

Adherence to dual antiplatelet therapy among outpatients after acute myocardial infarction in primary care

Sergey B. Fitilev^{1,2}, Alexander V. Vozzhaev¹, Irina I. Shkrebniova^{1,2}, Dmitry A. Klyuev¹, Anna O. Ovaeva¹, Darya K. Barsukova¹

1 Peoples' Friendship University of Russia named after Patrice Lumumba, Medical Institute, Department of Pharmacology and Clinical Pharmacology, 6 Miklukho-Maklaya St., Moscow 117198 Russian Federation;
2 City Polyclinic No 2 of Moscow Healthcare Department, 12 Fruktovalaya St., Moscow 117556 Russian Federation

Corresponding author: Alexander V. Vozzhaev (vozvhaev-av@rudn.ru)

Academic editor: Mikhail Korokin ♦ Received 05 June 2025 ♦ Accepted 11 September 2025 ♦ Published 27 September 2025

Citation: Fitilev SB, Vozzhaev AV, Shkrebniova II, Klyuev DA, Ovaeva AO, Barsukova DK (2025) Adherence to dual antiplatelet therapy among outpatients after acute myocardial infarction in primary care. Research Results in Pharmacology 11(3): 26–36. <https://doi.org/10.18413/rrpharmacology.11.752>

Abstract

Introduction: The efficacy outcomes of dual antiplatelet therapy (DAPT) observed in randomized controlled trials are often not replicated in real-world post-myocardial infarction (MI) patients due to suboptimal adherence to prescribed pharmacotherapy. This study aimed to assess DAPT adherence in outpatients after MI and evaluate its association with risk of major adverse cardiovascular events (MACE).

Material and Methods: This retrospective pharmacoepidemiologic study included 276 patients who experienced AMI between January 1, 2021, and December 31, 2023, based on electronic medical data. Adherence was measured using proportion of days covered (PDC) metric. Kaplan-Meier curves were constructed to evaluate the impact of DAPT adherence on the incidence of MACE over a 12-month period.

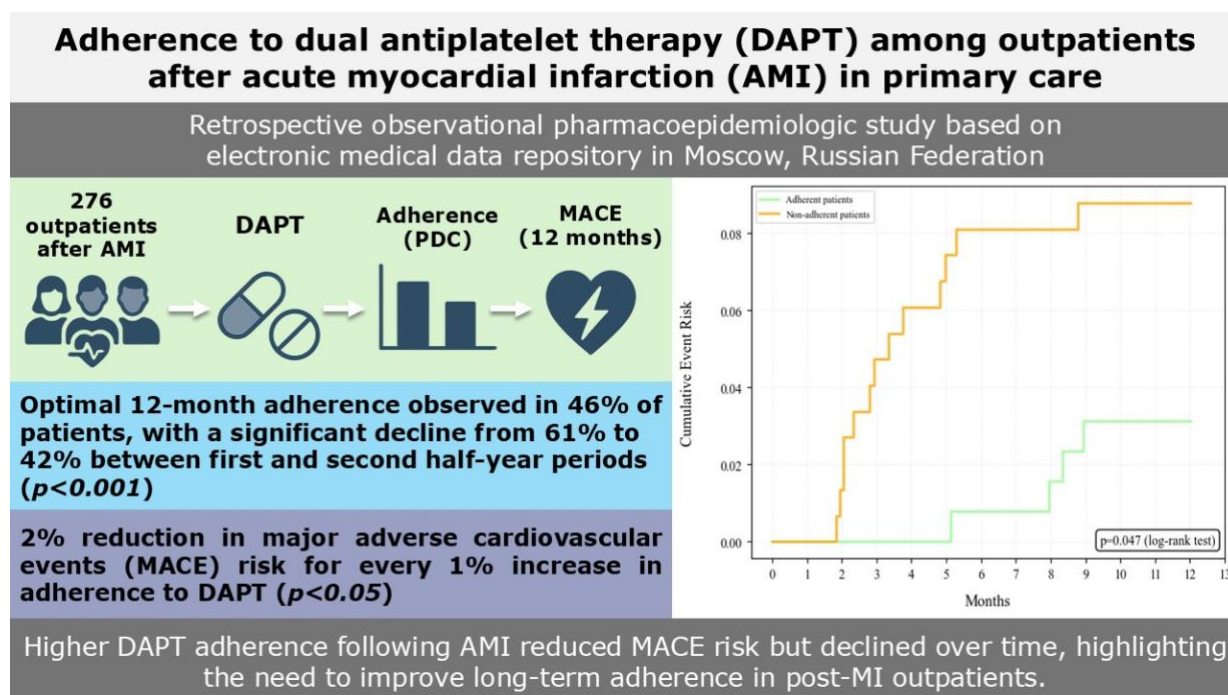
Results: Patients primarily received ASA 100 mg (91.3%) in combination with P2Y12 inhibitor ticagrelor (68.5%). The proportion of patients fully adherent to DAPT (PDC≥80% for both components) over 12 months was only 46.4%, with a significant decline from 60.9% to 42.0% between first and second half-year periods ($p<0.001$). Adherence to P2Y12 inhibitors was significantly higher compared to ASA ($87.8\pm18.9\%$ vs. $73.6\pm27.5\%$; $p<0.001$), largely due to high adherence to ticagrelor (PDC=92.5±12.8%). Post-MI patients fully adherent to DAPT had a lower probability of MACE compared to non-adherent ($p=0.047$). The protective effect of optimal adherence, adjusted for patient comorbidity, was also assessed using Cox regression, which demonstrated a 2% reduction in MACE risk for every 1% increase in PDC ($p<0.05$).

Conclusion: Higher adherence to DAPT following MI was associated with lower risk of MACE. However, adherence declined over time, underscoring the necessity of enhancing medication adherence in post-MI outpatients.



Copyright: © Sergey B. Fitilev et al.
This is an open access article
distributed under terms of the
Creative Commons Attribution
License (Attribution 4.0
International – CC BY 4.0).

Graphical Abstract



Keywords

acetylsalicylic acid; dual antiplatelet therapy; clopidogrel; medication adherence; myocardial infarction; prasugrel; prescription claims data; primary care; proportion of days covered (PDC); ticagrelor

Introduction

Dual antiplatelet therapy (DAPT) is an essential component of secondary prevention in patients after acute myocardial infarction (AMI). The duration of DAPT, as established by current clinical practice guidelines, is 12 months (Barbarash et al. 2024). Substantial evidence accumulated regarding this therapy, which might provide a reduction in the risk of recurrent thrombotic complications during the acute post-infarction period. However, the maximum benefit can only be achieved with optimal patient adherence to antiplatelet agents, which is often lacking in real-world clinical practice. According to the literature, adherence to antiplatelet therapy as part of DAPT averages between 40% and 80% (Hou et al. 2019; Huber et al. 2019; Soldati et al. 2021; Peasah et al. 2022; Dogan et al. 2023). Moreover, international studies have demonstrated that high adherence to DAPT was associated with a reduced risk of adverse cardiovascular outcomes after a coronary event (Hou et al. 2019; Chen et al. 2022; Almendro-Delia et al. 2024).

Notably, there is a paucity of studies in the Russian literature specifically addressing DAPT adherence. Only a few papers describe overall adherence to prescribed pharmacotherapy among post-infarction patients, in which medication adherence was assessed by patient questionnaires and scales (Davidovich et al. 2017; Kuzheleva et al. 2020; Pereverzeva et al. 2020; Kalaydzhyan et al. 2023) or pill counts (Khaisheva et al. 2019).

Along with this, the method for measuring medication adherence based on the analysis of electronic prescription claims data, previously applied for the first time in Russian practice (Fitilev et al. 2024), allows for the evaluation of adherence to individual drugs or their combinations over a specified period. Thus, the authors of this study sought to address the question of how adherent patients are to antiplatelets in real-world primary care setting and how this impacts the clinical effectiveness of DAPT.

The aim of this study was to assess the adherence to DAPT using the proportion of days covered (PDC) metric among patients after myocardial infarction over a 12-month observation period and its association with the risk of cardiovascular events.

Materials and Methods

Study design

A retrospective observational pharmacoepidemiologic study was conducted based on an electronic medical data repository.

Data source

The analysis was performed using patients' electronic medical records (EMR) stored on the Unified Medical Information and Analytical System (EMIAS) platform of Moscow city, which is integrated with the federal Unified State Health Information System of the Russian Federation. EMIAS platform contains comprehensive medical information on all residents of Moscow, collected from healthcare and pharmacy institutions across the city. For this study, data were examined for patients registered at a large outpatient setting, which provides primary care to nearly 200,000 individuals.

Study population

The study analyzed EMR data of patients that were put under the supervision of a primary care cardiologist after they suffered an acute myocardial infarction (AMI) from January 1, 2021, to December 31, 2023 (index MI). Each patient included in the study was observed for 12 months starting from the first visit to cardiologist following hospital discharge.

Inclusion criteria were as follows: men and women over 18 years of age; confirmed diagnosis of AMI; presence of active electronic subsidized prescriptions for antiplatelet agents (acetylsalicylic acid, clopidogrel, ticagrelor, prasugrel); initiation of DAPT (issuance or dispensing of the first prescription) no later than 14 days after hospital discharge; and the absence of anticoagulant prescriptions during the observation period. All patients were required to have subsidized prescriptions for secondary prevention medications (lipid-lowering agents, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, beta-blockers) or documented contraindications to these drugs. All relevant information was entered into individual case report forms.

Data collection from the EMR was conducted in two stages. At the first stage, demographic and medical history data, results of instrumental diagnostics (systolic and diastolic blood pressure, heart rate), hospitalizations, and cardiovascular events during the observation period were recorded. Based on demographic and medical history data, the Charlson comorbidity index was calculated according to the standard methodology (Charlson et al. 1987). Depending on the total score, patients were categorized as having low (1–2 points), moderate (3–4 points), or high comorbidity (5 points or more) (Huang et al. 2014). At the second stage, data on prescriptions for acetylsalicylic acid (ASA) and P2Y₁₂ receptor inhibitors (clopidogrel, ticagrelor, prasugrel) were collected from the specialized EMIAS electronic subsidized prescription module. The international nonproprietary names (INN) of the drugs, dates of prescription and dispensing, number of dispensed units, dosages, and dosing frequency were recorded.

Medication adherence analysis

Adherence to DAPT was evaluated using the analysis of EMIAS electronic prescription claims data by calculating the proportion of days covered (PDC) (Fitilev et al. 2025). The initial date of the calculation period corresponded to the first dispensing of DAPT prescriptions. Subsequent prescription refill dates were tracked, and the observation period ended at the 12-month follow-up. PDC was calculated with adjustments for overlapping prescription dates. PDC threshold of $\geq 80\%$ for each antiplatelet agent defined optimal adherence. Patients with $PDC \geq 80\%$ for both components of DAPT (ASA or P2Y₁₂ inhibitor) were classified as having optimal composite adherence to DAPT.

Survival assessment

Survival analysis assessed the impact of adherence on clinical outcomes. The primary endpoint was a composite major adverse cardiovascular event (MACE), encompassing recurrent MI, cardiovascular death, all-cause mortality, transient ischemic attack, ischemic or hemorrhagic stroke, acute heart failure, and decompensation of chronic heart failure. Kaplan-Meier curves were constructed based on time-to-event data for MACE, stratified by patient groups with varying levels of composite adherence to DAPT.

Statistical analysis

Python 3.11.12 libraries (SciPy 1.13.0, Lifelines 0.28.0, NumPy 1.26.0) were used. Continuous variables were reported as mean with standard deviation (SD) or median with interquartile range

(IQR), depending on distribution normality assessed by the Shapiro-Wilk test. Categorical variables were described as absolute counts and percentages. Group comparisons employed Student's t-test, Mann-Whitney U-test, or Wilcoxon signed-rank test for paired data. Differences in PDC variables among P2Y12 inhibitors were analyzed using one-way ANOVA with Tukey's post hoc test. Categorical differences were evaluated by Pearson's χ^2 or McNemar's test. Kaplan-Meier curves were compared using the log-rank test, and Cox proportional hazards regression quantified MACE risk. A significance threshold of $p < 0.05$ was applied.

Ethic statement

All data were anonymized, and each patient was assigned a unique identification number. The study was conducted in accordance with local standards for personal data protection and for retrospective analysis of anonymized data; approval by the Ethics Committee was not required.

Results

According to the selection criteria, 276 patients with a history of MI were included in the study. Their demographic, clinical, and laboratory characteristics at baseline are presented in Table 1. The cohort predominantly comprised elderly male patients. A majority (85%) experienced their first MI. Notably, 90% of patients underwent myocardial revascularization. Arterial hypertension was the most prevalent comorbidity (95%). Mean systolic (SBP) and diastolic blood pressure (DBP) values were at the upper limit of target ranges. Smoking was identified as a behavioral risk factor in 38% of patients. The Charlson Comorbidity Index revealed high comorbidity (≥ 5 points) in half of the study population.

Table 1. Baseline characteristics of the study cohort of outpatients after myocardial infarction (n=276)

Demographics	
Men, n (%)	178 (64.5)
Age, Me (IQR), years	65.0 (57.0-74.0)
Primary Disease	
Number of myocardial infarctions, n (%):	
1	234 (84.8)
2	39 (14.1)
3	3 (1.1)
Type of index myocardial infarction, n (%):	
ST-segment elevation	171 (62.0)
non-ST-segment elevation	105 (38.0)
Myocardial revascularization, n (%)	250 (90.6)
Comorbidities	
Arterial hypertension, n (%)	263 (95.3)
Chronic heart failure, n (%)	154 (55.8)
Chronic kidney disease, n (%)	86 (31.2)
Diabetes mellitus, n (%)	66 (23.9)
Respiratory diseases, n (%)	35 (12.7)
Charlson Comorbidity Index, Me (IQR), score	5.0 (3.0-6.0)
Charlson Comorbidity Index, n (%):	
1-2 points	38 (13.8)
3-4 points	98 (35.5)
≥ 5 points	140 (50.7)
Instrumental Diagnostics	
Systolic blood pressure, M \pm SD, mm Hg	130.2 \pm 18.6
Diastolic blood pressure, M \pm SD, mm Hg	79.4 \pm 11.0
Heart rate, M \pm SD, beats per minute	75.0 \pm 11.9
Risk Factors	
Smoking, n (%)	104 (37.7)
Alcohol consumption, n (%)	10 (3.6)

Note: M – mean value, SD – standard deviation; Me – median, IQR – interquartile range.

All patients in the study cohort received DAPT combining ASA with a P2Y12 inhibitor. Of these, 252 patients (91.3%) maintained the guideline-recommended ASA dose of 100 mg throughout the observation period. Dose adjustments occurred in 24 cases, with rare instances of patients receiving 50 mg, 125 mg, or 150 mg ASA during therapy optimization.

P2Y12 receptor inhibitors were administered at standard doses: ticagrelor (90 mg twice daily), clopidogrel (75 mg once daily), or prasugrel (10 mg once daily). 87.0% of patients (n=240) maintained the same P2Y12 inhibitor throughout the study, with ticagrelor being the most frequently prescribed agent (Table 2). Medication switches occurred in 36 patients, predominantly involving a transition from ticagrelor to clopidogrel (27 cases). Ticagrelor served as the initial P2Y12 inhibitor in 68.5% of patients at therapy start.

Table 2. Prescription patterns of P2Y12 inhibitors within dual antiplatelet therapy in the study cohort of outpatients after myocardial infarction (n=276) over the 12-month observation period

The medication was not changed during the observation period, n (%)	clopidogrel	62 (22.5)
	ticagrelor	158 (57.2)
	prasugrel	20 (7.2)
The medication was changed during the observation period, n (%)	ticagrelor, clopidogrel	27 (9.8)
	prasugrel, clopidogrel	5 (1.8)
	ticagrelor, prasugrel	4 (1.5)

The results of the PDC calculations were analyzed to assess patient adherence and its dynamics with respect to individual components of DAPT. The PDC values for each medication over the 12-month observation period are presented in Table 3. Notably, overall adherence to the P2Y12 inhibitor group was significantly higher than adherence to ASA ($p<0.001$). Further comparative analysis of PDC values for individual P2Y12 inhibitors demonstrated that this difference was primarily due to the high level of adherence to ticagrelor ($92.5\pm12.8\%$), whereas the PDC values for ASA and clopidogrel were comparable.

Table 3. Adherence to individual components of dual antiplatelet therapy in the study cohort of outpatients after myocardial infarction (n=276) over the 12-month observation period

Medication	12-Month PDC Value	
	M \pm SD, %	Me (IQR), %
Acetylsalicylic acid	73.6 \pm 27.5	80.5 (55.8-100.0)
P2Y12 inhibitors	87.8 \pm 18.9 [†]	95.5 (84.0-100.0)
Clopidogrel	74.1 \pm 23.6	78.5 (58.5-94.8)
Ticagrelor	92.5 \pm 12.8 [‡]	98.0 (92.0-100.0)
Prasugrel	80.0 \pm 28.7	95.0 (66.5-100.0)

Note: [†] – $p<0.001$ compared to PDC for acetylsalicylic acid; [‡] – $p<0.001$ compared to PDC for clopidogrel.

Optimal adherence (PDC $\geq 80\%$) to ASA was maintained by 51.4% of patients throughout the observation period, while adherence to P2Y12 inhibitors was significantly higher at 78.3% (Fig. 1). A negative dynamic in optimal adherence was observed when analyzing the first and second six-month intervals separately. The proportion of patients with optimal adherence to ASA decreased by 16.6% ($p<0.001$), and to P2Y12 inhibitors – by 11.2% ($p<0.001$). A similar pattern emerged in the assessment of composite adherence to DAPT. Only 46.4% of patients maintained optimal composite adherence over the full 12-month period. This metric decreased by 18.9% ($p<0.001$) in the second half of the observation period compared to the first.

Subsequent analysis compared patients with varying levels of composite adherence to DAPT in terms of demographics, medical history, and DAPT regimens to identify potential adherence-related factors that might influence the association between adherence and MACE risk (Table 4). The comparison revealed that the patient groups were comparable in terms of prior MI history, comorbidities, and behavioral risk factors. However, patients with suboptimal DAPT adherence were slightly older. Notably, age contributes to the Charlson Comorbidity Index, and its median score was 1 point higher in the suboptimal adherence group, though this difference lacked statistical significance. Additionally, the analysis highlighted differences in P2Y12 inhibitor prescribing patterns: ticagrelor was more frequently used among optimally adherent patients. As previously noted, ticagrelor demonstrated high annual adherence (PDC=93%).

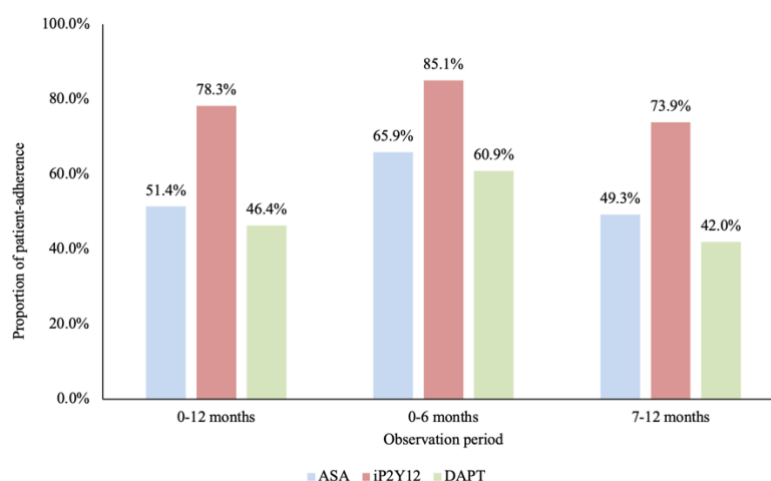


Figure 1. Proportion of patient optimal adherence (PDC \geq 80%) to dual antiplatelet therapy and its components for 1 year and by half-year in the study cohort of outpatients after myocardial infarction (n=276). **Note:** ASA – acetylsalicylic acid; iP2Y12 – P2Y12 receptor inhibitors; DAPT – dual antiplatelet therapy.

Table 4. Comparison of outpatients after myocardial infarction with optimal (PDC \geq 80%) and suboptimal (PDC<80%) composite adherence to dual antiplatelet therapy

Parameter	PDC≥80% (n=128)	PDC<80% (n=148)	<i>p</i>
<i>Demographics</i>			
Men, n (%)	90 (70.3)	88 (59.5)	0.080
Age, Me (IQR), years	64.0 (55.8-71.0)	67.0 (57.0-74.0)	0.045
<i>Primary disease and comorbidities</i>			
Number of myocardial infarctions, Me (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.858
Index MI with ST-segment elevation, n (%)	80 (62.5)	91 (61.5)	0.961
Myocardial revascularization, n (%)	116 (90.6)	134 (90.5)	1
Arterial hypertension, n (%)	122 (95.3)	141 (95.3)	1
Chronic heart failure, n (%)	68 (53.1)	86 (58.1)	0.478
Chronic kidney disease, n (%)	37 (28.9)	49 (33.1)	0.534
Diabetes mellitus, n (%)	33 (25.8)	33 (22.3)	0.593
Respiratory diseases, n (%)	13 (10.1)	22 (14.9)	0.296
Charlson Comorbidity Index, Me (IQR), score	4.0 (3.0-6.0)	5.0 (3.0-7.0)	0.261
Charlson Comorbidity Index, n (%): 1-3 points 3-4 points ≥5 points	18 (15.9) 47 (35.5) 63 (48.6)	20 (12.4) 51 (35.5) 77 (52.1)	0.896
<i>Risk factors</i>			
Smoking, n (%)	50 (39.1)	54 (36.5)	0.725
Alcohol consumption, n (%)	6 (4.7)	4 (2.7)	0.578
<i>DAPT patterns</i>			
Acetylsalicylic acid 100 mg throughout the observation period, n (%)	116 (90.6)	136 (91.9)	0.874
P2Y12 inhibitor unchanged during the observation period, n (%)	107 (83.6)	133 (89.9)	0.173
Clopidogrel use, n (%)	39 (30.5)	55 (37.2)	0.297
Prasugrel use, n (%)	14 (10.9)	15 (10.1)	0.984
Ticagrelor use, n (%)	96 (75.0)	93 (62.8)	0.041

Note: M – mean value, SD – standard deviation; Me – median, IQR – interquartile range.

Given the comparative analysis of patient groups with varying composite adherence to DAPT, the next phase of the study focused on survival analysis within the cohort. During the observation period, 17 patients (6.2%) experienced MACE. Of these, 13 events occurred in the

suboptimal adherence group, compared to 4 in the optimal adherence group. The median time-to-event was significantly shorter in the suboptimal adherence group: 89.0 (IQR 62.0-147.0) days vs. 248.0 (IQR 220.5-258.5) days in the optimal adherence group ($p=0.002$). Kaplan-Meier curves were constructed to evaluate cumulative MACE risk stratified by DAPT composite adherence (Fig. 2). Patients with suboptimal composite adherence demonstrated a significantly higher probability of MACE occurrence ($p=0.047$).

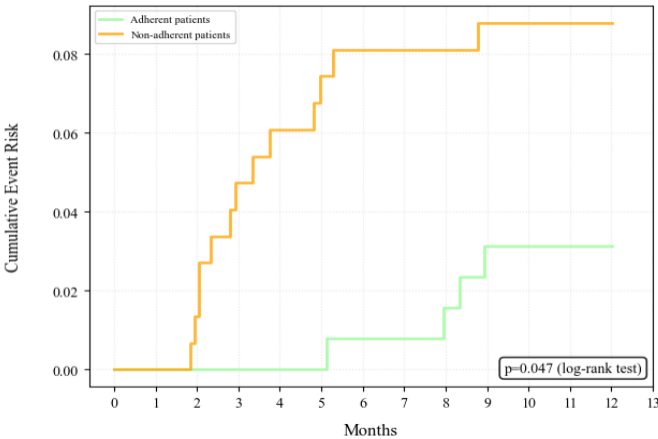


Figure 2. Kaplan-Meier curves for “time-to-MACE” based on optimal composite adherence to dual antiplatelet therapy in outpatients after myocardial infarction.

A Cox regression analysis was performed to assess the impact of composite DAPT adherence on MACE risk. Optimal composite adherence demonstrated a trend toward reducing MACE risk by 66% (HR 0.34; 95% CI 0.11-1.04; $p=0.058$). After adjusting for comorbidity burden (Charlson Comorbidity Index, CCI), optimal adherence remained associated with a 64% risk reduction (HR 0.36; 95% CI 0.12-1.13; $p=0.080$), though statistical significance also remained at the trend level. As expected, comorbidity severity significantly influenced outcomes: each additional point in CCI score increased MACE risk by 34% (HR 1.34; 95% CI 1.08-1.65; $p=0.010$).

A secondary regression analysis evaluated the relationship between adherence levels to individual DAPT components (PDC modeled as continuous variable) and MACE risk, with comorbidity index included as a covariate (Table 5). A 1% increase in PDC for ASA demonstrated a statistically significant protective effect, reducing the risk of MACE by 2%. A comparable magnitude and significance of effect were observed for P2Y12 inhibitors. In both regression models, the comorbidity index showed a significant adverse impact on event risk, as anticipated. However, higher adherence to antiplatelet agents reliably reduced MACE risk regardless of the patient’s comorbidity burden.

Table 5. Impact of adherence to individual components of dual antiplatelet therapy on MACE risk, adjusted for comorbidity, in the study cohort of outpatients after myocardial infarction (n=276) over the 12-month observation period

Variable	Hazard Ratio	95% CI	p
Model 1			
PDC for Acetylsalicylic acid	0.98	0.97-1.00	0.030
Charlson Comorbidity Index	1.31	1.06-1.60	0.010
Model 2			
PDC for P2Y12 receptor inhibitors	0.98	0.96-0.99	0.046
Charlson Comorbidity Index	1.31	1.08-1.60	0.010

Discussion

According to the literature, despite the well-established therapeutic benefits of antiplatelet therapy – particularly in the early period following AMI – there are several barriers to optimal medication adherence in routine clinical practice. These include safety concerns related to this drug class, socioeconomic factors, and a range of other obstacles (Mehran et al. 2013; Arora et al. 2019; LaRosa et al. 2022; Cohen and Jones 2024). As a result, the study of adherence to antiplatelet therapy has long been of interest to researchers. However, detailed investigations

describing adherence to both components of DAPT, as well as to individual agents, remain scarce even in the international literature.

For example, in Switzerland, post-MI patient adherence to DAPT was assessed using prescription refill data (medication possession ratio, MPR metric) over a one-year period (Huber et al. 2019). Low adherence (MPR<80%) was observed in 47.6% of patients. In another study, good adherence to antiplatelet agents (MPR≥75%) during the first six months after hospital discharge was reported in 69% of Italian post-MI patients, with lower adherence rates identified among those older than 65 years (Soldati et al. 2021). Our findings are comparable: optimal composite adherence to DAPT over one year was observed in 46.4% of patients, and in the first six months – in 60.9%. Notably, patients with suboptimal adherence were older, with a median age of 67 years.

Several international studies reported adherence rates to individual DAPT agents, particularly within the P2Y12 inhibitor class, allowing for direct comparison with our findings. For instance, an American study by Dayoub et al. (2018) demonstrated significantly higher 12-month adherence to *clopidogrel* (median MPR 76%) compared to *prasugrel* (MPR 71%) and *ticagrelor* (MPR 68%) among 55,340 post-PCI patients ($p<0.001$). The authors attributed these differences primarily to drug cost. Additionally, a decline in adherence was observed for all agents during the second half of the year compared to the first. Another US study by Peasah et al. (2022) found higher annual adherence to *ticagrelor* (mean MPR 88.1%) compared to *prasugrel* (MPR 79.1%) and *clopidogrel* (MPR 76.4%) among 948 patients after acute coronary syndrome (ACS), with 72.7% of patients overall demonstrating good adherence (MPR≥80%) to P2Y12 inhibitors. In a Turkish study by Dogan et al. (2023) involving 509 post-ACS patients, adherence (measured by PDC) to *clopidogrel* and *ticagrelor* over 12 months was identical – $81.3\pm 29\%$ vs. $81\pm 27.1\%$ ($p=0.9$).

In our study, the proportion of patients with optimal adherence to P2Y12 inhibitors over one year was comparable to the findings of Peasah et al. (2022), at 78.3%, and we also revealed a decrease in adherence during the second half of the observation period. Notably, we found the highest adherence rate for *ticagrelor* (mean PDC 92.5%) compared to *prasugrel* (PDC 80.0%) and *clopidogrel* (PDC 74.1%). It is important to remind that, in our study, all medications were provided to patients through a subsidized drug program.

Numerous studies investigating adherence to antiplatelet therapy have explored its relationship with clinical effectiveness, particularly regarding the risk of adverse outcomes. Thus, in the study by Huber et al. (2019), optimal DAPT adherence (MPR≥80%) was associated with a 32% reduction in cardiovascular event risk (HR 0.68; 95% CI 0.50-0.91). A Spanish cohort study of 2,180 post-ACS patients by Almendro-Delia et al. (2024) demonstrated that non-adherence to any P2Y12 inhibitor increased the composite endpoint risk (all-cause mortality, AMI, stroke, unplanned revascularization, or stent thrombosis) by 32% (HR 1.32; 95% CI 1.10-1.76), with nearly half of events (48.5%) occurring within the first 90 days. An Italian registry analysis of 5,932 post-MI patients revealed that high antiplatelet adherence (PDC≥75%) correlated with a 27% lower risk of all-cause mortality (OR 0.73; 95% CI 0.63-0.84; $p<0.001$) (Lenzi et al. 2015). The IMPACT study, involving 7,152 post-ACS patients, showed a 43% reduction in the composite endpoint (all-cause death, ACS, ischemic stroke) among adherent patients (PDC≥75%) compared to non-adherent (HR 0.57; 95% CI 0.50-0.66) (Sotorra-Figuerola et al. 2021). These findings collectively underscored the critical role of sustained antiplatelet therapy adherence in improving cardiovascular outcomes.

This aspect was further explored in a recent large-scale meta-analysis by Chinese researchers, encompassing 18 studies and 402,201 patients with coronary artery disease (primarily post-AMI) (Chen et al. 2022). The analysis revealed an 11% reduction in mortality risk (HR 0.89; 95% CI 0.85-0.92) with a 20% improvement in antiplatelet therapy adherence (measured by PDC).

In our study, patients with optimal composite adherence to DAPT (PDC ≥80% for both components) also demonstrated a lower risk of adverse cardiovascular events ($p=0.047$), with survival curves showing a pronounced protective effect of optimal adherence between the 2nd and 6th months of observation. Regression analysis indicated a 64% reduction in MACE risk with optimal adherence after adjusting for comorbidity, though this association did not reach high statistical significance.

One contributing factor to this result, beyond the limited sample size, might be the previously described in literature challenge of defining an appropriate threshold for “optimal” or “good” adherence. While researchers traditionally classify cardiological patients as adherent using PDC≥80%, several aforementioned studies adopted a 75% cutoff without clear justification. Furthermore, experts emphasize that adherence analysis in outcome-focused research should extend beyond binary categorization (adherent/non-adherent) and treat PDC as a continuous variable to capture nuanced relationships (Baumgartner et al. 2018; Loucks et al. 2022). Adopting this methodological approach, we incorporated the PDC parameter for DAPT agents

as a continuous variable in regression analysis of adverse cardiovascular outcomes risk. The analysis revealed a statistically significant protective effect of antiplatelet therapy adherence: each 1% increase in PDC for both ASA and P2Y12 inhibitors was associated with a 2% reduction in MACE risk.

These findings, largely consistent with international research data, underscore the critical challenge of suboptimal adherence to DAPT in Russia's clinical landscape. This issue warrants further investigation. The analysis of EMIAS electronic prescription claims data emerges as a robust and practical tool for real-world medication adherence studies. Its applications extend beyond adherence measurement to identifying non-adherence predictors, evaluating adherence-enhancing strategies, and optimizing methodological frameworks for implementation within Russia's healthcare system.

Some *limitations* of our research should be also acknowledged. First, medication adherence calculated from prescription claims data might not necessarily mean that patients took the drug. But this method has been widely used and validated as a good measure of medication adherence. Second, the study was conducted using electronic medical records of patients from a single healthcare institution. But it is a typical primary care setting in the Moscow region. Finally, the obtained results require further validation in a larger cohort of post-infarction patients.

Conclusion

The study characterized dual antiplatelet therapy (DAPT) patterns and evaluated 12-month adherence in post-MI outpatients. Most patients received ASA at 100 mg (91.3%) combined with the P2Y12 inhibitor ticagrelor (68.5%). Optimal composite adherence (PDC \geq 80% for both components of DAPT) was observed in 46.4% of patients over 12 months, with a significant decline in the proportion of adherent individuals during the second half of the year compared to the first (60.9% vs. 42.0%; $p<0.001$). Adherence differed markedly between DAPT components: P2Y12 inhibitors demonstrated higher ($p<0.001$) adherence (mean PDC = $87.8\pm18.9\%$) than ASA (mean PDC = $73.6\pm27.5\%$), driven primarily by high adherence to ticagrelor (mean PDC = $92.5\pm12.8\%$).

The study demonstrated that post-MI outpatients with optimal composite adherence to DAPT exhibited a significantly lower risk ($p=0.047$) of MACE compared to those with suboptimal adherence, particularly during the early post-discharge period (first six months). Regression analysis, adjusted for patient comorbidity burden, confirmed the protective effect of optimal medication adherence, revealing a 2% reduction in MACE risk for every 1% increase in PDC for antiplatelets ($p<0.05$). These findings highlight the critical role of sustained DAPT adherence in improving clinical outcomes, even when accounting for comorbid conditions.

Additional Information

Conflict of interest

The authors declare the absence of a conflict of interests.

Funding

The authors have no funding to report.

Acknowledgments

The authors have no support to report.

Data availability

All of the data that support the findings of this study are available in the main text.

References

- Almendo-Delia M, Padilla-Rodríguez G, Hernández-Meneses B, Blanco-Ponce E, Arboleda-Sánchez JA, Rodríguez-Yáñez JC, Soto-Blanco JM, Fernández-García I, Castillo-Caballero JM, García-Rubira JC, Hidalgo-Urbano R (2024) Nonadherence to ticagrelor versus clopidogrel and clinical outcomes in patients with ACS. Results from the CREA-ARIAM registry. *Revista Espanola De Cardiologia (English Ed.)* 77(2): 113–124. <https://doi.org/10.1016/j.rec.2023.05.011> [PubMed]
- Arora S, Shemisa K, Vaduganathan M, Qamar A, Gupta A, Garg SK, Kumbhani DJ, Mayo H, Khalili H, Pandey A, Das SR (2019) Premature ticagrelor discontinuation in secondary prevention of atherosclerotic CVD: JACC Review Topic of the Week. *Journal of the American College of Cardiology* 73(19): 2454–2464. <https://doi.org/10.1016/j.jacc.2019.03.470> [PubMed]

- Barbarash OL, Karpov YuA, Panov AV, Akchurin RS, Alekhan BG, Alekhin MN, Aronov DM, Harutyunyan GK, Belenkov YuN, Boytsov SA, Boldueva SA, Boschenko AA, Bubnova MG, Bulkina OS, Vasyuk YuA, Galyavich AS, Glezer MG, Golubev EP, Golukhova EZ, Grinstein Yul, Davidovich IM, Yezhov MV, Zavadovsky KV, Irtyuga OB, Karpov RS, Kozioleva VV, Kozioleva NA, Korennova OYu, Kosmacheva ED, Koshelskaya OA, Kukharchuk VV, Lopatin YuM, Merkulov EV, Mironov VM, Martsevich SYu, Mirolyubova OA, Mikhin VP, Nedoshivin AO, Nikulina NN, Nikulina SYu, Oleinikov VE, Panchenko EP, Perepech NB, Petrova MM, Protasov KV, Saidova MA, Samko AN, Sergienko IV, Sinitsyn VE, Skibitsky VV, Soboleva GN, Shalae SV, Shaposhnik II, Shevchenko AO, Shiryayev AA, Shlyakhto EV, Chumakova GA, Yakushin SS (2024) 2024 Clinical practice guidelines for Stable coronary artery disease. Russian Journal of Cardiology [Rossiiskii Kardiologicheskii Zhurnal] 29(9): 6110. <https://doi.org/10.15829/1560-4071-2024-6110> [in Russian]
- Baumgartner PC, Haynes RB, Hersberger KE, Arnet I (2018) A systematic review of medication adherence thresholds dependent of clinical outcomes. Frontiers in Pharmacology 9: 1290. <https://doi.org/10.3389/fphar.2018.01290> [PubMed] [PMC]
- Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. Journal of Chronic Diseases 40(5): 373–383. [https://doi.org/10.1016/0021-9681\(87\)90171-8](https://doi.org/10.1016/0021-9681(87)90171-8) [PubMed]
- Chen C, Li X, Su Y, You Z, Wan R, Hong K (2022) Adherence with cardiovascular medications and the outcomes in patients with coronary arterial disease: “Real-world” evidence. Clinical Cardiology 45(12): 1220–1228. <https://doi.org/10.1002/clc.23898> [PubMed] [PMC]
- Cohen M, Jones C (2024) Patient and physician perspectives on the benefits and risks of antiplatelet therapy for acute coronary syndrome. Cardiology and Therapy 13(3): 631–643. <https://doi.org/10.1007/s40119-024-00372-7> [PubMed] [PMC]
- Davidovich IM, Malay LN, Kutishenko NP (2017) The analysis of long-term outcomes and adherent to treatment in patients after myocardial infarction: Khabarovsk Register Data. The Clinician [Klinitsist] 11(1): 36–44. <https://doi.org/10.17650/1818-8338-2016-10-4-36-44> [in Russian]
- Dayoub EJ, Seigerman M, Tuteja S, Kobayashi T, Kolansky DM, Giri J, Groeneveld PW (2018) Trends in platelet adenosine diphosphate P2Y12 receptor inhibitor use and adherence among antiplatelet-naïve patients after percutaneous coronary intervention, 2008–2016. JAMA Internal Medicine 178(7): 943–950. <https://doi.org/10.1001/jamainternmed.2018.0783> [PubMed] [PMC]
- Dogan O, Bulat Z, Yildiz A, Abaci O, Barman HA, Kılıçarslan O, Yumuk MT, Mirzayev K, Kocas C (2023) Comparison of clopidogrel vs. ticagrelor medication adherence in patients with acute coronary syndrome. European Review for Medical and Pharmacological Sciences 27(15): 7309–7315. https://doi.org/10.26355/eurev_202308_33302 [PubMed]
- Fitilev SB, Kliuev DA, Shkrebniova II, Vozzhaev AV, Ovaeva AO (2025) Methodology for calculating the “proportion of days covered” to determine adherence to pharmacotherapy using data from the accounting of implemented electronic prescriptions of the EMIAS. Good Clinical Practice [Kachestvennaya Klinicheskaya Praktika] (4): 70–81. <https://doi.org/10.37489/2588-0519-2024-4-70-81> [in Russian]
- Fitilev SB, Vozzhaev AV, Shkrebniova II, Kliuev DA, Saakova LN, Ovaeva AO (2024) Electronic medical information and analytical system (EMIAS) as a tool for the new level of understanding and diagnosis of medication adherence in patients with myocardial infarction in primary care practice in Moscow. Good Clinical Practice [Kachestvennaya Klinicheskaya Praktika] (2): 16–32. <https://doi.org/10.37489/2588-0519-2024-2-16-32> [in Russian]
- Hou Y, Yue Y, Zhao M, Jiang S (2019) Prevalence and association of medication nonadherence with major adverse cardiovascular events in patients with myocardial infarction. Medicine 98(44): e17826. <https://doi.org/10.1097/MD.00000000000017826> [PubMed] [PMC]
- Huang Y, Gou R, Diao Y, Yin Q, Fan W, Liang Y, Chen Y, Wu M, Zang L, Li L, Zang J, Cheng L, Fu P, Liu F (2014) Charlson comorbidity index helps predict the risk of mortality for patients with type 2 diabetic nephropathy. Journal of Zhejiang University. Science. B 15(1): 58–66. <https://doi.org/10.1631/jzus.B1300109> [PubMed] [PMC]
- Huber CA, Meyer MR, Steffel J, Blozik E, Reich O, Rosemann T (2019) Post-myocardial infarction (MI) care: medication adherence for secondary prevention after MI in a large real-world population. Clinical Therapeutics 41(1): 107–117. <https://doi.org/10.1016/j.clinthera.2018.11.012> [PubMed]
- Kalaydzhyan EP, Kutishenko NP, Lukina YuV, Sichinava DP, Martsevich SYu, Drapkina OM (2023) The Study of adherence to drug therapy at the stage of outpatient follow-up in patients with acute myocardial infarction (Data from the PROFIL-IM Registry). Rational Pharmacotherapy in Cardiology [Ratsional'naya Farmakoterapiya v Kardiologii] 19(1): 50–57. <https://doi.org/10.20996/1819-6446-2023-02-04> [in Russian]
- Khaisheva LA, Glova SE, Suroedov VA, Samakaev AS, Shlyk SV (2019) Evaluation of drug therapy and adherence to it in patients after acute coronary syndrome in real clinical practice (Results of One Year Observation). Rational Pharmacotherapy in Cardiology [Ratsional'naya Farmakoterapiya v Kardiologii] 14(6): 852–857. <https://doi.org/10.20996/1819-6446-2018-14-6-852-857> [in Russian]
- Kuzheleva EA, Alexandrenko VA, Kondratiev MYu, Aptekar VD, Garganeeva AA (2020) Prediction of adverse cardiovascular events in the post-infarction period, taking into account treatment compliance. Russian Medical Review [RMZh. Meditsinskoe Obozrenie] 4(7): 431–436. <https://doi.org/10.32364/2587-6821-2020-4-7-431-436> [in Russian]
- LaRosa AR, Swabe GM, Magnani JW (2022) Income and antiplatelet adherence following percutaneous coronary intervention. International Journal of Cardiology. Cardiovascular Risk and Prevention 14: 200140. <https://doi.org/10.1016/j.ijcrp.2022.200140> [PubMed] [PMC]
- Lenzi J, Rucci P, Castaldini I, Protonotari A, Di Pasquale G, Di Martino M, Perrone E, Forti P, Fantini MP (2015) Does age modify the relationship between adherence to secondary prevention medications and mortality after acute myocardial infarction? A nested case-control study. European Journal of Clinical Pharmacology 71(2): 243–250. <https://doi.org/10.1007/s00228-014-1793-8> [PubMed]
- Loucks J, Zuckerman AD, Berni A, Saulles A, Thomas G, Alonzo A (2022) Proportion of days covered as a measure of medication adherence. American Journal of Health-system Pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists 79(6): 492–496. <https://doi.org/10.1093/ajhp/zxab392> [PubMed]
- Mehran R, Baber U, Steg PG, Ariti C, Weisz G, Witenbichler B, Henry TD, Kini AS, Stuckey T, Cohen DJ, Berger PB, Iakovou I, Dargas G, Waksman R, Antoniucci D, Sartori S, Krucoff MW, Hermiller JB, Shawl F, Gibson CM, Chieffo A, Alu M, Moliterno DJ, Colombo A, Pocock S (2013) Cessation of dual antiplatelet treatment and cardiac

events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. *Lancet* (London, England) 382(9906): 1714–1722. [https://doi.org/10.1016/S0140-6736\(13\)61720-1](https://doi.org/10.1016/S0140-6736(13)61720-1) [PubMed]

- Peasah SK, Mager D, Munshi KD, Huang Y, Henderson R, Swart ECS, Neilson L, Good CB (2022) Real-world use and outcomes of oral antiplatelets among patients with acute coronary syndrome: A retrospective cohort study. *Drugs – Real World Outcomes* 9(1): 121–127. <https://doi.org/10.1007/s40801-021-00283-2> [PubMed] [PMC]
- Pereverzeva KG, Yakushin SS, Loukianov MM, Drapkina OM (2020) Adherence to the treatment of patients in the long-term supervision period after myocardial infarction (according to the REGATA register). *Kardiologiia* [Kardiologiya] 60(10): 66–72. <https://doi.org/10.18087/cardio.2020.10.n1264> [in Russian]
- Soldati S, Di Martino M, Castagno D, Davoli M, Fusco D (2021) In-hospital myocardial infarction and adherence to evidence-based drug therapies: a real-world evaluation. *BMJ Open* 11(2): e042878. <https://doi.org/10.1136/bmjopen-2020-042878> [PubMed] [PMC]
- Sotorra-Figuerola G, Ouchi D, Giner-Soriano M, Morros R (2021) Impact of adherence to drugs for secondary prevention on mortality and cardiovascular morbidity: A population-based cohort study. *IMPACT study. Pharmacoepidemiology and Drug Safety* 30(9): 1250–1257.

Author Contribution

- **Sergey B. Fitilev**, Doctor Habilitated of Medical Sciences, Professor; Professor of the Department of Pharmacology and Clinical Pharmacology, Medical Institute, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation; Clinical pharmacologist, City Polyclinic No 2 of Moscow Healthcare Department, Moscow, Russian Federation; e-mail: fitilev-sb@rudn.ru; **ORCID ID:** <https://orcid.org/0000-0001-8395-419X>. The author contributed to the concept and design of the study and final approval of the manuscript.
- **Alexander V. Vozzhaev**, Doctor Habilitated of Pharmaceutical Sciences, Associate Professor; Professor of the Department of Pharmacology and Clinical Pharmacology, Medical Institute, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation; e-mail: vozzhaev-av@rudn.ru; **ORCID ID:** <https://orcid.org/0000-0002-2687-5986>. The author contributed to the analysis and interpretation of study results, prepared the draft version of the article, and translated the final version of the article into English.
- **Irina I. Shkrebniova**, Candidate of Medical Science, Associate Professor; Associate Professor of the Department of Pharmacology and Clinical Pharmacology, Medical Institute, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation; Clinical pharmacologist, City Polyclinic No 2 of Moscow Healthcare Department, Moscow, Russian Federation; e-mail: shkrebniova-ii@rudn.ru; **ORCID ID:** <https://orcid.org/0000-0002-0070-3115>. The author contributed to optimization of data collection tools, contributed to interpretation of the results of the study and scientific editing of the article.
- **Dmitry A. Klyuev**, Candidate of Pharmaceutical Sciences; Assistant Professor of the Department of Pharmacology and Clinical Pharmacology, Medical Institute, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation; e-mail: klyuev-da@rudn.ru; **ORCID ID:** <https://orcid.org/0000-0003-2400-3938>. The author contributed to statistical data processing, analysis and interpretation of the study results.
- **Anna O. Ovaeva**, Assistant Professor of the Department of Pharmacology and Clinical Pharmacology, Medical Institute, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation; e-mail: ovaeva_ao@pfur.ru; **ORCID ID:** <https://orcid.org/0009-0006-5245-3791>. The author contributed to data collection and analysis of literary data.
- **Darya K. Barsukova**, student of Pharmacy, Department of Pharmacology and Clinical Pharmacology, Medical Institute, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation; e-mail: funchozabarsuk@mail.ru; **ORCID ID:** <https://orcid.org/0009-0003-5709-0609>. The author contributed to data collection.