

# The Association Between Schizophrenia and Cardiovascular Diseases: A Retrospective Cohort Study of Primary Care Routine Data in Germany

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## Introduction

Cardiovascular diseases (CVDs) remain among the leading causes of mortality worldwide [1,2].

Although overall CVD-related mortality has declined in recent years, CVDs continue to significantly impact individuals with schizophrenia, contributing to a notably reduced life expectancy – estimated between 13 to 25 years in this population [3,4].

## Methods

- Retrospective cohort study with IQVIA Disease Analyzer
- Data from 1,209 general practices in Germany between 2005-2023
- 12,527 patients aged  $\geq 18$  years with schizophrenia, matched 1:5 with individuals without schizophrenia
- Exclusion of patients with ischaemic heart disease, atrial fibrillation or heart failure prior to, on or within three months after the index date
- CVDs cumulative incidence via Kaplan-Meier curves and hazard ratios (HRs), using univariable Cox regression analysis

Table 1. Baseline characteristics of the study sample, N (%) after 1:5 propensity score matching

Variable	Patients with SZ (N=12,527)	Patients without SZ (N=62,635)	Standardized Mean Difference
<b>Age in years</b>			
Mean (SD)	49.8 (16.9)	50.0 (16.9)	
18 - 40	4,067 (32.5)	20,091 (32.1)	
41 - 50	2,481 (18.8)	12,091 (19.3)	
51 - 60	2,823 (21.4)	13,657 (21.8)	-0.010
61 - 70	1,864 (14.1)	8,706 (13.9)	
> 70	1,923 (14.6)	8,090 (12.9)	
<b>Sex</b>			
Female	6,180 (49.3)	31,130 (49.7)	
Male	6,347 (50.7)	31,505 (50.3)	-0.007
<b>Annual consultations during the follow-up, mean (SD)</b>			
Mean (SD)	6.5 (4.6)	6.6 (4.6)	-0.007
<b>Chronic conditions</b>			
Essential (primary) hypertension	3,398 (27.1)	16,935 (27.0)	-0.002
Disorders of lipoprotein metabolism and other lipidemias	2,010 (16.1)	9,943 (15.9)	-0.005
Obesity	1,334 (10.7)	6,482 (10.4)	-0.010
<b>Index year</b>			
2005-2008	1,047 (8.4)	5,209 (8.3)	
2009-2012	1,542 (12.3)	7,653 (12.2)	
2013-2016	2,462 (19.7)	12,356 (19.7)	-0.002
2017-2020	3,531 (28.2)	17,646 (28.2)	
2021-2023	3,945 (31.5)	19,771 (31.6)	

Proportions of patients in N, % given, unless otherwise indicated. SD: standard deviation. The standardized mean difference is commonly used to compare the distribution of covariates included in the propensity score matching, with differences greater than 0.1 indicating a degree of imbalance. Regarding age and index year, the standardized mean difference was computed for the continuous variable only.

Over a 10-year follow-up, schizophrenia was significantly associated with a higher risk of heart failure (HR: 1.33, 95% CI: 1.20–1.48) and a lower risk of atrial fibrillation and flutter (HR: 0.77, 95% CI: 0.67–0.89). No significant associations were observed for acute myocardial infarction (HR: 0.97, 95% CI: 0.76–1.25), angina pectoris (HR: 0.78, 95% CI: 0.63–0.96), or chronic ischaemic heart disease (HR: 0.91, 95% CI: 0.82–1.02). Stratified analyses showed that schizophrenia was most strongly associated with heart failure in women aged 41–50 years (HR: 3.34, 95% CI: 2.11–5.31), followed by women aged 61–70 years (HR: 1.88, 95% CI: 1.45–2.44) and men aged 51–60 years (HR: 1.81, 95% CI: 1.34–2.45).

## Conclusion

This study highlights the elevated cumulative incidence of cardiovascular disease among individuals with schizophrenia. It is essential to raise awareness—not only among affected individuals but also among their social environment and healthcare providers—that this population might not only be at increased risk for cardiovascular diseases, in general, but also less likely to be diagnosed and receive adequate treatment. As a result, severe cardiovascular outcomes such as HF may occur more frequently and could potentially be prevented through routine cardiovascular screening in this vulnerable population. To address these disparities, targeted prevention strategies and integrated care models are needed. Moreover, future research should further explore the underlying mechanisms driving the associations observed in this study, including genetic, behavioral, and systemic factors.

[1] Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2021 (GBD 2021) Results.

[2] World Health Organization. Cardiovascular diseases (CVDs). 2025.

[3] Goldfarb, M. et al. Severe Mental Illness and Cardiovascular Disease. *J. Am. Coll. Cardiol.* 2022, 80, 918–933.

[4] Rafcikova, J.; Novakova, M.; Stracina, T. Exploring the Association between Schizophrenia and Cardiovascular Diseases: Insights into the Role of Sigma 1 Receptor. *Physiol. Res.* 2023, 72, S113–S126.

## Objective

This novel study addresses the question of whether schizophrenia is associated with an increased risk of CVDs by controlling for metabolic syndrome-related conditions, using real-world primary care data from Germany.

Specifically, the relationship between schizophrenia and five major cardiovascular outcomes were examined: angina pectoris, acute myocardial infarction, chronic ischaemic heart disease, atrial fibrillation and flutter, and heart failure.

## Results

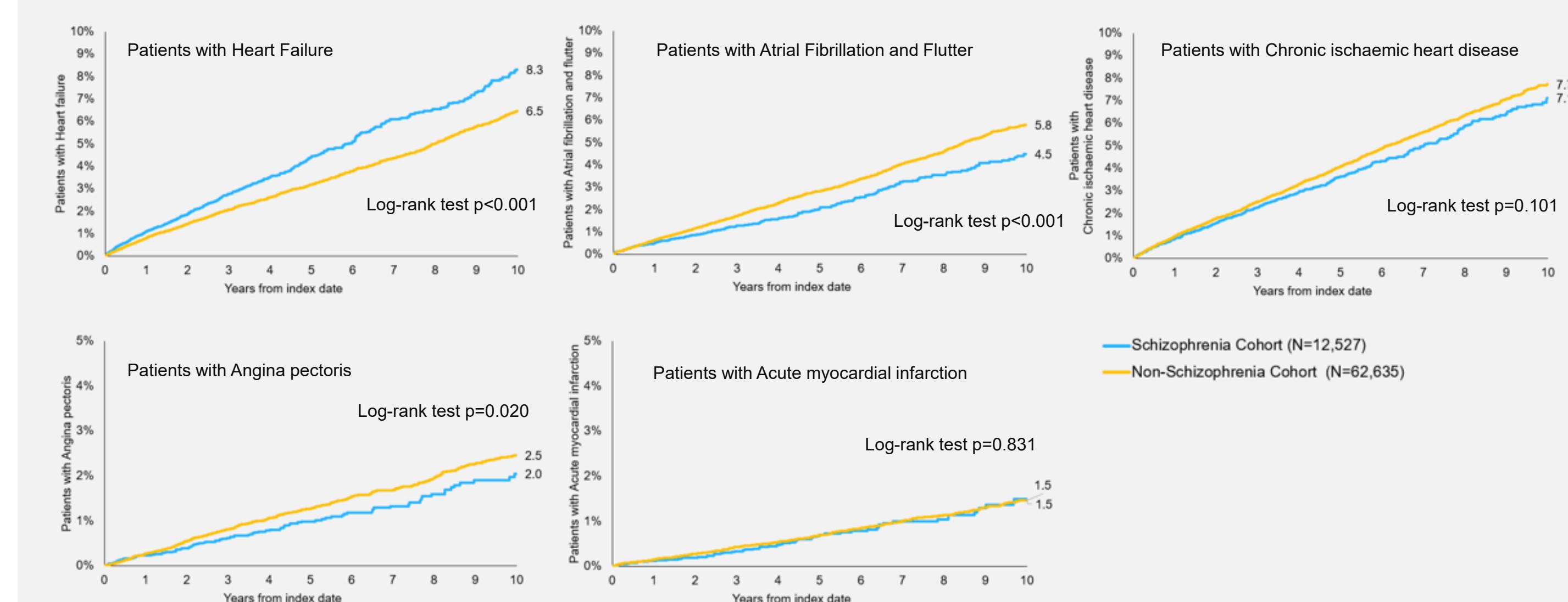


Figure 1. Kaplan-Meier curves for cumulative incidence of CVDs

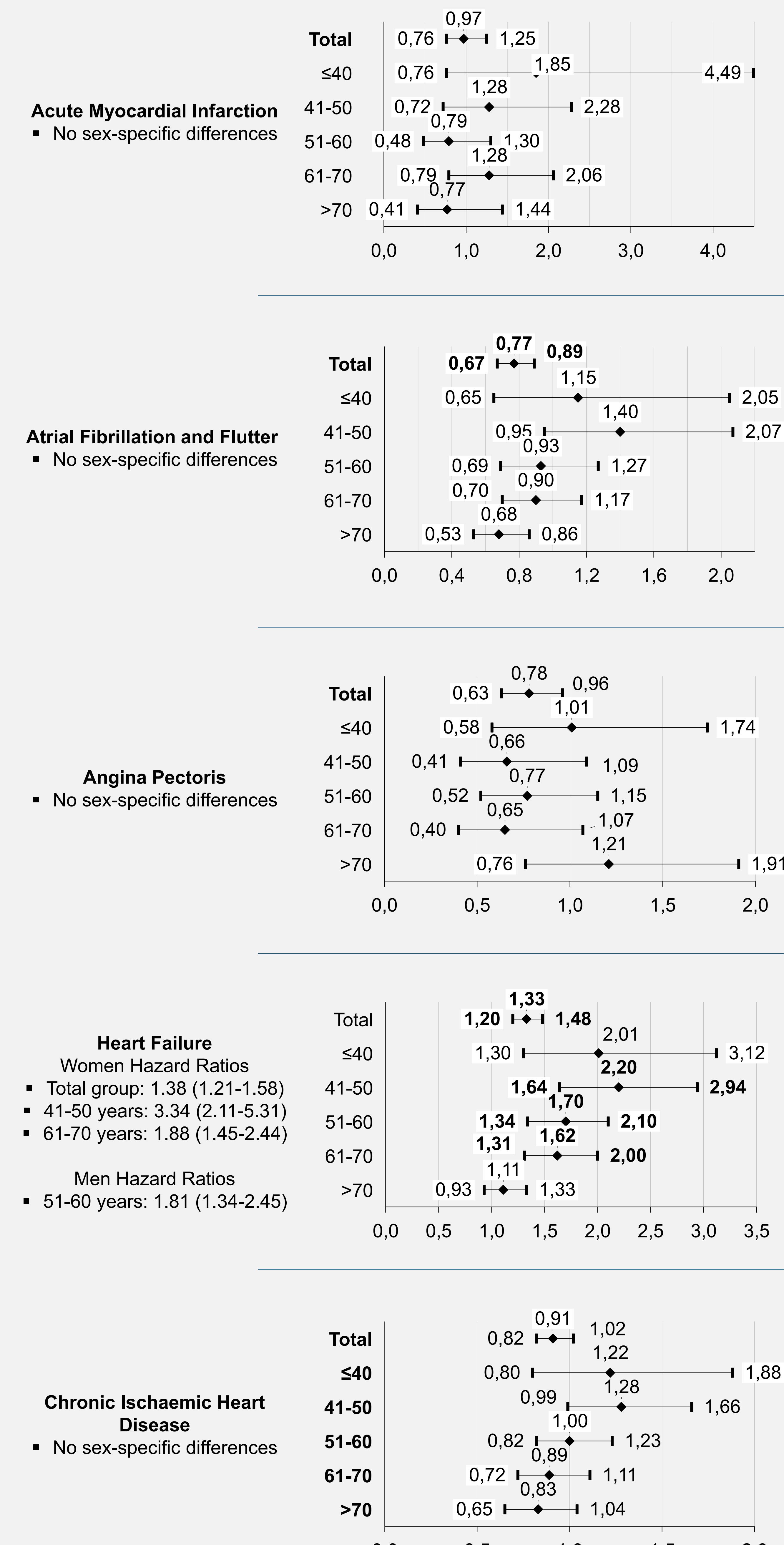


Figure 2. Association between schizophrenia and CVDs (Hazard Ratios) with differences in sex. Bold values denote statistical significance at the p < 0.001 level.