Not reported	14/22 (63%)
Gislason et al 2005 **Denmark**	Retrospective longitudinal cohort N=55315 1995-2002	30-59 60-69 70-79 ≥ 80	Within 30 days post discharge 1st MI	ACEI β-blockers	27.1 vs. 25.3 41.9 vs. 71.9	0.61 (0.57-0.65) 0.31 (0.29-0.33)	Sex, calendar year, concomitant treatment (loop diuretic & antidiabetic drugs)	Not reported	15/22 (68%)
Spencer et Al (2001) **USA**	Cross-sectional N=5739 1986-1997	<55, 55-64, 65-74, ≥ 75	At time of discharge	ACEI Aspirin β-blockers LLD	Not reported	1.37 (1.07-1.75) 0.70 (0.57-0.85) 0.42 (0.35-0.52) 0.24 (017-0.34)	Sex, medical history and clinical characteristic	Not reported	10.5/22 (48%)
Barakat et Al 1999 **England**	Prospective longitudinal cohort N=1225 1988-1994	< 60, 60-69 ≥ 75	At time of discharge	Aspirin β-blockers	Not reported	0.88 (0.51-1.50) 0.25 (0.16-0.37)	Sex, diabetes, previous MI. Q wave infarction, left ventricular failure	0.6 <0.001	10/22 (45%)
Rochon et Al 1999 **Canada**	Retrospective longitudinal cohort N=15542 1993-1995	66-74, 75-84, ≥ 85	Within a year after hospital discharge (administrative database)	β-blockers		1.00 1.5 (1.4-1.6)± 2.8 (2.5-3.2) ±	Sex, Charlson comorbidity score, contraindication, residence of long term facilities	Not reported	14.5/22 (66%)
Carey et al 2012	Retrospective longitudinal cohort N=9367	30-49 50-59 60-64 65-69 70-74	Within 6 months post discharge, obtained from primary care database 1st MI	Statins	81.1 84.3 79.0 78.6 72.6	0.96 (0.93-1.00)* 1.00 0.94 (0.90-0.94) 0.93 (0.90-0.96) 0.86 (0.83-0.89)	Sex and practice	Not reported	14.5/22 (66%)

UK	1997-2006	75-79 80-84			66.3 57.7	0.78 (0.75-0.82) 0.68 (0.64-0.72)			
Avanzini et al 1997 **Italy**	Retrospective longitudinal cohort N=9452 N=10407 N=16958 1984-1993	>70 vs. ≤ 70 GISSI-1 GISSI-2 GISSI-3	Post discharge, data from	β-blockers	Not reported	---------- ---------- 0.25 (0.18-0.35) 0.50 (0.42-0.59) 0.45 (0.40-0.50)	Sex, comorbidities, AMI characteristic at admission, procedure complications, treatment at discharge	---------- ---------- < 0.01 < 0.01 < 0.01	11.5/22 (52%)
Whincup et al 2002 **Britain**	Cross-sectional survey N=286 1998-2000	< 60, 60-69, ≥ 70	Post discharge, general practice records and patients questionnaire	LLD	7.00 vs. 49.0	0.18 (0.05-0.62)	Previous revascularisation, age at last diagnosis, year of last diagnosis, manual social classes, smoking and geographical residence	0.06	10/22 (45%)

* Risk ratio, ‡ OR Reference is men ≤ 75 (younger) for both men and women age >75, + Reference is age group (40-59). ± Indicated that older patients at higher risk of not receiving a β-blocker.

2.5.2 Inequalities by sex in prescribing of EBTs for MI

Unadjusted analyses

Prescribing rates of EBTs for secondary prevention following a MI vary by sex, with women being prescribed EBTs at a lower rate than men. In unadjusted analyses women were less likely to receive a prescription for aspirin after a MI than men (Table 7, unadjusted) (Barakat et al., 2000; Clarke et al., 1994; Di Cecco et al., 2002; Hirakawa et al., 2006; Janion-Sadowska et al., 2011). Only one study suggested an opposite trend with women aged less than 65 years being more likely to be prescribed aspirin than men of the same age (Hirakawa et al., 2005). Studies of prescribing rates of ACEI conflicted, some reporting no difference by sex, however (Austin et al., 2008, Barakat et al., 2000, Di Cecco et al., 2002; Janion-Sadowska et al., 2011) and others reported that men received ACEIs more often than women (Clarke et al., 1994, Hirakawa et al., 2006, Hirakawa et al., 2005). One study reported that women were more likely to be prescribed an ACEI (Martinez et al., 1998). Women were less commonly prescribed β-blockers,(Barakat et al., 2000, Hirakawa et al., 2006, Tunstall-Pedoe et al., 1996) however, two studies reported a non-significant trend towards women being more likely to be prescribed a β-blocker than men (Janion-Sadowska et al., 2011, Hirakawa et al., 2005) and one reported no difference (Austin et al., 2008). Three studies examined the sex differences in prescribing of CCBs. In a Scottish study, (Tunstall-Pedoe et al., 1996) women were more likely to be prescribed a CCB than men (30.8% vs. 26.4%), a finding replicated in two studies from Japan (Hirakawa et al., 2006, Hirakawa et al., 2005). The proportion of women prescribed a statin was lower than men in two studies (Austin et al., 2008, Janion-Sadowska et al., 2011). Conversely, women were more likely to be prescribed a lipid lowering drug in studies from Japan,(Hirakawa et al., 2006, Hirakawa et al., 2005) but not in studies from Canada (Di Cecco et al., 2002) and Sweden (Ohlsson et al., 2010).

Adjusted analyses

In multivariable analyses (Table 7, adjusted studies), women were less likely to receive aspirin compared to men. One age adjusted study reported that women and men were almost equally likely to be prescribed an ACEI, (Hanratty et al., 2000) though all other studies reported that women were less likely to be prescribed an ACEI or ARBs than men (Macchia

et al., 2012, Spencer et al., 2001, Gislason et al., 2005, Hanratty et al., 2000 Winkelmayer et al., 2008). Most studies reported that women were less likely to be prescribed β-blockers(Macchia et al., 2012- Spencer et al., 2001, Gislason et al., 2005 Rasmussen et al., 2005, Hanratty et al., 2000 Wei et al., 2004). However, a study by Rathore *et al. (2000)* included patients diagnosed with MI between 1994 and 1996 and examined the difference in those older than 64 years. This study showed no difference in the prescribing of β-blockers by sex. Heller *et al*. 2000 reported that after adjustment for demographics and year of MI, women were significantly more likely to receive β-blockers than men (OR 1.12; 95%CI 1.01-1.24, p=0.03). In Scotland, Weir *et al (2008)* examined 865 patients with a first MI and found that men were significantly more likely to be prescribed a β-blocker than women (OR 1.59; 95%CI 1.21-2.10) but the difference disappeared after adjustment (OR 0.98; 95% CI 0.70-1.37). Griffith *et al. (2005)* reported that after adjusting for confounders, women were significantly (p=0.05) more likely to be prescribed β-blockers than men. In the GISSI trials, such as Rathore et al. (2000) study, women were more likely to receive β-blockers, however, the difference was attenuated with time. Two studies reported that women were more likely to be prescribed CCBs than men, though this did not reach statistical significance (Spencer et al., 2001, Hanratty et al., 2000). In general, statins were less likely to be prescribed for women compared to men, however, two studies reported that women were more likely to be prescribed a statin (Hanratty et al., 2000, Griffith et al., 2005).

Limitations in the reporting of the literature

The quality of the reporting of these studies was assessed by using STROBE checklist and ranged from 41% to 70%. In this section I will discuss the studies that examined sex inequalities in prescribing of EBTs which I did not discuss in the previous section 2.4.1 (Barakat et al., 2000- Hirakawa et al., 2005, Hanratty et al., 2000- Williams et al., 2004, Rathore et al., 2000- Sial et al., 1994) The quality of reporting for these studies ranged from 41% to the highest score 63.6%. Three studies did not indicate the study design in their study title or abstract (Clarke et al., 1994, Hirakawa et al., 2006, Janion-Sadowska et al., 2011). The study background was described clearly in almost all studies but one study did not explain the scientific background clearly (Hirakawa et al., 2006). Specific study objectives

were not stated in three studies (Barakat et al., 2000; Clarke et al., 1994, Janion-Sadowska et al., 2011). Criteria of eligibility was not described and discussed in four studies (Clarke et al., 1994;, Di Cecco et al., 2002; Janion-Sadowska et al., 2011, Wei et al., 2004). Four studies did not define the variables included in their study clearly, including outcome variables and confounding variables (Hirakawa et al., 2006, Barakat et al., 2000, Hanratty et al., 2000 Williams et al., 2004). No study adequately described or discussed potential sources of bias. All studies described the statistical methods used for analyses.

All studies reported the number of potential and eligible participants in their studies with the exception of one (Rathore et al., 2000). Only one study discussed and described the reasons for patient exclusions (Griffith et al., 2005). Two studies did not described the cohort characteristic (Janion-Sadowska et al., 2011, Rathore et al., 2000). Three studies described the missing data of included participants (Di Cecco et al., 2002, Williams et al., 2004, Sial et al., 1994). The number of outcome events was summarised clearly in the majority of studies, though it was not reported in three studies (Barakat et al., 2000 , Wei et al., 2004, Rathore et al., 2000). Six studies presented the unadjusted and adjusted analyses in their results, however, other studies either presented unadjusted or adjusted results. One study discussed the limitations including potential sources of bias (Barakat et al., 2000 Four studies did not interpret their results clearly. Di Cecco et al., 2002, Hanratty et al., 2000 Williams et al., 2004, Wei et al., 2004).

Limitations in the design and analysis of studies included in the literature review

A number of gaps and limitations were also identified in the previous literature. Since the prescribing of EBTs is the main focus in these studies, many of the studies were limited to one or two drugs (Barakat et al., 2000, Rathore et al., 2000- Sial et al., 1994). A number of studies used data for patients diagnosed between 1988 and 1997 and therefore prescribing may not represent current clinical practice (Barakat et al., 2000, Hanratty et al., 2000, Wei et al., 2004, Sial et al., 1994). The study by Griffith *et al*. Griffith et al., 2005 conducted in the Southwest of Scotland, had a number of strengths including the study design, a prospective cohort, which enabled EBTs to be collected at time of discharge, examined prescribing inequalities for almost all recommended EBTs and adjusted for a wide range of confounders

that were included in the analyses. Its only weakness was its relatively small sample size though this is inevitable in a study that collects such detail. Unfortunately, they did not clearly describe whether they excluded patients who did not survive 30 days. A number of conducted studies used primary or secondary care data sets making the generalisability of results difficult. The age of patients included in the study was not mentioned in two studies. Finally, one study was subject to selection bias as they did not include patients who did not survive more than 30 days. Williams et al., 2004

In summary, there were a number of limitations in the literature surrounding the association between sex and prescribing of EBTs in MI. There was also a wide range in the quality of reporting of studies as assessed by the STROBE guidelines. Few studies achieved a quality score of over 63.6%, however, these studies were associated with a number of limitations that have already has discussed above such as selection bias and a small sample size. The study by Gislason *et al. (2005)* had a number of strengths over other studies. This study adjusted for a wide range of confounders, although not socioeconomic status, and used nationwide population data sets for all hospitals in Denmark, making results generalizable. In general women were less likely to receive appropriate EBTs following MI than men.

Table 2 Inequalities by sex in prescribing of EBTs after myocardial infarction

Study	Design/year	subject	Prescribing	Medications	Prescribing percentage Women vs. men	OR, 95% CI Women vs. men	Adjustment	P values / statistical significance	STROBE Score (%)
Martinez et al 1998	Retrospective cross-sectional	324 and 190	At time of discharge from hospital chart	ACEI	Not reported	4.45 (2.16-9.14)	Unadjusted	Not reported	11/22
Spain	1989-91/ 1994	N=514							(50%)
Austin et al 2008	Retrospective population cohort	Age ≥ 65	Within 90 days post-discharge	ACEI β-blockers Statins	78.5 vs. 78.5 78.1 vs. 78.4 76.7 vs. 82.0	Not reported	Unadjusted	Not reported	12/22
Canada	2005-06	N=8706							(54.5%)
Sadowska et al 2011	Retrospective cross-sectional	N=420	At time of discharge from data centre	ACEI Aspirin Clopidogrel β-blockers Statins Nitrates	90.4 vs. 90.9 89.2 vs. 94.1 16.9 vs. 28.7 81.9 vs. 77.6 78.9 vs. 85.8 54.8 vs. 49.2	Not reported	Unadjusted	0.84 0.06 0.005 0.28 0.06 0.26	8.5/22
Poland	2005-06	(Cardiology centre)							(39%)
Hirakawa et al 2006	Prospective cross-sectional	< 65	At time of discharge Detailed chart review & questionnaire	ACEI Aspirin CCB β-blockers LLD Nitrates	42.6 vs. 46.6 80.5 vs. 89.6 14.8 vs. 18.6 4.14 vs. 7.7 43.2 vs. 35.8 46.7 vs. 49.8	Not reported	Unadjusted	NS < 0.01 NS‡ NS NS NS	11/22
	2001-2003	Women= 169 Men= 1246							(50%)
Japan		≥ 65		ACEI Aspirin CCB β-blockers LLD Nitrates	34.7 vs. 41.7 72.4 vs. 81.2 14.3 vs. 16.5 5.40 vs. 5.97 26.6 vs. 22.4 44.8 vs. 49.8			< 0.01 < 0.01 NS NS < 0.05 < 0.05	
		Women=616 Men=1240							
Barakat et al 2000	Retrospective cohort study	Women=463 Men=1274	At time of discharge	ACEI Aspirin β-blockers	34.3 vs. 32.9 90.0 vs. 92.9 31.6 vs. 44.9	Not reported	Unadjusted	NS 0.08 < 0.001	12/22
England	1988-97								(54.5%)
Di Cecco et al 2002	Audit	≥ 60	Chart review	ACEI Anticoagulant Aspirin	57.0 vs. 56.0 17.0 vs. 11.0 77.0 vs. 82.0	Not reported	Unadjusted	Not reported	11.5/22
		Women=81							(52%)

				β-blockers	72.0 vs. 75.0				
		Men= 142		LLD	33.0 vs. 48.0				
Canada	2000			Nitrates	77.0 vs. 66.0				
Clarke et al 1994	Retrospective cross-sectional	Women=424	At time of discharge	Aspirin	75.0 vs. 79.7 28.7 vs. 42.2	Not reported	Unadjusted	< 0.01	11.5/22
		Men= 997		β-blockers				< 0.01	(52%)
UK	1998-90								
Hirakawa et al 2005	Retrospective cross-sectional	< 65	At time of discharge Detailed chart	ACEI	33.5 vs. 40.1	Not reported	Unadjusted	NS	11/22
				Aspirin	71.3 vs. 64.1			NS	
		Women= 143	review &	CCB	51.1 vs. 46.8			NS	(50%)
			questionnaire	β-blockers	7.70 vs. 5.23			NS	
		Men= 822		LLD	17.5 vs. 12.4			NS	
Japan	1995-97			Nitrates	39.8 vs. 38.2			NS	
		≥ 65		ACEI	31.7 vs. 30.5			< 0.01	
				Aspirin	68.5 vs. 67.7			< 0.01	
		Women=319		CCB	35.3 vs. 38.4			NS	
				β-blockers	3.60 vs. 2.72			NS	
		Men=661		LLD	8.95 vs. 5.57			< 0.05	
				Nitrates	31.4 vs. 32.5			< 0.05	
Ohlesson et al 2010	Retrospective cohort	N=1364	Within three months post discharge 1st MI	ACEI	63.0 vs. 72.0	Not reported	Unadjusted	Not reported	15.5/22
				LLD	82.0 vs. 87.0				(70%)
	2006		Income						
Sweden									
Macchia et al 2012	Three cohorts		Post-discharge follow for one year	ACEI/ARBs	81.3 vs. 79.3	0.94 (0.84-1.04)	Age, previous CHD, diabetes, stroke, TIA, atrial fibrillation, COPD, depression and malignancy	Not reported	15/22
		Age ≤ 75		Aspirin	83.2 vs. 87.0	0.72 (0.65-0.81)			
	2003-04			β-blockers	73.9 vs. 73.1	0.99 (0.90-1.08)			(68%)
	2005-06	N=21423		Statins	81.1 vs. 85.6	0.70 (0.63-0.78)			
Italy	2007-08								
Heller et al 2000	Retrospective Cohort study	≥ 65	Outpatients prescription database with 90 days post discharge	β-blockers	Not available	1.12 (1.01-1.24)	Demographic and year of MI	0.03	11.5/22
		N=9534							(52%)
USA	1994-1997								
Rasmussen et al 2005	Retrospective cohort	1995-97	Within 6 months post discharge	Statins	Not reported	1.29 (1.18-1.45)	Age, concomitant medications, hospital type	Not reported	15/22
		1998-99	Follow statins purchased			1.26 (1.18-1.38)			(68%)
		2000-02				0.95 (0.88-1.03)			
	1995-2002		1st MI						
Denmark		N=17875							

Winkelmayer et al 2008 **Austria**	Retrospective cohort 2004	N=4105	Within 120 days post discharge 1st MI	ACEI/ARBs β-blockers statins	Not reported	0.93 (0.80-1.09) 0.87 (0.74-1.03) 0.90 (0.77-1.06)	Age, length of stay at hospital, concomitant medications	Not reported	12.5/22 (57%)
Gislason et al 2005 **Denmark**	Retrospective cohort 1995-2002	Men vs. women N=55315	Within 30 days post discharge 1st MI	ACEI β-blockers	28.8 vs. 29.8 52.2 vs. 62.6	0.85 (0.82-0.89) 0.80 (1.21-1.30)	Age, calendar year, concomitant treatment (loop diuretic & antidiabetic drugs)	<0.001	15/22 (68%)
Spencer et al 2001 **USA**	Cross-sectional 1986-1997	N=5739	At time of discharge	ACEI Aspirin CCB β-blockers LLD*	Not reported	0.86 (0.74-1.01) 0.86 (0.78-1.01) 1.06 (0.92-1.20) 0.83 (0.73-0.94) 0.92 (0.73-1.16)	Age, medical history and clinical characteristic	Not reported	10.5/22 (48%)
Griffith et al 2005 **Southwest Scotland**	Prospective cohort 1994-2000 follow up to end of 2001	Women= 458 Men= 821	At time of discharge 1st MI	ACEI Aspirin β-blockers Statins	49.6 vs. 52.0 86.7 vs. 90.3 38.0 vs. 48.8 23.8 vs. 23.8	0.85 (0.66- 1.08)+ 0.90 (0.62- 1.32) 0.78 (0.60- 1.00) 1.48 (1.10- 1.98)	Age, smoking, comorbidity, previous angina, revascularisation PAD, DM, HTN, and social deprivation	0.18 0.60 0.05 0.001	9/22 (41%)
Sial et al **USA**	Retrospective cross-sectional 1990-1991	N=444	At time of discharge from medical records	β-blockers	Not reported	0.52 (0.30- 0.88)	Age, race, comorbidities, other medications, MI characteristic, physician	Not reported	13.7/22 (62%)
Rathore et al 2000 **USA**	Retrospective cross-sectional 1994-96	≥ 65 N=169079	At time of discharge from medical records database 1st MI	Aspirin β-blockers	Not reported	0.98 (0.96-0.99) 1.00 (0.97-1.02)	Age, illness severity, doctor speciality, live rural area, US census region of residency	Not reported	12.5/22 (57%)
Hanrratty et al 2000 **England**	Prospective cohort study Sep-Nov 1995	Women=850 Men=1303	At time of discharge	ACEI Anticoagulant Aspirin CCB β-blockers Nitrates Statins	Not reported	1.01 (0.82-1.26) 1.40 (0.97-2.03) 0.91 (0.68-1.23) 1.25 (0.96-1.63) 0.84 (0.67-1.07) 0.85 (0.69-1.06) 1.37 (0.92-2.03)	Age	0.91 0.07 0.55 0.09 0.15 0.15 0.12	11/22 (50%)
Williams et al 2004 **Wales**	Retrospective cross-sectional Jan, Feb, July and Aug 1999	Women=438 Men= 819	Case notes Exclude patients died within 30 days	ACEI Aspirin β-blockers Statins	Not reported	0.83 (0.63-1.10) 0.93 (0.65-1.32) 0.97 (0.73-1.28) 0.98 (0.74-1.30)	Age	Not reported	10/22 (45.5%)
Carey et al 2012	Retrospective cohort N=9367	Women=3107 Men=6210	Within 6 months post discharge, obtained from	Statins	72.0 vs. 75.9	1.01 (0.98-10.3)‖	Age, and practice	Not reported	14.5/22 (66%)

	1997-2006		primary care database 1st MI						
UK									
Avanzini et al 1997 Italy	Retrospective cohort 1984-1993	GISSI-1 (N=9452) GISSI-2 (N=10,407) GISSI-3 (N=16,958)	Post discharge, data from	β-blockers	Not reported	1.15 (0.93-1.24) 1.06 (0.92-1.22) 1.03 (0.93-1.14)	Age, comorbidities, AMI characteristic at admission, procedure complications, treatment at discharge	No significant	11.5/22 (52%)
Weir et al 2004 Scotland	Retrospective cohort 1994-1995	Age 30 -93 N=865	Post discharge, use record linkage database 1st MI	β-blockers	Not reported	1.02 (073-1.42)¶	Age, deprivation, obstructive airway disease, diabetes mellitus, PAD, prior beta blockers, prior of CCB, ACEI, alpha blockers, thiazide diuretic, loop diuretic, nitrates, antiplatelet drug, lipid lowering drug, steroid.	Not reported	14/22 (63.5%)

*LLD=Lipid lowering drug, ‡ Not significant, ǀ Risk ratio, ¶ Unadjusted OR 0.62 (0.48-0.82), + Unadjusted ACEI (OR 0.91, 0.72-1.14), aspirin (OR 0.70, 0.49-1.00), blockers (OR 0.64, 0.51-0.81), statins (OR 1.00, 0.76-1.30).

Inequalities by socioeconomic status in prescribing of EBTs for MI

The association between the prescribing of EBTs and socioeconomic status has only been examined in a few studies (Table 8).

Unadjusted analyses

In an unadjusted analyses Hawkins *et al. (2013)* reported that the most deprived were more likely to be prescribed aspirin, though this difference became non-significant over time (RR 1.28; 95% CI 1.08-1.53) in 1999 and (RR 1.01; 95% CI 0.76-1.34) in 2007. In the same study ACEI/ARBs were prescribed similarly for the most and least deprived. Hawkins et al., 2013 Although this study was not adjusted, it has a number of strengths such as large sample size obtained from the general practice database, including all EBTs, and it used a deprivation measurement based on different domains. In contrast, a Swedish study Ohlsson et al., 2010 using routinely collected regional data reported that the least deprived were more likely to be prescribed an ACEI than the most deprived (66.0 vs. 74.0). No studies reported a significant difference in prescribing rates of β-blockers between the most and least deprived groups (Ohlsson et al., 2010, Hawkins et al., 2013). Hawkins *et al. (2013)* reported that statins were less commonly prescribed for the most versus the least deprived patients post-MI but this was not statistically significant (RR 0.67; 95% CI 0.45-1.01).

Adjusted analyses and limitations of the published literature

In the multivariable adjusted analyses examining the relationship between socioeconomic status and the prescription of aspirin, more deprived patients were not significantly less likely to be prescribed aspirin (OR 0.98; 95% CI 0.96-1.00). However, this study used a single deprivation measurement and only included patients aged ≥ 65 years in the study (Rathore et al., 2000). Reid *et al. (2011)* reported that the least deprived were more likely to be prescribed an ACEI. Conversely, prescribing of β-blockers was higher among the least deprived patients after adjustment (Rathore et al., 2000, Reid et al., 2011).

Although these studies adjusted their results for a wide range of confounders and examined prescribing inequalities for more than one drug, they were subject to a number of limitations such as limiting the study to patients aged ≥ 65 years, (Rathore et al., 2000) excluding patients who did not survive more than 120 days leading to selection bias, Reid et al., 2011 and using one measure to determine socioeconomic deprivation (Rathore et al., 2000, Reid et al., 2011). Carey *et al.*'s (2012) study avoided these limitations using a measurement based on different domains of deprivation, though it was adjusted for only a few confounders. This study reported no difference in statin prescribing rates by socioeconomic status (Carey et al., 2012). Reid *et al. (2011)* reported that statins were significantly more likely to be prescribed for men with high income than those with lower income.

Limitations in the reporting of the literature

The quality of the reporting of these studies was assessed by using STROBE checklist and ranged from 45% to 70%. All studies indicated their study design using common terms either in the title or in the abstract. Three studies did not state their objectives (Whincup et al., 2002, Carey et al., 2012, Reid et al., 2011). The study design was not described clearly in the methods for one study (Rathore et al., 2000). One study did not report the eligibility criteria for patients included in their analyses (Hawkins et al., 2013). Two studies did not describe the statistical methods included in the analyses (Whincup et al., 2002, Hawkins et al., 2013). All studies reported the number of individuals included in the study and those included in the analyses, however one study did not (Hawkins et al., 2013). Three of the six studies did not describe the demographic characteristics of the patients (Carey et al., 2012 Rathore et al., 2000, Hawkins et al., 2013). Only one study described and discussed the potential sources of bias in the limitation section (Ohlsson et al., 2010).

In summary, there were a number of limitations in the literature surrounding the association between socioeconomic and prescribing of EBTs in MI. There was also a wide range in the quality of reporting of studies as assessed by the STROBE guidelines. One study achieved a quality score of over 70%. In those studies that did adjust their analyses the most deprived individuals were less likely to receive appropriate EBTs following a MI.

Table 3 Inequalities by socioeconomic status in prescribing of EBTs after myocardial infarction

Study	Design /year/	Reference/ subject	Prescribing/ Deprivation measure	Medications	Prescribing percentage Affluent vs. deprived	OR, 95% CI Affluent vs. deprived	Adjustment	P values / statistical significance	STROBE Score (%)
Ohlesson et al 2010	Retrospective cohort	high income vs. Low income	Within three months post discharge	ACEI LLD	74.0 vs. 66.0 91.0 vs. 82.0	Not reported	Unadjusted	Not reported	15.5/22 (70%)
		Age 40-100	1st MI						
	2006	N=1364	Income						
Sweden									
Hawkins et al 2013	Cross-sectional	Less deprived vs. Most deprived	General practice research database	ACEI/ARBs Aspirin β-blockers statins	17.5 vs. 18.8 33.7 vs. 43.3 32.1 vs. 32.9 45.2 vs. 30.3	0.92 (0.73-1.19)‡ 1.28 (1.08-1.53) 0.98 (0.52-1.82) 1.49 (0.99-2.22)	Unadjusted	Not reported	13.5/22 (61%)
	1999	N=32976							
UK									
	2007		IMD*	ACEI/ARBs Aspirin β-blockers statins	56.1 vs. 57.3 63.5 vs. 64.3 49.7 vs. 52.7 74.6 vs. 67.8	0.98 (0.76-1.26) 1.01 (0.76-1.34) 0.94 (0.72-1.25) 1.10 (0.85-1.41)			
Rathore et al 2000	Retrospective cross-sectional	Affluent vs. deprived	At time of discharge	Aspirin β-blockers	Not reported	1.02 (1.00-1.04) 1.05 (1.01-1.09)	Age, illness severity, doctor speciality, live rural area, US census region of residency	Not reported	12.5/22 (57%)
		≥ 65							
USA	1994-96	N=169079	Household income						
Whincup et al 2002	Cross-sectional survey	Non-manual vs. Manual	Post discharge, general practice records and patients questionnaire	LLD	49.0 vs. 49.0	1.45 (0.82-2.56)	Previous revascularisation, age at last diagnosis, year of last diagnosis, manual social classes, smoking and geographical residence	0.2	10/22 (45%)
		N=286							
		Men							
	1998-2000		*Occupation*						
UK									
Carey et al 2012	Retrospective cohort	Least deprived vs. Most deprived	Within 6 months post discharge, primary care database	Statins	72.0 vs. 75.9	1.01 (0.98-1.03)‖	Age, sex and practice	Not reported	14.5/22 (66%)
		Women=3107	1st MI						
	1997-2006	Men=6210	IMD*						
UK									

Reid RJ et al 2011 **Canada**	Cross-sectional 1999-2006	High income vs. low income Men N=28216	Within 120 days post discharge administrative database	ACEI β-blockers Statins	Not reported	1.37 (1.24-1.51) 1.50 (1.35-1.68) 1.71 (1.53-1.90)	Age using 5 years age bands, urban residence and general health status	Not reported	15.2/22 (69%)
		Women	Income	ACEI β-blockers Statins		1.04 (0.89-1.20) 1.25 (1.06-1.47) 1.32 (1.12-1.54)			

* Index of Multiple deprivation, ‡ Rate ratio, ǁ Risk ratio

2.5.4 Trends in prescribing of EBTs for MI

Several studies have reported that the use of EBTs for secondary prevention post-MI has improved over the last decade (Table 9). Prescribing of EBTs at discharge or shortly after discharge has been examined in a number of studies.

Unadjusted analyses

Prescribing of aspirin or any antiplatelet agent at any time point post discharge increased over time in the studies (Macchia et al., 2012, Spencer et al., 2001, Austin et al., 2008- Setoguchi et al., 2007). Only one study reported that prescribing of aspirin declined at time of discharge, though the sample size was very small in this study compared to other studies. Martinez et al., 1998 Prescribing of ACEI/ARBs similarly improved over time. Since the 1990s the prescribing of β-blockers has improved (Macchia et al., 2012, Spencer et al., 2001, Martinez et al., 1998, Austin et al., 2008- De Ruijter et al., 2010). The largest increases in prescribing were seen with statins (Macchia et al., 2012 Spencer et al., 2001; Austin et al., 2008; Setoguchi et al., 2007). Although all above studies were unadjusted, they have a number of strengths. Almost all of these studies included all recommended EBTs after MI, however, a few did not. Long time periods of the trend were examined in the majority of these studies, which helps to demonstrate how far prescribing EBTs has improved. A recent report published in 2014 by British Heart Foundation (BHF), reported that the prescription used in the prevention and treatment of cardiovascular diseases in England, Wales and Scotland increased over the time (British Heart Foundation, 2014).

Adjusted analyses

Few studies used multivariable analyses to examine the prescribing trends for EBTs after MI. Of the studies that did adjust for other confounders they all reported that prescribing rates improved over time for all of the above drugs. However, they only adjusted for a limited number of covariates or were limited to one or two drugs. One study Sarah et al., 2010 with a large sample size, included all patients diagnosed with MI from age 35 years and above, and examined prescribing trends for all recommended EBTs. This study, however, adjusted for limited confounders and was not specific for statins examining all lipid lowering drugs.

This study showed that prescribing EBTs increased significantly from 1991 to 2002 for all secondary prevention therapies.

Limitations in the reporting of the literature

A number of studies were identified that examined the trends in prescribing after diagnosis with MI. In this section, I will focus my discussion on the studies that explicitly examined trends in prescribing of EBTs after MI (Austin et al., 2008- De Ruijter et al., 2010، Sarah et al., 2010- Barron et al., 1998). The quality of the reporting of studies describing the prescribing trends over the time was assessed using the STROBE checklist and ranged from 36% to 74%. Two studies did not indicate the study design using common terms in the title or abstract (Perschbacher et al., 2004، De Ruijter et al., 2010). The majority of studies provided a clear summary in the abstract including background, methods, results and conclusion (Austin et al., 2008- Setoguchi et al., 2007، Sarah et al., 2010- Barron et al., 1998). Study objectives were not described clearly in three studies (Austin et al., 2008، De Ruijter et al., 2010، Barron et al., 1998). Study design was not clearly described in one study (Barron et al., 1998). The eligibility criteria of patients for inclusion in the study was not described in three studies (Masoudi et al., 2006 Perschbacher et al., 2004، De Ruijter et al., 2010). The outcome, exposure and potential predictors were not described clearly in one study (De Ruijter et al., 2010).

Statistical methods were described in all but one study not (De Ruijter et al., 2010). Furthermore, none of the studies described any further analyses or explained how missing data were addressed. All studies reported the number of eligible patients included in the study. Four studies did not describe the reasons for those who were excluded from the analyses (Austin et al., 2008- Masoudi et al., 2006، De Ruijter et al., 2010). The number of outcome events was not indicated in five studies (Austin et al., 2008، Setoguchi et al., 2007، Setoguchi et al., 2008، Barron et al., 1998). Three studies presented the unadjusted and adjusted analyses in their results (Perschbacher et al., 2004، Setoguchi et al., 2007، Setoguchi et al., 2008). Other studies, however, either presented unadjusted or adjusted results. Two studies failed to discuss the source of the potential bias in their limitations (Sarah et al., 2010، Setoguchi et al., 2008).

Limitations in the design and analysis of studies included in the literature review

A number of gaps and limitations were identified in the literature. Few studies examined prescribing trends using all EBTs and most limited their analyses to select groups of drugs. The majority of previous studies reported unadjusted analyses and therefore results were not adjusted for potential confounders. The results of some studies may not represent current clinical practice as they measured the trends using older data sets. De Ruijter *et al. (2010)* did not explain how the practices included in the study were selected. In addition, this study examined prescribing at three different points but did not clarify whether they avoided double counting of individuals between periods. Selection bias was identified in two studies (Sarah et al., 2010 Setoguchi et al., 2008).

In summary, a number of limitations were identified in the previous studies of trends in prescribing EBTs after MI. There was variation in the quality of reporting of studies as assessed using STROBE guidelines. There was, however, a general consensus in the literature that the prescribing of EBTs has improved over time.

Table 4 Trends in prescribing of EBTs after myocardial infarction

Study	Design/year	Reference/ Subject	Prescribing	Medications	Prescribing percentage	OR, 95% CI	Adjustment	P values / statistical significance	STROBE Score (%)
Spencer et al (2001)	Cross-sectional	1986 vs. 1997	At time of discharge	ACEI Aspirin	0.00 vs. 40.0‡ 15.0 vs. 77.0	Not reported	Unadjusted	Not reported	10.5/22
		N=5739		β-blockers CCB	35.0 vs. 70.0 50.0 vs. 15.0				(48%)
	1986-1997			LLD*	1.00 vs. 20.0				
USA									
Perschbacher et al 2004	Cross-sectional	1979 vs. 1998	At time of discharge, medical records database	ACEI Aspirin	0.00 vs. 39.0 10.0 vs. 88.0	Not reported	Unadjusted	Not reported	13/22
	1979-1998	N= 2093		β-blockers	25.0 vs. 73.0				(59%)
USA									
De Ruijter et al 2010	Cross-sectional	2000 vs. 2007	Post discharge, obtained from medical records of GP	ACEI β-blockers	30.0 vs. 47.0 40.0 vs. 58.0	Not reported	Unadjusted	Not reported	8/22
	2000-2007	N=800		Statins	44.0 vs. 71.0				(36%)
Netherlands									
Gasse et al 2008	Retrospective longitudinal cohort	1997 vs. 2003	Within 6 months post discharge	ACEI/ARBs Aspirin	35.0 vs. 52.7 38.0 vs. 83.0	Not reported	Unadjusted	Not reported	15/22
		N=11927		β-blockers	74.0 vs. 76.2				(68%)
Denmark	1997-2003			Statins	17.0 vs. 70.5				
Masoudi et al 2006	Retrospective cohort	1992 vs. 2001	At time of discharge, used patients Medical records	ACEI Aspirin	47.3 vs. 64.6 66.0 vs. 79.4	Not reported	Unadjusted	< 0.001 < 0.001	11.5/22
		N=20550		β-blockers	33.1 vs. 71.4			< 0.001	(52%)
	1992-2001								
USA									
Macchia et al 2012	Three cohorts	2003 vs. 2007	Within 1 year after discharge	ACEI/ARBs Aspirin	73.1 vs. 82.1 76.4 vs. 85.7	Not reported	Unadjusted	Not reported	15/22
	2003-04 2005-06	N=21423		β-blockers Statins	59.3 vs. 71.2 67.0 vs. 80.6				(68%)
Italy	2007-08								
Setoguchi et al 2008	Retrospective cohort study	1995 vs. 2004	Within 30 days post discharge	ACEI/ARBs Antiplatelet	39.2 vs. 50.0 2.60 vs. 50.9	Not reported	Unadjusted	<0.0001 <0.0001	13.7/22
		N=21484		β-blocker	41.5 vs. 71.6			<0.0001	
	1995-2004			Statins	7.60 vs. 50.7			<0.0001	(62%)
USA									

Austin et al 2008 **Canada**	Cross-sectional 1992-2005	1992 vs. 2005 Age ≥ 65 years N=132778	Within 90 days post discharge from Ontario MI database,1st MI	ACEI/ARBs β-blocker statins	42.0 vs. 78.4 42.6 vs. 78.1 4.20 vs. 79.2	Not reported	Unadjusted	< 0.001	12.5/22 (57%)
Barron et al 1998 **USA**	Cross-sectional 1994-1996	1994 vs. 1996 N=190015	At discharge, from national registry for MI2	ACEI	25.0 vs. 30.7	Not reported	Unadjusted	Not reported	12/22 (54.5%)
Setguchi et al 2007 **USA**	Retrospective cohort 1995-2004	1995 vs. 2004 N=19368	Within 90 days post discharge	ACEI/ARBs β-blockers Statins	46.0 vs. 58.0 47.0 vs. 80.0 11.0 vs. 61.0	Not reported	Unadjusted	<0.001 <0.001 <0.001	13/22 (59%)
Martinez et al 1998 **Spain**	Retrospective cross-sectional 1989-91/ 1994	1989 vs. 1994 324 and 190	At discharge	ACEI β-blocker Aspirin CCB	14.0 vs. 23.0 62.0 vs. 63.0 75.0 vs. 71.0 20.0 vs. 17.0	Not reported	Unadjusted	Not reported	11/22 (50%)
Avanzini et al. 1997 **Italy**	Retrospective cohort 1984-1993	1984 vs. 1993 N=36817	Post discharge, data from GISSI-1 GISSI-2 GISSI-3	β-blockers	8.50 vs. 31.4	5.73 (5.23-6.26)	Age, sex, comorbidities, AMI characteristic at admission, procedure complications, treatment at discharge	Not reported	11.5/22 (52%)
Heller et al 2000 **USA**	Retrospective Cohort study 1994-1997	1994 1995 1996 1997 N=9534 (≥ 65)	Outpatients prescription database with 90 days post discharge	β-blockers	Not reported	1.00 1.36 (1.20-1.53) 1.72 (1.50-1.97) 2.33 (2.03-2.67)	Demographic and year of MI	--------- 0.0001 0.0001 0.0001	11.5/22 (52%)
Gislason et al 2005 **Denmark**	Retrospective cohort 1995-2002	1995 vs. 2002 N=55315	Within 30 days post discharge 1st MI	ACEI β-blockers	24.5 vs. 35.5 38.1 vs. 67.9	1.86 (1.73-2.01) 3.84 (3.58-4.13)	Age, sex, calendar year, concomitant treatment (loop diuretic & antidiabetic drugs)	<0.001	15/22 (68%)
Carey et al 2012 **UK**	Retrospective cohort N=9367 1997-2006	1997-1998 1999-2000 2001-2002 2003-2004 2005-2006	Within 6 months post discharge, from primary care database, 1st MI	Statins		1.00 1.34 (1.31-1.47)* 1.68 (1.58-1.79) 1.93 (1.81-2.07) 1.97 (1.84-2.11)	Age, sex and practice	Not reported	14.5/22 (66%)
Hardoon et al 2010	Retrospective cohort N=10,352	1991 vs. 2002	Within 90 days post discharge, general	ACEI Antiplatelet	11.0 vs. 71.0 46.0 vs. 86.0	1.28 (1.26-1.30) 1.20 (1.17-1.23)	Age, sex, and GP	Not reported	16/22 (74%)

	1991-2002	≥ 35 years	practice (GP) database	β-blocker LLD	26.0 vs. 68.0 3.00 vs. 79.0	1.23 (1.20-1.26) 1.79 (1.73-1.85)		
UK								
		Men=6586		ACEI	11.6 vs. 72 .7	1.30 (1.27-1.32)	< 0.001	
				Antiplatelet	47.7 vs. 87.1	1.20 (1.18-1.22)	< 0.001	
				β-blocker	32.9 vs. 73.3	1.22 (1.20-1.24)	< 0.001	
				LLD	3.90 vs. 83.1	1.83 (1.78-1.89)	< 0.001	
		Women=3766		ACEI	10.2 vs. 67.1	1.25 (1.22-1.28)	< 0.001	
				Antiplatelet	42.3 vs. 83.5	1.20 (1.17-1.23)	< 0.001	
				β-blocker	12.8 vs. 59.7	1.24 (1.21-1.27)	< 0.001	
				LLD	1.28 vs. 71.7	1.72 (1.66-1.79)	< 0.001	
Gale C et al. 2011	Cross-sectional	2003 vs. 2010	At time of				Not reported	16/22
		<55	discharge, obtained	Aspirin	95.8 vs. 82.5	0.20 (0.19-0.22)*		
	N=612995	>85	from electronic data		81.1 vs. 71.6	0.59 (0.55-0.63)		(74%)
England and Wales			base					
		<55		ACEI	81.4 vs. 76.5	1.35 (1.27-1.42)		
		>85			57.4 vs. 55.9	1.06 (1.01-1.12)		
		<55		β-blockers	85.5 vs. 75.3	0.52 (0.49-0.55)		
		>85			49.1 vs. 56.7	1.35 (1.29-1.43)		
		<55		Clopidogrel	56.1 vs. 97.3	28.48 (20.64-39.69)		
		>85			28.1 vs. 89.1	81.31 (59.06-112.26)		
		<55		Statins	94.2 vs. 82.4	0.29 (0.26-0.31)		
		>85			61.3 vs. 68.6	1.38 (1.31-1.46)		

*Relative risk, ‡ result approximated from a figure.

Prescribing of EBTs for MI by comorbidities

Prescribing of EBTs post-MI may be influenced by the presence of concomitant disease. One study reported that aspirin was less commonly prescribed in patients with end stage renal disease (ESRD) post MI. Berger et al., 2003 Prescribing rates of ACEIs were lower among patients with the comorbidities of diabetes mellitus, HF, cancer, stroke, chronic kidney disease (CKD) and RF.Similar trends have been reported for β-blockers and statins (Austin et al., 2008, Berger et al., 2003, Younis et al., 2001).

A number of studies examined the effect of comorbidities using adjusted multivariable analyses and reported that the presence of concomitant disease was associated with a lower rate of prescribing of EBTs (Table 10). Aspirin was prescribed less commonly among patients with diabetes than without (Norhammar et al., 2003). ACEI/ARBs were prescribed more commonly in patients with respiratory disease, diabetes and HF (Gislason et al., 2005, Norhammar et al., 2003). However, rates of prescribing of ACEI/ARBs were lower in those with CKD and RF (Winkelmayer et al., 2008). The most widely studied group of drugs was β-blockers. The presence of a number of comorbidities (asthma, COPD, diabetes, PAD, HF and atrial fibrillation) was associated with lower rates of prescribing of β-blockers (Gislason et al., 2005; Heller et al., 2000, Sial et al., 1994, Norhammar et al., 2003). Two comorbidities were associated with higher rates of prescribing of β-blockers, these were hypertension (Sial et al., 1994) and CKD (Winkelmayer et al., 2008). One study, Winkelmayer et al. (2008) reported that statins were more commonly prescribed in patients with CKD. Other studies, however, reported that statins were less likely to be prescribed in the presence of comorbidities (Winkelmayer et al., 2008; Norhammar et al., 2003).

Limitations in the reporting of the literature

Few studies examined the relationship between comorbidities and the prescribing of EBTs following a diagnosis of MI. The STROBE scores for literature that described the association between comorbidities and prescribing of EBTs after MI ranged from 45% to 68% (Table 10). Four studies did not mention their study design either in the title or in the abstract (Heller et al., 2000, Berger et al., 2003, Younis et al., 2001; Norhammar et al., 2003). Four authors did not state their study objectives (Gislason et al., 2005, Winkelmayer et al., 2008;

Norhammar et al., 2003). One study did not report the eligibility criteria for patients included in their analyses. Wei et al., 2004. The outcome, exposure, predictors and potential confounder's variables were not defined clearly in one study (Wei et al., 2004). No studies discussed or identified potential sources of bias, though all studies reported how the statistical analysis was conducted. One study described a subgroup analysis (Winkelmayer et al., 2008). Four studies did not report the number of individuals included in the study and the patient population was not clearly described in other studies (Austin et al., 2008, Heller et al., 2000, Berger et al., 2003, Younis et al., 2001, Sial et al., 1994, Sial et al., 1994; Norhammar et al., 2003).

The rationale of excluding participants from a study was explained in four studies (Gislason et al., 2005, Winkelmayer et al., 2008, Berger et al., 2003; Norhammar et al., 2003). Two studies did not describe the baseline characteristics of the included population (Berger et al., 2003; Norhammar et al., 2003). Missing variables were only reported in one study (Sial et al., 1994). Four studies presented the unadjusted and adjusted analyses in their results (Winkelmayer et al., 2008, Winkelmayer et al., 2008, Sial et al., 1994, Wei et al., 2004). Other studies, however, either presented unadjusted or adjusted results. Three studies discussed the limitations including the source of potential biases (Gislason et al., 2005, Winkelmayer et al., 2008, Berger et al., 2003).

Limitations in the design and analysis of studies included in the literature review

A number of gaps and limitations were also identified in the previous literature. Three studies were subject to bias. Norhammar *et al. (2003)* obtained comorbidity diagnosis from patients and is therefore subject to "recall bias". They also excluded patients aged 80 years and older. Winkelmayer *et al. (2008)* excluded patients who did not survive more than 30 days after diagnosis "survivor bias" and Berger *et al (2003)* excluded patients younger than 65 years selection bias. Limiting the study sample to one area, or one hospital will limit the generalisability of the results to the whole population. Younis *et al. (2001)* examined the association between comorbidities and prescribing EBTs after MI in a small sample recruited from one hospital. A number of studies were limited to one disease such as RF or diabetes (Berger et al., 2003; Norhammar et al., 2003).

In summary, there were a number of limitations in the literature surrounding the association between comorbidities and prescribing of EBTs in MI. There was also a wide range in the quality of reporting of studies as assessed by the STROBE guidelines. Only a few studies achieved a quality score of over 70%. The presence of comorbidities was generally associated with lower rates of prescribing of EBTs.

Table 5 Inequalities in prescribing of EBTs after MI by comorbidities

Study	Design/year/ Subject	Reference/	Prescribing	Medications	Prescribing percentage	OR, 95% CI	Adjustment	P values / statistical significance	STROBE Score (%)
Berger et al 2003	Retrospective cohort	ESRD vs. No	Not reported	ACEI Aspirin	27.6 vs. 37.2 62.0 vs. 78.9	Not reported	Unadjusted	Not reported	
	N=146765	ESRD=1025		β-blockers	37.7 vs. 45.8				
USA	1994-1996	≥ 65							
Austin et al 2008	Retrospective population cohort	DM vs. No DM	Within 90 days post-discharge	ACEI β-blockers Statins	69.7 vs. 79.0 79.4 vs. 78.2 77.9 vs. 79.6	Not reported	Unadjusted	Not reported	12/22
	N=8706	Age ≥ 65	Used linked administrative database						(54.5%)
	2005-06	HF vs. No HF		ACEI β-blockers Statins	77.0 vs. 79.0 75.5 vs. 79.2 71.8 vs. 82.1				
Canada		Cancer vs. No cancer		ACEI β-blockers Statins	64.9 vs. 78.9 72.1 vs. 78.5 64.1 vs. 80.0				
		Stroke		ACEI β-blockers Statins	75.0 vs. 78.6 75.4 vs. 78.4 75.8 vs. 79.6				
		CKD		ACEI β-blockers Statins	59.7 vs. 80.3 75.8 vs. 78.5 74.6 vs. 80.0				
Younis et al 2001	Retrospective cross-sectional	DM vs. not	At discharge obtained from the case sheet 1st MI	β-blockers	23.4 vs. 52.3	Not reported	Unadjusted	Not reported	10/22
	N=400 1995-1999	DM=201							(45.5%)
Norhammar et al 2003	Retrospective longitudinal cohort	DM vs. Not	At discharge, Medical records database (RIKS-HIA)	ACEI Aspirin	50.0 vs. 34.0 80.0 vs. 84.0	1.45 (1.33-1.58) 0.97 (0.87-1.08)	Adjusted different confounders, however not particularly mentioned	Not reported	10/22
	N=25633 1995-1998	DM=5193 < 80 years		β-blockers Statins	75.0 vs. 80.0 25.0 vs. 28.0	0.97 (0.87-1.07) 0.88 (0.80-0.97)			(45.5%)
Sweden									
Heller et al 2000	Retrospective longitudinal cohort study	AF vs. No AF	Outpatients prescription database with 90	β-blockers	Not reported	0.86 (0.76-0.97)	Demographic and year of MI	0.01 <0.01	11.5/22
		HF vs. No HF				0.52 (0.47-0.58)		<0.01 <0.01	(52%)

	N=9534	COPD vs. No Asthma vs. No	days post discharge			0.49 (0.44-0.56) 0.32 (0.22-0.47)			
USA	1994-1997	≥ 65							
Winkelmayer et al 2008	Retrospective cohort N=4105	Asthma/COPD vs. No	Within 120 days post discharge 1st MI	ACEI/ARBs β-blockers statins	Not reported	1.07 (0.86-1.34) 0.67 (0.55-0.83) 0.87 (0.71-1.07)	Age, sex, length of stay at hospital, concomitant medications	Not reported	12.5/22 (57%)
Austria	2004								
Gislason et al 2005	Retrospective longitudinal cohort N=55315	DM vs. No DM HF vs. No HF	Within 30 days post discharge 1st MI	ACEI β-blockers ACEI β-blockers	Not reported	1.48 (1.40-1.58) 0.79 (0.74-0.84) 3.32 (3.19-3.47) 0.71 (0.68-0.74)	Age, sex, calendar year, concomitant treatment (loop diuretic & antidiabetic drugs)	Not reported	15/22 (68%)
Denmark	1995-2002								
Sial et al 1994	Cross-sectional N=444	COPD vs. Non HTN vs. Non	At time of discharge from medical records	β-blockers	Not reported	0.21 (0.07- 0.60) 1.86 (1.11- 3.12)	Gender, age, race, comorbidities, other medications, MI characteristic, physician	Not reported	13.7/22 (62%)
USA	1990-1991	HF vs. Non				0.46 (0.27-0.79)			
Wei et al 2004	Retrospective longitudinal cohort N=865	OAD vs. Not DM vs. Not HF vs. Not	Post discharge, use record linkage database 1st MI	β-blockers	Not reported	0.30 (0.15-0.60)* 0.93 (0.57-1.65) 0.33 (0.19-0.60)	Age, sex, deprivation, obstructive airway disease, diabetes mellitus, PAD, prior beta blockers, prior use of CCB, ACEI, alpha blockers, thiazide diuretic, loop diuretic, nitrates, antiplatelet drug, lipid lowering drug, steroid.	Not reported	14/22 (63.5%)
Scotland	1994-1995	PAD vs. Not Age 30 -93				0.64 (0.31-1.32)			
Winkelmayer et al 2008	Retrospective longitudinal cohort N=21484	CKD vs. Not CKD=3645	Within 30 days post discharge	ACEI/ARBs β-blockers Statins	38.0 vs. 45.0 55.0 vs. 58.0 28.0 vs. 26.0	0.78 (0.75-0.82)+ 1.00 (0.96-1.03) 1.02 (0.96-1.08)	Demographic, discharge year, comorbidities, health service measure, in-hospital procedures		15/22 (68%)
USA	1995-2004	≥ 65							
		ESRD vs. Not ESRD=436		ACEI/ARBs β-blockers Statins	28.0 vs. 45.0 57.0 vs. 58.0 22.0 vs. 26.0	0.57 (0.49-0.66) 0.94 (0.86-1.04) 0.83 (0.70-0.99)			

* Unadjusted OR: OAD 0.24 (0.15-0.39), DM 0.83 (0.51-1.35), HF 0.27 (0.16-0.46), PAD 0.52 (0.28-0.94), + Risk ratio,

OAD=obstructive airway disease, HF=heart failure, PAD=peripheral vascular disease, DM=diabetes mellitus,

RIKS-HIA= Register of information and knowledge about Swedish heart intensive care admissions, ESRD=End stage renal disease, CKD=chronic kidney disease

Conclusions:

In conclusion, the systematic review of prescribing trends of evidence-based pharmacotherapy post-myocardial infarction (MI) has illuminated age-based inequalities in the administration of essential medications. Our findings reveal a concerning pattern where certain age groups may be systematically undertreated, potentially compromising the post-MI care continuum. This discovery emphasizes the necessity for targeted interventions and educational efforts to ensure that evidence-based therapies are uniformly prescribed across all age categories, addressing disparities and optimizing outcomes for the broader demographic spectrum of post-MI patients.

Furthermore, our research has unveiled gender-based inequalities in the prescription of evidence-based therapies (EBTs) following MI. These disparities underscore the need for a gender-sensitive approach to post-MI care, addressing factors that may contribute to differential prescribing patterns. Future interventions should prioritize gender-specific educational initiatives for healthcare providers to mitigate these discrepancies and promote equitable access to evidence-based pharmacotherapy, thereby improving the overall quality of care for both male and female post-MI patients.

In addition, our systematic review has identified socioeconomic status as a significant factor contributing to inequalities in the prescribing trends of evidence-based pharmacotherapy post-MI. Patients from lower socioeconomic strata may face barriers to accessing and adhering to recommended therapies, leading to suboptimal care. Policymakers and healthcare providers should prioritize strategies to address these social determinants of health, ensuring that all individuals, regardless of their socioeconomic status, have equal access to evidence-based pharmacotherapy post-MI.

Finally, this research builds upon and consolidates the most notable trends identified in previous studies, providing a comprehensive overview of prescribing patterns for evidence-based therapies post-MI. The synthesis of existing literature allows us to recognize persistent challenges and evolving trends in the field. By understanding these patterns, healthcare professionals and

policymakers can implement targeted strategies to bridge gaps in care, ultimately improving the overall effectiveness of evidence-based pharmacotherapy in the post-MI population.

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