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Do statins reduce hospital admissions for cardiovascular diseases?☆

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ABSTRACT

Managing cardiovascular risk is a major concern for healthcare systems. Statins are lipid-lowering drugs used to prevent adverse cardiovascular events. Using an instrumental variables approach, this study provides district-level evidence consistent with a causal effect of statin prescribing on hospitalisation rates for cardiovascular disease. By exploiting variation in prescribing patterns and physicians' preferences to construct an instrument for district-level statin consumption, we move beyond the correlational evidence from existing ecological studies. We focus on the Emilia-Romagna region (Italy) from 2010 to 2019, using district-level longitudinal data. We consider two study populations to measure hospitalisations among individuals aged 50 and over: firstly, the general population living in the region; secondly, those on statin therapy (statin users). The IV estimates show that increasing statin use at the district level is linked to reduced cardiovascular hospitalisation rates, with effects varying by diagnosis and type of admission. Comparing district-level measures of coverage and average treatment intensity, we find more consistent evidence for the coverage-based specification, while intensity estimates based on DDDs per treated patient are less stable and require cautious interpretation. Exploratory analyses by recent hospitalised vascular-event history suggest some differences across treated users, but formal tests provide limited evidence of statistically significant heterogeneity. Overall, the findings support population-level pharmaceutical prevention while cautioning against interpreting aggregate coverage–intensity margins as clean individual-level mechanisms.

1. Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality in the European Union (EU) and account for 11% of total health expenditure in 2021 (Timmis et al., 2024). While poor lifestyle factors contribute to increased cardiovascular (CV) risk, medical treatments nonetheless play a significant role in tackling these adverse events (Vancheri et al., 2022).[1] As CV prescription drugs are a key instrument to contain disease prevalence and progression, there is an interest in evaluating their contribution to population health in the context of rising chronic conditions (e.g., Moscone et al., 2026).

The impact of CV medications has been examined from various perspectives. A body of literature has studied the relationship between pharmaceutical innovation and outcomes (e.g., Lichtenberg, 2009; Lichtenberg and Pettersson, 2014). Other studies have examined the impact of adherence on ischaemic heart disease mortality (Haukka et al., 2012) and non-fatal coronary events in primary prevention (Bouchard et al., 2007). Yet, adherence itself can be related to the treatment benefits: Depalo (2020) shows that adherence to statins is higher among patients with greater benefits. Furthermore, Atella et al. (2017) document that in Italy, unobserved physician heterogeneity remains an important determinant of health status, with adherence effects varying substantially across doctors.

Among drugs targeting CV risk, statins hold a prominent position. By lowering low-density lipoprotein cholesterol (LDL-C), they mitigate the risk of adverse CV events. Randomised controlled trials substantiate

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[1] According to Palmieri et al. (2010), in Italy between 1980 and 2000, 40% of the drop in mortality rates for ischaemic heart disease can be attributed to advancements in medical therapies. Yet, in some circumstances, drugs may also act as substitutes rather than complements to better lifestyles (Kaestner et al., 2014).

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their clinical efficacy, with benefits typically emerging within one to two years following treatment initiation (Shepherd et al., 1995; Baigent et al., 2005). Physicians, acting as gatekeepers, determine whether the level of CV risk warrants initiating therapy, then set the individual dosage, shaping both the extent of population coverage and the intensity of therapy for patients under treatment.[2]

Real-world evidence on the impact of statin utilisation on CVDs in large populations remains limited. By linking prescriptions to health outcomes at the area level, ecological studies can inform on the effectiveness of interventions aimed at curbing cardiovascular risk, with effects that vary depending on the scale of the policy and the target population. To date, ecological studies examining the relationship between statins and CVD outcomes have yielded mixed, context-specific findings. Moreover, the existing body of work on the association between statins and CVDs has not established whether prescriptions causally affect health outcomes.

Nilsson et al. (2011) employ cross-sectional data for Sweden, showing no correlation between statins and incidence/mortality of acute myocardial infarction (AMI), in contrast to earlier studies in the same country reporting a reduction in mortality for ischaemic heart disease (IHD) (Merlo et al., 1999). Also, Vancheri et al. (2016) do not find associations between statin use levels and IHD mortality rates in cross-sectional, country-level data from 12 European countries. According to Bijlsma et al. (2015), statins contributed to the decline in CV mortality in the Netherlands between 1994 and 2010. Medrano et al. (2014) found that statins were negatively associated with IHD hospitalisations in Spain between 1996 and 2006. Using country-level data from 2000 to 2020, Treciokiene et al. (2024) find an inverse association between statins and IHD mortality in Sweden, but not in Lithuania. Existing studies rely mainly on cross-sectional or time-series data: the former lack a longitudinal dimension, while the latter cannot capture heterogeneity across jurisdictions. Moreover, evidence often focuses on homogeneous episodes, although effects may differ by condition and event type. Our study aims to contribute to the real-world evidence on the impact of prescription drugs on population health. We utilise longitudinal quarterly data from the Emilia-Romagna region of Italy between 2010 and 2019, exploiting district-level variation over time to identify the parameters of interest. The analysis, therefore, focuses on the relationship between local prescribing settings and hospitalisation rates among district residents. To the best of our knowledge, this is the first ecological study to exploit an IV design to provide evidence consistent with a causal effect of district-level statin prescribing on district-level CVD hospitalisation rates, under the identifying assumptions. We do so by leveraging prescribing patterns in very low–risk groups to capture physicians' prescribing styles that would otherwise go unobserved. Provided that the identification conditions hold, this strategy allows us to interpret the estimates as causal district-level effects of prescribing variation on hospitalisation rates, rather than as correlational associations.

We provide more comprehensive evidence on the area-level preventive role of prescription drugs against CVDs than commonly available, by accounting for variation across jurisdictions and over time, and by distinguishing between conditions (ischaemic heart diseases-IHDs and cerebrovascular diseases-CDs). Separating IHDs from CDs is important because the relationship between statin prescribing and hospitalisation outcomes need not be homogeneous across cardiovascular domains. Statins have a well-established role in vascular prevention, but cardiovascular disease remains a clinically heterogeneous category and depends on several pathways beyond lipid levels (Cholesterol Treatment Trialists' Collaboration, 2012; Kleindorfer et al., 2021).[3] Distinguishing IHDs from CDs allows us to examine whether aggregate CVD effects mask distinct patterns across clinically distinct hospitalisation outcomes. On the same line, we also distinguish between elective and emergency episodes.

A further feature of our study is the separate analysis of two aggregate prescribing indicators: treatment coverage in the resident population and average treatment intensity among statin users. These measures provide insights into different aspects of local prescribing behaviour, although they should not be seen as a precise breakdown of individual treatment decisions. Considering them separately is policy-relevant because local practices may more directly influence treatment coverage than the treatment intensity among already-treated patients, which is more closely tied to clinical indications. We also conduct a further district-level analysis of CV hospitalisations separately for patients with a recent hospitalised major adverse cardiovascular event (MACE) and for those with no hospitalised MACE in the previous three years. This allows us to describe how the relationship between drug prescribing and hospitalisations varies across populations with different recent vascular event histories.[4]

We find that district-level statin prescribing is linked to lower CVD hospitalisation rates, with substantial heterogeneity across diseases and admission types. In the overall population, the IV estimates indicate reductions in elective IHD admissions and emergency CD admissions. A very similar pattern emerges when coverage is used as the district-level prescribing indicator. Among statin users, the evidence for average treatment intensity is less consistent and should be interpreted with more caution. Exploratory analyses by recent hospitalised vascular-event history suggest some differences across treated-user groups, but formal tests offer limited evidence of statistically significant heterogeneity.

2. Institutional background and the statin market

The Italian National Health Service (NHS) is tax-funded and provides hospital and primary care, mostly free at the point of need. Local Health Authorities (LHAs) are funded to cover services included in the national benefit package ("Essential Levels of Care"). Health Districts (HDs), territorial sub-units of LHAs serving around 100,000–120,000 residents, manage community care policies, set local primary-care priorities and targets, and fund ad-hoc local initiatives. As a result, policies may vary substantially across districts.

Medications are prescribed by specialists and general practitioners (GPs), who are self-employed physicians contracted with the NHS and mainly paid through capitation. GPs may also receive remuneration for locally promoted activities (Iezzi et al., 2014). This design allows local heterogeneity in prescription strategies, especially when decisions depend not only on guidelines but also on patient risk and the expected benefits of pharmacological versus alternative interventions.

Statins are included in Class A medications, which are covered by the NHS and comprise life-saving drugs together with treatments for chronic conditions. For certain chronic diseases, the Italian Pharmaceutical Agency (AIFA) releases *Notes* specifying the conditions under which a drug is reimbursed. For statins, AIFA has issued *"Note 13"* specifying the CV risk conditions required for coverage by the NHS.[5] Cardiovascular drugs were the second-largest therapeutic category in terms of public expenditure in 2023 (13.7% of the total) (AIFA - Italian Medicines Agency, 2024). Within this group, statins display the highest utilisation rate and the highest expenditure per capita. The family of

[2] Statin prescribers act as double agents for both their patients and the payer, and typically weigh the expected gains from pharmaceutical prevention against the responsible use of healthcare resources (Crea et al., 2019).

[3] They include, among others, blood pressure control, atrial fibrillation, anticoagulation, diabetes, smoking, and broader vascular-risk management.

[4] MACE episodes correspond to myocardial infarction and stroke. Because our data do not record the occurrence of these events directly, we proxy them using hospital admissions with the corresponding diagnoses.

[5] Statin prescriptions outside the conditions specified in *Note 13* are almost absent, implying that patients are entitled to free access to the medication. Copayments are required only for those who choose the branded product when generic alternatives are available.

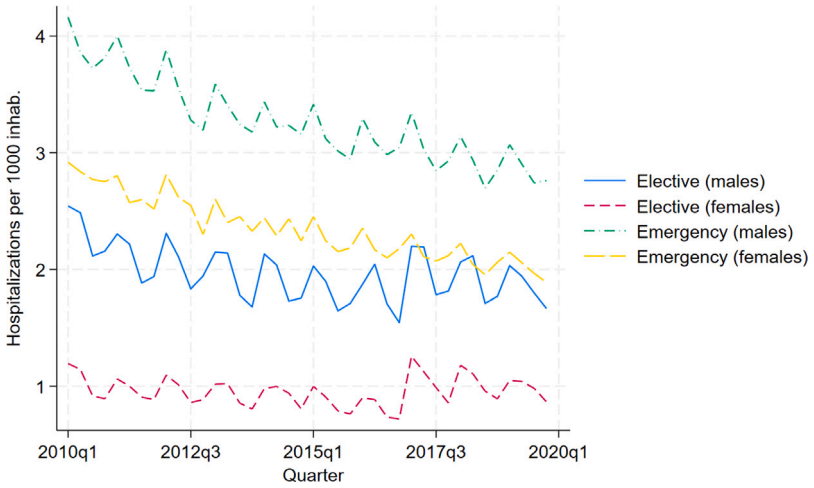


Fig. 1. CVDs hospital admissions in Emilia-Romagna (2010–2019).

statins includes various active principles, each with varying potency in lowering lipid concentrations.[6] Three of them, simvastatin, atorvastatin and rosuvastatin, rank among the top five active substances in terms of per-capita expenditures in Italy (AIFA - Italian Medicines Agency, 2018). Simvastatin is the earliest compound, while rosuvastatin is the most recent and highest-potency option.

Decisions regarding therapy initiation, compound, and dosage depend on the prescriber and are typically based on cholesterol levels, cardiovascular risk, patient characteristics, and clinical history. Some substitutability across active ingredients remains, especially between simvastatin and atorvastatin. Rosuvastatin differs, as AIFA recommends it only as second-line therapy for highest-risk patients who do not respond to lower-intensity treatments (Fiorentini et al., 2022).

3. Data

3.1. Population of interest

The population of interest comprises residents aged 50 and above. Large-scale pharmaceutical prevention is expected to affect CVD hospitalisation rates primarily through treatment coverage among at-risk residents, which may vary across areas with local physicians' practice styles. We first focus on CVD hospitalisations in the entire regional population aged 50 and over, including both statin users and non-users. This approach allows us to evaluate how area-level variation in treatment volume and coverage influences hospitalisation rates.

Subsequently, we restrict the analysis to statin users. Linking district-level prescriptions to hospitalisations among the treated population, we focus on an aggregate measure of treatment intensity. Heterogeneity among statin users may also arise from differences in recent cardiovascular history. Although we cannot reconstruct patients' full clinical histories, we observe hospitalisations for patients who experienced a hospitalised MACE in the previous year and for those with no hospitalised MACE in the past three years. Patients with a recent hospitalised MACE are likely to be managed within a secondary-prevention pathway. The complementary group may include patients with vascular events occurring before the lookback window and should therefore not be interpreted as a pure primary-prevention group.[7]

3.2. Variables description

We use administrative data from Emilia-Romagna for the period 2010–2019. Hospitalisations come from discharge records and drug dispensing from purchases at retail pharmacies. The data is available at the health district level (38 HDs), and the information is complemented by contextual indicators. The variables are measured at a quarterly frequency.[8]

3.2.1. Hospital admissions

To measure adverse events related to CVDs, we use inpatient admissions among Emilia-Romagna residents, occurring both within and outside the region and grouped by the patient's district of residence. Hospital inpatient admissions are identified by primary diagnosis based on the International Classification of Diseases, 9th Revision (ICD-9). We focus on Ischaemic Heart Diseases (ICD-9 410–414) and Cerebrovascular Diseases (ICD-9 430–438), as these conditions are directly linked to the risks associated with high LDL cholesterol levels. We also distinguish between elective admissions and those initiated through the emergency department (ED).[9]

AMI is the most prevalent diagnosis (21.6%). Among cardiac diseases, the other conditions contributing most to hospital admissions are angina and other forms of chronic IHD; among CD, the main drivers of hospitalisation are arterial occlusions and intracerebral haemorrhages. Admission type reflects clinical features: AMI is mostly emergency-based (89.5%), while elective cardiovascular admissions are less frequent and mainly due to angina. Emergency admissions also prevail for cerebrovascular diseases (70.6%), especially cerebral artery occlusions and intracerebral haemorrhages; elective cases mainly involve precerebral artery occlusions and late disease effects.[10]

Hospital admissions are expressed as the number of CVD hospitalisations per 1000 inhabitants, when we consider the entire population, and as the number of CVD hospitalisations for 1000 patients treated, when we focus on statin users. Statin users at time t are defined as

[6] The Italian market includes six compounds, identified by the Anatomical Therapeutic Chemical (ATC) codes: simvastatin (C10AA01), lovastatin (C10AA02), pravastatin (C10AA03), fluvastatin (C10AA04), atorvastatin (C10AA05), rosuvastatin (C10AA07).

[7] This grouping provides an operational distinction based on observed recent hospitalised events, and not a complete characterisation of patients' underlying cardiovascular risk.

[8] Indicators of hospitalisations, statin consumption, average age of naïve patients, demand and supply of hospital services, and "Community Health Centres" (CHCs) have a quarterly variation. The other indicators have been transformed to induce a quarterly variation by interpolating annual data. We assume that, in each quarter of a given year, a quarter of the annual variation occurs.

[9] We exclude day cases and ED visits that do not lead to hospital admission. The former are used for sensitivity checks.

[10] A detailed breakdown by ICD-9 code and gender is reported in the Appendix in Table A.1.

distinct residents recording at least one statin purchase in the previous calendar year. Admissions are then counted in quarter t and assigned to the district of residence, regardless of the hospital where they occur.[11] The measures for hospital admissions are recorded quarterly for each HD, diagnosis group, and type of admission. Fig. 1 displays CVD hospitalisations in the population aged 50+ years at the regional level. We observe a pronounced seasonal component and a declining trend in emergency admissions, whereas elective cases remain fairly stable. Hospitalisations are consistently higher for men compared to women.

3.2.2. Statin consumption

Drug consumption for each HD is calculated from dispensed prescriptions in both public and private retail pharmacies and is assigned to districts based on patients' residence, regardless of the pharmacy's location.[12] When hospital admissions cover the entire regional population, statin use is expressed as Defined Daily Doses (DDDs) per 1000 inhabitants per day, dispensed each quarter to residents of each HD. In the main analysis, the measure is lagged by four quarters relative to hospital admissions, as it has been documented that statins take at least 12 months to reduce CVD risk. However, we also examine the robustness of our findings by extending the lag to eight quarters and by considering a measure of cumulative exposure.

The volume indicator combines treatment coverage in the population and the average dispensed DDDs per treated patient. Decisions regarding the share of patients treated are more likely to reflect prescribers' professional views and their interactions with local policymakers than decisions concerning individual dosage, which are shaped by stricter clinical recommendations. We therefore also assess whether similar patterns emerge when using a related aggregate prescribing indicator, the number of patients receiving statin treatment per 1000 inhabitants, as an alternative to DDDs.

When the population of interest comprises patients under therapy, statin use is measured as the number of DDDs per 1000 treated patients per day. This variable offers an aggregate indicator of treatment intensity, but its interpretation may also mirror changes in the composition of the treated population. Table 1 reports the evolution of the main characteristics of statin users over time. The treated population increases, especially in the early years, while the share of naïve patients declines, suggesting a gradually more consolidated treated population.[13] The share of patients aged 75 and above rises both among all statin users and among users aged 50+, consistently with treatment increasingly involving older age groups. The number of treated users with a recent hospitalised MACE declines over the period. Overall, these indicators evolve smoothly, including average age, indicating gradual changes in patient composition rather than sudden shifts.

Fig. 2 displays DDDs per 1000 inhabitants per day at the regional level, showing an upward trend in volumes for both genders between 2010 and 2019, with males being more intensive users and the gender gap widening over time.

[11] For example, for admissions observed in 2015Q4, residents identified as statin users are those who had been dispensed the drug in 2014. The corresponding hospitalisation rate is defined as the number of admissions in 2015Q4 per 1000 statin users, where the numerator is the number of admissions observed among these patients in the same quarter, while the denominator is the number of distinct residents classified as statin users on the basis of drug purchases recorded from 2014Q1 to 2014Q4. Treatment discontinuations within the look-back window cannot be separately tracked with the available data, while switching across statin molecules does not imply exit from the statin-user group.

[12] Due to data limitations, we are unable to measure in-hospital consumption of statins and those dispensed directly by hospital pharmacies.

[13] Naïve patients are individuals initiating statin treatment. Patients are classified as naïve in the quarter in which they receive statins for the first time.

3.2.3. Contextual factors

We complement the measures of statin use with contextual information. We consider proxies for the demographic structure of the HDs, including gender-specific shares of age groups (75+; 65–74; and 50–64) and the share of foreigners aged 50+. Socio-economic characteristics and local living standards, deemed to affect lifestyle and local health needs, are captured by per-capita taxable income and by the share of individuals enrolled in higher education over the number of inhabitants aged 19–30.

The provision of hospital services reflects the local availability of hospital inputs. Accordingly, we include standardised measures of hospital human and physical capital, such as the number of acute-care inpatient beds per 1000 inhabitants and the number of physicians employed in public hospitals. To account for the availability of specialist care, we consider the number of cardiology-specialised doctors. Hospital output is measured by the total number of inpatient days per 1000 inhabitants, controlling for both days of care provided to district residents, regardless of where treatment occurs, and days delivered within the district, regardless of patients' place of residence. Lastly, to account for organisational changes in primary care services, we control for the number of CHCs per 1000 inhabitants operating in each quarter within the HD.

Table 2 shows descriptive statistics for the variables used in the empirical analysis, both for the overall population aged 50 and above and for the population of statin users.

4. Methods

4.1. Empirical strategy

We analyse hospital admissions for two target populations: the overall population aged 50 and above, and individuals in the same age range receiving statin therapy. For the former group, we first investigate the relationship between total hospital admissions for CVD-related conditions and the volume of statins dispensed. To capture potential heterogeneous effects of medication use, we analyse inpatient stays separately for the two major categories of CVDs (Ischaemic Heart Disease and Cerebrovascular Disease). We present separate analyses for males and females, and distinguish between elective and emergency admissions.

We estimate the effects of interest using a longitudinal model with district fixed effects on quarterly data aggregated at the district level.

The model specification reads as follows:

$$hosp_{it} = \beta_1\, DDDs_{i(t-4)} + \beta_2\, rosu_{it} + \beta_3\, age_nai_{i(t-4)} + \boldsymbol{\gamma}\, \boldsymbol{X_{it}} + \boldsymbol{\delta_i} + \boldsymbol{\tau}_t + \epsilon_{it} \quad (1)$$

where $i = 1, \ldots, 38$ identifies the HDs, $t = 1, \ldots, 40$ represents the quarters, $\boldsymbol{\delta}_i$ is a district fixed effect, $\boldsymbol{\tau}_t$ is a vector of additively included seasonal $(q_1, \ldots, q_4)_t$ and year $(y_1 \ldots y_9)_t$ dummies, and ϵ_{it} is an error term. $hosp_{it}$ is hospitalisations in HD i and quarter t; $DDDs_{i(t-4)}$ is statin consumption in HD i and quarter $(t-4)$; $rosu_{it}$ is the share of rosuvastatin consumption in HD i and quarter t; $age_nai_{i(t-4)}$ is the average age of naïve patients in HD i and quarter $(t-4)$; $\boldsymbol{X}_{it}$ is a vector of control variables in HD i and quarter t. The inclusion of a 1-year lag in statin consumption is intended to capture the effect of the treatment within the shortest time horizon before one can expect statins to be effective.

Standard errors are clustered at the district level. For the main analyses, inference is based on the wild cluster bootstrap procedure with clustering at the district level, as a finite-sample refinement to conventional cluster-robust inference. In these cases, statistical significance is determined using wild cluster bootstrap p-values, and we report 95% confidence intervals.

District fixed effects help control for time-invariant differences among districts that might jointly affect statin consumption and CVD hospitalisations, thus removing cross-sectional confounding. These unobserved characteristics that stay constant within districts include longstanding disparities in demographic composition, socioeconomic

Table 1
Statin users.

Year	N. of patients	Avg age	Share 75+	Share 85+	N. of naïves	Share naïves	N. of patients 50+	Share 50+	Avg age 50+	Share 75+ (out of 50+)	N. of patients with MACE
2010	375 631	68.45	0.34	0.07	50 684	0.13	356 144	0.95	69.94	0.36	9151
2011	399 629	68.71	0.35	0.07	49 079	0.12	379 174	0.95	70.19	0.37	9260
2012	415 889	68.99	0.36	0.08	47 300	0.11	395 080	0.95	70.44	0.38	9176
2013	416 377	69.77	0.38	0.09	39 991	0.10	396 768	0.95	71.10	0.40	8731
2014	415 245	70.05	0.39	0.09	36 394	0.09	396 387	0.95	71.36	0.41	8347
2015	422 348	69.87	0.40	0.10	38 419	0.09	403 536	0.96	71.19	0.42	8316
2016	428 003	69.96	0.41	0.10	40 944	0.10	409 157	0.96	71.27	0.42	7608
2017	440 878	70.09	0.41	0.10	42 053	0.10	421 782	0.96	71.39	0.43	7953
2018	450 765	70.22	0.41	0.11	42 555	0.09	431 621	0.96	71.50	0.43	8002
2019	456 153	70.28	0.41	0.11			436 607	0.96	71.57	0.43	
% change 2010–19	21.44%	2.66%	20.72%	68.08%	−16.04%[a]	−30.03%[a]	22.59%	0.99%	2.33%	19.08%	−12.56%[a]
CAGR	2.18%	0.29%	2.11%	5.94%	−1.92%[a]	−3.89%[a]	2.29%	0.11%	0.26%	1.96%	−1.48%[a]

Patients are counted as distinct individuals with at least one statin purchase during the year. CAGR = Compound Annual Growth Rate.
[a] Rate computed over the period 2010–2018.

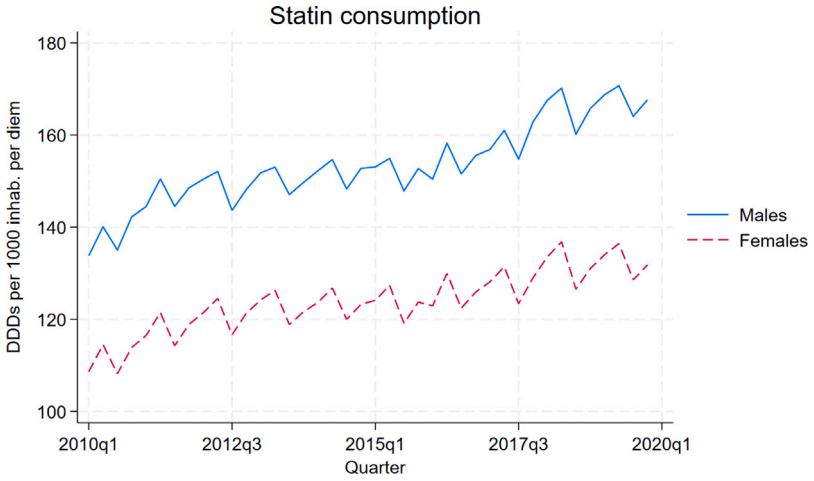


Fig. 2. Statin consumption in Emilia-Romagna (2010–2019).

conditions, baseline cardiovascular risk, health behaviours, disease prevalence, persistent social and cultural norms, and local health system features.

We include year fixed effects and quarter fixed effects. Year fixed effects capture trends and policy changes influencing statin use and cardiovascular outcomes across all districts, while quarter fixed effects account for recurring seasonal patterns in cardiovascular hospitalisations and statin consumption.[14]

We also control for the average age of statin initiators (naïve patients) at the district-quarter level as a proxy for time-varying underlying CV risk and patient composition. Conditional on district- and time-fixed effects, variations in the average age at which treatment starts mainly reflect shifts in the age distribution and risk profile of individuals newly starting statin therapy, as well as differences in when CV risk becomes clinically significant. The variable helps account for remaining within-district variation in CV risk that could be related to both statin use and hospitalisations.[15] Moreover, to account for potential local variation in the prevalence of highly complex patients, we include the share of rosuvastatin use relative to total statin use.

Finally, the inclusion of contextual factors is intended to control for variations in the underlying determinants that may affect population health and the supply of health services. They cover domains related to the demographic composition, socioeconomic conditions, and the supply of healthcare services, both in hospitals and in the community.

4.2. Instrumental variable estimation

Several challenges remain in causally interpreting the relationship between statin use and cardiovascular hospitalisations at the district-quarter level. In real-world settings, statin use is not randomly assigned; instead, it reflects patients' underlying risk, physicians' judgement, and local clinical practices and policies. Although our main specification controls for multiple confounding factors and time-invariant district-specific heterogeneity, and we include a one-year lag in statin consumption to mitigate simultaneity, a significant risk of endogeneity persists.

A source of endogeneity in statin use is reverse causality from hospitalisations to prescriptions. The latter may reflect the endogenous therapeutic response to underlying CV risk. When hospital episodes for cardiovascular events increase at the local level due to changes in underlying risk, prescribers might respond by starting new patients on statins or increasing the average dose. As a result, statin use may increase following a rise in CV risk and in subsequent hospitalisations.

[14] Accounting for seasonality is relevant because CV risk varies by season, as do statin purchases. In Italy, AMI events are characterised by a winter peak (e.g. Stewart et al., 2017), and there is evidence of stockpiling ahead of holiday seasons (e.g. Fiorentini et al., 2022). By including additive year and quarter fixed effects, our specification assumes that seasonal patterns are stable across years, a claim which is supported by an inspection of our data.

[15] This measure is useful for capturing short-term variations in underlying risk, as the characteristics of newly treated patients can quickly change due to demographic shifts or evolving screening methods.

Table 2
Descriptive statistics.

Part A: Variables by gender	Men				Women			
	Mean	St. dev.	Min	Max	Mean	St. dev.	Min	Max
Elective admissions per 1000 inhab.	1.99	0.65	0.22	5.98	0.95	0.41	0.09	3.69
Emergency admissions per 1000 inhab.	3.28	0.72	1.36	5.85	2.35	0.58	0.52	4.84
Elective IHD admissions per 1000 inhab.	1.27	0.55	0.11	5.13	0.38	0.21	0.00	1.66
Emergency IHD admissions per 1000 inhab.	1.61	0.47	0.33	3.47	0.79	0.27	0.00	2.03
Elective CD admissions per 1000 inhab.	0.72	0.33	0.00	2.84	0.57	0.35	0.00	2.90
Emergency CD admissions per 1000 inhab.	1.66	0.45	0.39	3.84	1.56	0.45	0.26	3.56
Elective IHD admissions per 1000 pat.	3.71	1.98	0	15.13	1.17	0.88	0	6.39
Emergency IHD admissions per 1000 pat.	3.77	1.66	0	11.71	1.87	1.00	0	7.33
Elective CD admissions per 1000 pat.	1.78	1.02	0	8.07	1.27	0.94	0	8.14
Emergency CD admissions per 1000 pat.	2.93	1.13	0	9.03	2.65	1.09	0	8.79
DDDs per 1000 inhab. per diem	156.39	36.01	57.69	237.64	125.18	25.39	50.05	186.97
DDDs per 1000 patients	897.74	79.39	698.11	1122.91	775.11	47.73	657.94	915.48
Patients per 1000 inhab.	172.79	30.91	72.02	226.93	160.94	28.92	73.19	222.98
Share of rosuvastatin consumption	17.61	6.18	6.60	41.16	18.35	6.26	6.80	43.20
Avg age naïves	62.27	1.67	55.89	68.38	65.01	1.64	59.98	70.40
Share of individuals aged 75+	24.17	1.70	20.34	28.47	31.23	2.23	25.81	36.68
Share of individuals aged 65–74	26.01	1.03	23.57	29.10	24.54	0.85	22.43	27.31
Higher education proxy	16.22	3.80	11.02	29.88	21.71	3.52	15.40	35.59
Share of foreign population	3.18	0.94	0.96	6.70	4.86	1.28	2.03	8.40

Part B: Variables on the total population	Mean	St. dev.	Min	Max
Income per capita	15 527.39	1651.02	11 980.95	20 039.02
Hospital days per 1000 inhab. (res.)	231.77	34.41	139.11	337.17
Hospital days per 1000 inhab. (hosp.)	211.60	138.58	0.00	661.08
NHS Hospital beds per 1000 inhab.	2.08	2.47	0.00	10.56
NHS Hospital doctors	199.00	338.49	0.00	1936.31
Doctors specialised in cardiology	24.14	17.27	4.09	103.09
CHCs per 1000 inhab.	0.02	0.02	0.00	0.09

All variables are measured at the district level.

Furthermore, even after accounting for district- and time-fixed effects, unobservable factors influencing health outcomes vary heterogeneously across districts over time. They can include changes in lifestyle and risky behaviours, screening practices, health literacy, and the organisation of community services. Since they potentially affect both statin prescription and cardiovascular hospitalisations, a correlation between statin consumption and the regression error term may arise. Overall, drug purchases result from a combined decision-making process involving doctors and patients. They reflect clinical risk assessment, prescribing decisions, patient adherence, local policies, and potentially other factors. Two main factors contribute to statin prescription: first, cardiovascular risk, which drives CVD-related episodes and hospitalisations; and second, prescribing habits and preferences, which affect statin use but do not directly cause CVD episodes. To support a causal interpretation, variation in statin consumption that reflects such differences in prescribing should be isolated from variation in underlying cardiovascular risk.

To this end, we adopt an IV approach that leverages variation in aggregate statin purchases plausibly driven by local prescribing behaviour rather than by unobserved cardiovascular risk. We base our instrument on quarterly statin prescriptions among individuals under 50 living in the district, measured as DDDs per 1000 inhabitants per day.

We estimate the model in Eq. (1) by exploiting an FE-IV (2SLS) estimator. The first stage specification reads as follows:

$$DDDs_{i(t-4)} = \pi\, DDDs_under50_{i(t-4)} + \gamma_1\, rosu_{it} + \gamma_2\, age_nai_{i(t-4)} + \boldsymbol{\varphi}\, \boldsymbol{X_{it}} + \boldsymbol{\mu_i} + \boldsymbol{t_t} + \varepsilon_{it} \quad (2)$$

where $i = 1, \ldots, 38$ identifies the HDs, $t = 1, \ldots, 40$ represents the quarters, $\boldsymbol{\mu}_i$ is a district fixed effect, $\boldsymbol{t}_t$ is a vector of additively included seasonal $(q_1, \ldots, q_4)_t$ and year $(y_1 \ldots y_9)_t$ dummies, and ε_{it} is an error term. $DDDs_{i(t-4)}$ is statin consumption in HD i and quarter $(t-4)$; $DDDs_under50_{i(t-4)}$, the IV, is statin consumption of individuals under 50 in HD i and quarter $(t-4)$; $rosu_{it}$ is the share of rosuvastatin consumption in HD i and quarter t; $age_nai_{i(t-4)}$ is the average age of naïve patients in HD i and quarter $(t-4)$; $\boldsymbol{X}_{it}$ is the vector of exogenous variables in HD as in Eq. (1).

The second stage is the following:

$$hosp_{it} = \beta_1\, \widehat{DDDs}_{i(t-4)} + \beta_2\, rosu_{it} + \beta_3\, age_nai_{i(t-4)} + \boldsymbol{\gamma}\, \boldsymbol{X_{it}} + \boldsymbol{\delta_i} + \boldsymbol{\tau}_t + \epsilon_{it} \quad (3)$$

where $\widehat{DDDs}_{i(t-4)}$ denotes the fitted values from the first-stage equation.

Several arguments support our choice of the instrument in terms of relevance and validity.

The under-50 age group has a minimal risk of CV hospitalisation and accounts for a small share of observed CVD admissions. Statin use in this population can be seen as a proxy for physicians' prescribing behaviours and preferences, treatment aggressiveness, and local clinical practices, rather than a response to acute cardiovascular conditions and events. According to this argument, prescriptions in the low-risk population are driven by clinical preferences rather than by an actual need for treatment. In our IV analysis, we therefore utilise an age-separation design to distinguish the two components mentioned above. The population for which we calculate the instrument does not directly contribute to the outcome.

GPs treat patients across various age groups, and prescribing decisions are shaped by shared information, guidelines, and local professional practices. Other things equal, including underlying risk, districts where doctors are more prone to prescribe statins to younger, low-risk individuals can also be expected to show higher statin use among older and higher-risk populations. Variations in prescribing behaviour towards younger patients offer insights into prescription attitudes for the overall (older) population. This approach leverages shocks to prescribing style rather than to the underlying cardiovascular risk. Empirically, this hypothesis would be confirmed by a strong first-stage relationship between statin use among under-50 and among 50+ individuals,

supporting the idea that districts with more aggressive prescribing to low-risk individuals also have higher statin use among higher-risk groups.

The exclusion restriction assumes there is no direct link between prescriptions for patients under 50 and CVD events among those aged 50 or older. It is justified on the grounds that preference-driven variation, such as prescribing patterns for the under-50 population, is unrelated to health outcomes for the high-risk population, once key confounders are accounted for. The validity of the instrument relies on the assumption that statin use among people under 50 affects cardiovascular hospitalisations of higher-risk (older) individuals only through its influence on their statin use. This assumption is plausible for several reasons. Firstly, individuals under 50 are a very low-risk group and account for a tiny portion of cardiovascular hospitalisations, which, in any case, do not contribute to the outcome, calculated only for those aged 50 and over. Additionally, there is no reason to expect that their drug utilisation directly affects the health outcomes of older patients. Secondly, shocks that increase cardiovascular hospitalisations among the elderly do not have feedback effects on statin prescriptions for younger people, given the very different risk levels for the two groups, which makes direct reverse causality less plausible. At the same time, we cannot entirely rule out shared changes in cardiovascular risk or care across age groups. For this reason, we complement the IV analysis with a rich set of validation and robustness checks. Finally, the instrument reflects variation in prescribing styles rather than differences in underlying risk or health severity, since risk in the younger population is negligible across the board.

The IV estimates identify a local average treatment effect (LATE) (Imbens and Angrist, 1994) for districts where changes in prescribing behaviour towards low-risk individuals lead to variations in statin use among higher-risk populations (compliers). The LATE parameter reflects the causal effect of marginal shifts in prescribing habits within districts, rather than changes in underlying cardiovascular risk. Prescribing behaviour is precisely what local policies can influence. While prescribing styles appear to be correlated across age groups across all districts, the strength of this relationship may differ, suggesting that the IV assigns greater weight to districts in which prescribing behaviour is more responsive to such variation. If treatment effects are fairly homogeneous across districts, the estimated LATE may be informative about broader average effects.

One might still be concerned that prescriptions to younger individuals could reflect unobserved CV risk or early disease onset. However, the very low CV risk of individuals under 50 is corroborated by the negligible proportion of CV-related hospitalisations they account for.[16] Furthermore, any time-invariant differences in underlying risk are captured by district fixed effects and identification hinges on within-district variability in prescribing towards low-risk groups, rather than on risk differences across districts. We measure the outcome and the IV on separate groups of individuals. However, using longitudinal data, we cannot exclude that some younger patients may later contribute to hospitalisations among patients aged 50+. This is not worrisome as long as we work with aggregated data and the identification relies on temporal variation. Our approach is based on splitting the patient population into low- and high-risk groups. This strategy may be threatened if risk increases gradually and an intermediate-risk group exists. To avoid overlap and to ensure that the two subpopulations significantly differ in terms of CVD risk, we replicate the main IV analysis with an "age-*donut*": we use prescriptions for individuals under 50 as an IV but calculate the outcome for the population above 65, excluding individuals in the intermediate age and risk group. The age-*donut* design is more conservative than the main analysis; while it strengthens the exclusion restriction, it could weaken the relevance of the instrument in the first-stage regression.

[16] Table A.2 in the Appendix shows that hospitalisation rates for those under 50 are up to 10 times lower than for the 50–64 age group.

5. Results

5.1. Regression analysis: general population

5.1.1. Statin volumes (DDDs): Fixed-effects estimates

Throughout the results section, coefficients are interpreted as district-level changes in hospitalisation rates associated with district-level prescribing variation. We first explore the association between district-level statin use and CVD hospital admission rates in the general population aged 50+. In panel A of Table 3, we consider hospitalisations for the combined set of the CVD conditions of interest (i.e., IHD+CD). The first two columns present the estimates of Eq. (1) for the district-level population covering residents aged 50+, while the following columns display the results separately by gender.

The primary variable of interest is the volume of drug prescriptions, expressed as DDDs per 1000 inhabitants per day, lagged by 4 quarters. The results outline a negative association between DDDs and CVD hospitalisations for both genders, with broadly similar magnitudes across admission types. Prima facie, such evidence suggests a "protective" effect of statin use against major adverse events, as measured by hospitalisation rates for IHD and CD. However, this association cannot be interpreted causally, as drug volumes may be endogenous.

A higher share of rosuvastatin prescriptions is positively associated with emergency admissions, possibly reflecting a higher concentration of patients at elevated CV risk. The effect is smaller and not statistically significant for elective conditions. The average age of naïve patients exhibits a different pattern across genders or types of admissions. For men, earlier treatment initiation is associated with a higher (marginally significant) frequency of elective CVD admissions and a lower frequency of emergency admissions, while no statistically significant effect is detected for women.

To gain further insight into the relationship between statin use and hospital admissions, we estimate Eq. (1) separately for IHDs and CDs. The results reveal strikingly different patterns between emergency and elective episodes. Table 3 (Panel B) shows the estimates for IHD hospitalisations. Volume coefficients indicate a negative, significant association between DDDs and admission rates for elective procedures, with a larger effect among males. However, higher drug use is not significantly associated with emergency admissions except for women. Regarding CD hospitalisations (Panel C): DDDs are negatively associated with emergency admissions for both genders, while elective treatments are largely unaffected. The reduction in emergency CD hospitalisations is similar across genders.

5.1.2. Statin volumes (DDDs): Fixed-effects IV estimates

Since potential endogeneity of prescriptions threatens the identification of the parameter of interest, we implement an IV strategy that allows us to interpret the estimates as district-level effects of statin use on hospitalisation rates. Table 4 presents the IV estimates based on Eqs. (2) and (3). The results are reported following the same structure as in Table 3.

The first-stage coefficient on the instrument is statistically significant across all specifications and is positively associated with the endogenous variable. The F-statistic is well above the conventional threshold of 10. This evidence supports the instrument's relevance, as statin use among individuals under 50 is a good predictor of prescription rates in older groups.

Turning to the second-stage estimates, accounting for the potential endogeneity of statin prescribing, we continue to find a statistically significant negative effect of DDDs on hospital admissions among individuals aged 50+. The absolute values of the estimated coefficients are slightly larger than their non-instrumented counterparts. The differences in magnitude between the IV estimates and the FE estimates are consistent with a potential reverse-causality mechanism from hospitalisations to statin consumption, which could attenuate the estimated effect of statin use. The IV approach identifies a LATE for districts

Table 3
DDDs and hospitalisations for various diagnostic categories: FE estimation.

Dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)					
	All 50+		Men 50+		Women 50+	
	Elective	Emergency	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)						
DDDs$_{t-4}$	−0.0045***	−0.0042***	−0.0034**	−0.0039**	−0.0041***	−0.0049**
WB 95% CI	[−0.0074, −0.0016]	[−0.0071, −0.0013]	[−0.0067, −0.0002]	[−0.0067, −0.0008]	[−0.0066, −0.0017]	[−0.0093, −0.0011]
Share Rosuvast$_t$	0.0067	0.0112**	0.0091	0.0119**	0.0024	0.0094*
WB 95% CI	[−0.0033, 0.0146]	[0.0021, 0.0276]	[−0.0053, 0.0200]	[0.0022, 0.0320]	[−0.0082, 0.0112]	[−0.0010, 0.0202]
Avg age naives$_{t-4}$	0.0141*	−0.0202*	0.0217*	−0.0215**	0.0027	−0.0071
WB 95% CI	[−0.0012, 0.0287]	[−0.0413, 0.0002]	[−0.0002, 0.0429]	[−0.0396, −0.0049]	[−0.0083, 0.0131]	[−0.0253, 0.0106]
R^2 (within)	0.3358	0.4953	0.2724	0.4001	0.2547	0.3447
Panel B: pat. codes 410–414 (IHD)						
DDDs$_{t-4}$	−0.0035***	−0.0010	−0.0038***	−0.0007	−0.0022**	−0.0015**
WB 95% CI	[−0.0063, −0.0011]	[−0.0024, 0.0004]	[−0.0068, −0.0012]	[−0.0025, 0.0010]	[−0.0042, −0.0002]	[−0.0029, −0.0001]
Share Rosuvast$_t$	0.0025	0.0009	0.0047	0.0025	−0.0004	−0.0013
WB 95% CI	[−0.0048, 0.0101]	[−0.0034, 0.0062]	[−0.0058, 0.0152]	[−0.0045, 0.0115]	[−0.0061, 0.0056]	[−0.0051, 0.0032]
Avg age naives$_{t-4}$	0.0188**	−0.0052	0.0249**	−0.0033	0.0002	−0.0098**
WB 95% CI	[0.0048, 0.0312]	[−0.0148, 0.0045]	[0.0052, 0.0440]	[−0.0151, 0.0084]	[−0.0058, 0.0058]	[−0.0180, −0.0016]
R^2 (within)	0.2967	0.3814	0.2684	0.3074	0.1695	0.2520
Panel C: pat. codes 430–438 (CD)						
DDDs$_{t-4}$	−0.0010	−0.0032**	0.0004	−0.0032***	−0.0020	−0.0034**
WB 95% CI	[−0.0032, 0.0009]	[−0.0054, −0.0009]	[−0.0012, 0.0019]	[−0.0051, −0.0011]	[−0.0051, 0.0009]	[−0.0067, −0.0004]
Share Rosuvast$_t$	0.0044	0.0103**	0.0046*	0.0095***	0.0029	0.0106*
WB 95% CI	[−0.0019, 0.0095]	[0.0013, 0.0240]	[−0.0014, 0.0079]	[0.0033, 0.0234]	[−0.0055, 0.0095]	[−0.0001, 0.0208]
Avg age naives$_{t-4}$	−0.0048	−0.0150*	−0.0032	−0.0181***	0.0026	0.0027
WB 95% CI	[−0.0131, 0.0035]	[−0.0312, 0.0013]	[−0.0126, 0.0062]	[−0.0321, −0.0050]	[−0.0059, 0.0111]	[−0.0125, 0.0189]
R^2 (within)	0.4126	0.3399	0.2556	0.2335	0.3426	0.2305
Other controls	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520

Statistical significance is based on district-level wild cluster bootstrap p-values. ***, **, and * denote significance at the 1%, 5%, and 10% levels, respectively. Brackets report 95% confidence intervals. DDDs = DDDs per 1000 inhabitants per day.

in which statin consumption among higher-risk patients responds to changes in prescribing behaviour towards the low-risk group. These marginal shifts in treatment intensity are likely to produce larger effects on cardiovascular hospitalisation rates than the average variation across all HDs. For the sum of IHD+CD, no marked gender differences are observed, except for emergency admissions, which show no significant association for the male group.[17]

Disaggregating by diagnostic category confirms substantial heterogeneity across conditions in the effect of area-level dispensing on hospitalisation rates, with DDD coefficients differing sharply by admission type. For IHD, no effect is observed on emergency conditions, whereas elective admission rates decline.[18] For CD-related events, higher district-level statin volumes reduce emergency admission rates, while no significant effect is found for elective ones.[19]

In Columns 7–8, we carry out a robustness check, focusing on DDD prescribing and CVD hospitalisations among individuals aged 65 and above. In doing so, we introduce a wedge between the high-risk group that contributes to the outcome (individuals aged 65+) and the low-risk group on which the instrument is constructed (individuals younger than 50). Excluding individuals aged 50–64 eliminates any overlap between the instrument and outcome populations over the entire ten-year period and further separates the CVD risk profiles of the estimation sample from those of the population used to instrument the DDD coefficient.

Leaving an age-donut between the instrument and the outcome strengthens instrument validity, but at the cost of excluding an important patient segment responsible for a sizeable share of CV admissions. Individuals aged 50–64 constitute a relevant target for prevention policies. Still, across all three panels, the volume coefficients are similar to those for the 50+ population in sign, significance, and magnitude. Overall, this supports the empirical strategy and corroborates the preceding results.

5.1.3. Threats to identification and validation checks

The IV strategy assumes that district-level statin prescribing among residents under age 50 influences CVD hospitalisation rates in older residents only through its relationship with statin use in the older population. However, although the under-50 group does not contribute to the outcome and has lower cardiovascular risk, statin prescribing in this group may also reflect time-varying aspects of local healthcare practices, including chronic disease management, prevention, or hospital admission patterns. Therefore, we supplement the baseline IV analysis with further validation checks.

First, we present reduced-form estimates from regressions of CVD hospitalisations on the instrument, including the same controls, district fixed effects, and time effects as in the baseline specification. This exercise does not directly test the exclusion restriction, but it shows whether the instrument predicts CVD outcomes consistently with the main IV estimates. Table 5 shows that the association between under-50 prescribing and CVD hospitalisations closely mirrors the main analysis-by-admission-type pattern. The instrument does not predict all CVD hospitalisations uniformly but is significantly associated with the same outcome categories as those for which the main analysis finds significant effects.

[17] We report in Table 4 only the coefficients for the regressors related to statin use. Table A.3 in the Appendix displays the results for the full set of regressors for Panel A (columns 1–2).

[18] A 1% increase in DDDs per 1000 inhabitants per diem is associated with a −0.84% change in IHD elective admissions per 1000 inhabitants (Panel B, column 1).

[19] A 1% increase in DDDs per 1000 inhabitants per diem corresponds to a −0.28% change in CD emergency admissions per 1000 inhabitants (Panel C, column 2). Elasticities are calculated at mean values for all covariates.

Table 4
DDDs and hospitalisations for various diagnostic categories: IV FE estimation.

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective	Emergency	Elective	Emergency	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs$_{t-4}$	−0.0056***	−0.0040**	−0.0049**	−0.0026	−0.0050***	−0.0057***	−0.0038**	−0.0049**
WB 95% CI	[−0.0091, −0.0019]	[−0.0076, −0.0006]	[−0.0094, −0.0004]	[−0.0061, 0.0010]	[−0.0084, −0.0018]	[−0.0101, −0.0016]	[−0.0076, −0.0001]	[−0.0090, −0.0010]
Share Rosuvast$_t$	0.0064	0.0112**	0.0086	0.0124**	0.0021	0.0090*	0.0036	0.0166**
WB 95% CI	[−0.0067, 0.0142]	[0.0020, 0.0283]	[−0.0108, 0.0192]	[0.0012, 0.0354]	[−0.0101, 0.0108]	[−0.0015, 0.0196]	[−0.0253, 0.0167]	[0.0009, 0.0381]
Avg age naives$_{t-4}$	0.0135*	−0.0201*	0.0211*	−0.0210**	0.0026	−0.0072	0.0197*	−0.0314**
WB 95% CI	[−0.0024, 0.0277]	[−0.0412, 0.0003]	[−0.0005, 0.0423]	[−0.0395, −0.0041]	[−0.0081, 0.0134]	[−0.0253, 0.0109]	[−0.0045, 0.0420]	[−0.0643, −0.0002]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	17.5209***	17.5209***	21.2868***	21.2868***	14.3563***	14.3563***	23.7248***	23.7248***
F-stat.	158.50	158.50	146.12	146.12	173.46	173.46	143.97	143.97
Panel B: pat. codes 410–414 (IHD)								
DDDs$_{t-4}$	−0.0049***	−0.0007	−0.0056***	0.0001	−0.0035**	−0.0016	−0.0043**	−0.0010
WB 95% CI	[−0.0084, −0.0014]	[−0.0030, 0.0014]	[−0.0096, −0.0019]	[−0.0025, 0.0027]	[−0.0062, −0.0004]	[−0.0040, 0.0007]	[−0.0078, −0.0009]	[−0.0036, 0.0014]
Share Rosuvast$_t$	0.0020	0.0010	0.0040	0.0028	−0.0009	−0.0013	−0.0017	0.0007
WB 95% CI	[−0.0076, 0.0090]	[−0.0034, 0.0070]	[−0.0111, 0.0142]	[−0.0051, 0.0130]	[−0.0076, 0.0050]	[−0.0053, 0.0031]	[−0.0218, 0.0082]	[−0.0085, 0.0093]
Avg age naives$_{t-4}$	0.0180**	−0.0050	0.0242**	−0.0030	0.0000	−0.0098**	0.0281**	−0.0095
WB 95% CI	[0.0045, 0.0308]	[−0.0150, 0.0044]	[0.0051, 0.0424]	[−0.0152, 0.0085]	[−0.0062, 0.0059]	[−0.0178, −0.0018]	[0.0086, 0.0453]	[−0.0266, 0.0064]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	17.5340***	17.5340***	21.3080***	21.3080***	14.3569***	14.3569***	23.7536***	23.7536***
F-stat.	159.20	159.20	147.00	147.00	173.73	173.73	145.38	145.38
Panel C: pat. codes 430–438 (CD)								
DDDs$_{t-4}$	−0.0008	−0.0034***	0.0006	−0.0028**	−0.0016	−0.0041***	0.0005	−0.0040**
WB 95% CI	[−0.0031, 0.0012]	[−0.0057, −0.0008]	[−0.0012, 0.0022]	[−0.0053, −0.0001]	[−0.0050, 0.0012]	[−0.0073, −0.0012]	[−0.0017, 0.0023]	[−0.0072, −0.0010]
Share Rosuvast$_t$	0.0044*	0.0103**	0.0047*	0.0097***	0.0030	0.0103*	0.0053	0.0160**
WB 95% CI	[−0.0012, 0.0093]	[0.0011, 0.0233]	[−0.0001, 0.0080]	[0.0032, 0.0245]	[−0.0049, 0.0096]	[−0.0004, 0.0201]	[−0.0084, 0.0139]	[0.0012, 0.0367]
Avg age naives$_{t-4}$	−0.0047	−0.0151*	−0.0031	−0.0180***	0.0026	0.0027	−0.0085	−0.0219
WB 95% CI	[−0.0132, 0.0039]	[−0.0307, 0.0006]	[−0.0127, 0.0065]	[−0.0315, −0.0044]	[−0.0060, 0.0108]	[−0.0130, 0.0184]	[−0.0235, 0.0057]	[−0.0486, 0.0047]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	17.5242***	17.5242***	21.2879***	21.2879***	14.3586***	14.3586***	23.7189***	23.7189***
F-stat.	158.20	158.20	145.79	145.79	173.47	173.47	143.54	143.54
Other controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

2nd stage: statistical significance is based on district-level wild cluster bootstrap p-values; brackets report 95% confidence intervals. 1st stage: statistical significance is based on conventional district-level cluster p-values. ***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. DDDs = DDDs per 1000 inhabitants per day.

Table 5
Reduced form: FE estimation.

Dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)	Elective (7)	Emergency (8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs under50$_{t-4}$	−0.0979***	−0.0706**	−0.1039**	−0.0561	−0.0716***	−0.0825***	−0.0892**	−0.1166**
	[0.0278]	[0.0277]	[0.0427]	[0.0363]	[0.0210]	[0.0266]	[0.0413]	[0.0447]
Share Rosuvast$_t$	0.0067*	0.0115**	0.0091**	0.0127**	0.0023	0.0093**	0.0048	0.0181**
	[0.0034]	[0.0048]	[0.0045]	[0.0061]	[0.0036]	[0.0044]	[0.0061]	[0.0074]
Avg age naives$_{t-4}$	0.0093	−0.0231**	0.0180*	−0.0227**	0.0006	−0.0095	0.0153	−0.0372**
	[0.0070]	[0.0098]	[0.0100]	[0.0085]	[0.0050]	[0.0085]	[0.0110]	[0.0153]
R^2 (within)	0.3367	0.4904	0.2755	0.3933	0.2542	0.3439	0.2649	0.4642
Panel B: pat. codes 410–414 (IHD)								
DDDs under50$_{t-4}$	−0.0859***	−0.0121	−0.1193***	0.0024	−0.0496***	−0.0231	−0.1018***	−0.0230
	[0.0248]	[0.0174]	[0.0364]	[0.0246]	[0.0150]	[0.0142]	[0.0352]	[0.0259]
Share Rosuvast$_t$	0.0024	0.0010	0.0046	0.0028	−0.0007	−0.0013	−0.0003	0.0010
	[0.0030]	[0.0023]	[0.0041]	[0.0036]	[0.0022]	[0.0020]	[0.0046]	[0.0037]
Avg age naives$_{t-4}$	0.0143**	−0.0055	0.0207**	−0.0029	−0.0014	−0.0104**	0.0230**	−0.0106
	[0.0063]	[0.0050]	[0.0086]	[0.0055]	[0.0030]	[0.0043]	[0.0091]	[0.0087]
R^2 (within)	0.3031	0.3799	0.2743	0.3067	0.1774	0.2512	0.2270	0.3761
Panel C: pat. codes 430–438 (CD)								
DDDs under50$_{t-4}$	−0.0135	−0.0588***	0.0131	−0.0592**	−0.0227	−0.0592***	0.0112	−0.0944***
	[0.0165]	[0.0204]	[0.0159]	[0.0264]	[0.0191]	[0.0200]	[0.0222]	[0.0347]
Share Rosuvast$_t$	0.0045**	0.0105***	0.0046**	0.0100**	0.0031	0.0105**	0.0052	0.0173***
	[0.0021]	[0.0038]	[0.0018]	[0.0039]	[0.0028]	[0.0040]	[0.0043]	[0.0063]
Avg age naives$_{t-4}$	−0.0053	−0.0176**	−0.0027	−0.0197***	0.0020	0.0010	−0.0079	−0.0266**
	[0.0040]	[0.0074]	[0.0047]	[0.0065]	[0.0038]	[0.0076]	[0.0072]	[0.0126]
R^2 (within)	0.4108	0.3353	0.2558	0.2250	0.3392	0.2303	0.3541	0.3069
Other controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. DDDs under50 = DDDs per 1000 inhabitants per day (population age < 50).

Second, we perform falsification exercises using non-CV hospitalisations to assess whether the instrument also predicts outcomes that should not respond to statin therapy through the CV-prevention channel. Our primary falsification tests are reduced-form regressions where placebo outcomes are regressed on under-50 statin prescribing (Table 6). We also report in Appendix placebo IV estimates, replacing the CV outcome with each falsification outcome while instrumenting over-50 statin use with under-50 prescribing (Table A.4).[20]

The outcomes are organised into three groups. The first group includes clean placebo outcomes: appendicitis, kidney stones, and diseases of the oral cavity. These conditions are clinically distant from lipid-lowering therapy and cardiovascular prevention and provide a baseline check of whether the instrument is associated with hospitalisations in unrelated clinical domains.[21] The second group includes care-sensitive outcomes (pressure ulcers, skin and subcutaneous tissue infections, influenza, and dehydration) which are not directly statin-responsive but are informative about whether the instrument is associated with broader differences in community care delivery.[22] The third group includes orthopaedic outcomes: osteoarthritis and traumatic non-pathological fractures. These are unlikely to operate through a cardiovascular statin channel, but are imperfect placebos because they may reflect local orthopaedic practices, trauma patterns, or hospital supply. We therefore treat them as additional checks.

The instrument does not systematically predict non-CV hospitalisations. For the clean placebo outcomes, the coefficients are small and generally not significant, with only isolated weak associations. Care-sensitive outcomes lead to similar conclusions: the effects on pressure ulcers and dehydration are never significant, while the few significant coefficients for skin infections and influenza show no consistent admission-type pattern. Orthopaedic outcomes are less definitive but also reveal no systematic association between the instrument and unrelated hospital use. Overall, these results reduce the concern that the instrument captures broader differences in hospital use or community care management.

Third, we test whether elective results depend on the allocation of planned care between overnight and day-hospital (DH) settings. We re-estimate the IV-FE specification using an expanded outcome that combines standard elective admissions and DH episodes for the same CVDs (Table A.5 in Appendix). Adding DH and overnight elective admissions leaves the estimates largely unchanged. Statin use remains negatively and significantly associated with IHD hospitalisations, while CD coefficients are not significant. This is consistent with elective CVD findings not being driven by local substitution between overnight and DH admissions.

These exercises cannot definitively validate the exclusion restriction. However, they offer valuable evidence of the instrument's behaviour. Reduced-form estimates show that the instrument predicts cardiovascular outcomes within the same diagnosis-by-admission-type cells as the main IV analysis. Falsification tests reveal no systematic association with unrelated or care-sensitive non-CV hospitalisations.

[20] Since the placebo IV estimates employ the same instrument, we consider them as complementary evidence; the reduced-form placebo estimates offer a more direct way to check if the instrument itself predicts unrelated hospital use.

[21] Appendicitis is a sudden-onset surgical condition, kidney stones represent urological events, and diseases of the oral cavity refer to a clinical area largely unrelated to cardiovascular pharmacological prevention.

[22] Pressure ulcers may reflect frailty management and continuity of care for vulnerable patients; skin and subcutaneous infections may depend on timely wound care and access to outpatient treatment; influenza admissions are related to vaccination uptake, seasonal-risk management, and timely treatment; dehydration is linked to monitoring and support for frail older individuals before clinical deterioration requires hospital care.

Table 6
Falsification tests: placebo outcomes (reduced form).

Dep. var.	Hospitalisations, (per 1000 inhabitants)					
	All 50+		Men 50+		Women 50+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)
Panel A: clean falsification outcomes						
Appendicitis	0.0001	−0.0016	−0.0000	−0.0020	0.0000	0.0007
	[0.0003]	[0.0014]	[0.0004]	[0.0029]	[0.0005]	[0.0017]
Kidney stones	0.0061	−0.0047	0.0130	−0.0087*	−0.0003	−0.0020
	[0.0041]	[0.0037]	[0.0079]	[0.0049]	[0.0049]	[0.0038]
Diseases of the oral cavity	0.0020	−0.0000	0.0020	0.0010	0.0024	−0.0008
	[0.0016]	[0.0008]	[0.0025]	[0.0010]	[0.0022]	[0.0009]
Panel B: care-sensitive falsification outcomes						
Pressure ulcers	0.0002	−0.0007	0.0003	−0.0004	0.0000	−0.0004
	[0.0008]	[0.0010]	[0.0013]	[0.0012]	[0.0008]	[0.0015]
Infections of the skin and subcutaneous tissue	0.0001	0.0019	−0.0016	0.0012	0.0013	0.0032*
	[0.0010]	[0.0017]	[0.0016]	[0.0025]	[0.0009]	[0.0017]
Influenza	0.0009**	0.0033	0.0008*	0.0031	0.0009*	0.0033
	[0.0004]	[0.0033]	[0.0005]	[0.0029]	[0.0005]	[0.0042]
Dehydration	−0.0013	0.0020	−0.0012	−0.0022	−0.0011	0.0069
	[0.0014]	[0.0051]	[0.0016]	[0.0037]	[0.0017]	[0.0072]
Panel C: supplementary analysis						
Osteoarthritis	0.0214	0.0005	0.0202	−0.0011	0.0306*	0.0022
	[0.0137]	[0.0008]	[0.0163]	[0.0010]	[0.0164]	[0.0013]
Traumatic non-pathological fractures	−0.0125	−0.0181	−0.0053	−0.0346**	−0.0186	0.0030
	[0.0083]	[0.0162]	[0.0064]	[0.0137]	[0.0118]	[0.0265]
All controls	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. The coefficients reported in the table are those associated to the variable "DDDs under50_{t-4}" (i.e. DDDs in the under-50 population per 1000 inhabitants per day at t–4.). The regressions use the same control variables as in the specification adopted in the analysis for the over-50 population in Table 4 (Panel A).

Total elective admissions confirm that the IHD result is not driven by differences in the allocation of planned care across regimes of hospital care. All these findings together support the interpretation that the instrument reflects variation in statin-prescribing behaviour rather than broader differences in hospital use.

5.2. Extensions

5.2.1. Spatial dependence and cross-district hospital use

Hospitalisations are assigned to the patient's HD of residence, regardless of where care is delivered, because cardiovascular prevention is organised around the resident population and anchored in primary care at the HD level. However, HDs are not self-contained hospital markets, as patients are not bound by legally defined catchment areas. This may generate spatial dependence in hospitalisations if admissions, bed pressure, care pathways, or discharge management are partly shared across HDs that rely on the same hospital network.

The spatial health economics literature argues that health outcomes and care use may be spatially correlated due to contextual factors, patient interactions, provider networks, and shared institutions (Baltagi et al., 2018). Interdependence may also arise when hospitals operate in connected local markets or respond to neighbouring providers (Lippi Bruni and Mammi, 2017; Gravelle et al., 2014). In our setting, a channel could operate through residents of neighbouring districts being treated in shared hospital facilities. Spillovers from common GP prescribing practices are less likely, since GP activity is coordinated within HDs. Although residence-based assignment remains appropriate for pharmaceutical prevention, spatial dependence may affect inference, especially for elective admissions. We address this issue through several checks.

First, we test for residual spatial dependence using Moran's I, based on a row-normalised contiguity matrix of neighbouring HDs and computed separately by quarter. As common time shocks are already absorbed by time fixed effects, the statistic captures remaining local spatial correlation across neighbouring districts. For the specifications corresponding to Columns 1–2 of Tables 3 and 4 of the main analysis, Table 7 reports the mean and median Moran's I across the 40 quarters and the number of quarters in which the null of no spatial correlation is rejected. It shows limited evidence of residual spatial dependence, with Moran's I statistics being generally small and rejections more frequent for elective than emergency admissions, which is institutionally plausible. In the IV specifications, residual spatial correlation is very limited for emergency admissions. For elective IHD admissions, Moran's I statistics are significant in only 5 of 40 quarters, with small mean and median values. Significant tests are most frequent for elective CD admissions, where the main IV estimates show no significant association with statin prescribing. Furthermore, significant statistics are scattered over time, suggesting occasional local spatial correlation rather than a persistent spatial error structure.

We have then performed two additional sensitivity checks, reported in Appendix. First, we use aggregate patient-mobility data to identify districts with very low internal provision of CVD hospital care. While most districts provide a substantial share of their residents' CVD admissions internally, three HDs rely almost entirely on facilities located elsewhere, treating less than 10% of these admissions within the district. These jurisdictions are the most exposed to the concern that admission outcomes may be shaped by hospital practices outside the patient's district of residence. As shown in Table A.6, excluding the three high-outflow districts broadly confirms the baseline IV estimates. Second, we re-estimate the IV fixed-effects specification, clustering standard errors at the LHA level. This allows for correlation in unobserved hospital-practice shocks across HDs belonging to the same

Table 7
Moran's I on residuals of regressions from Tables 3–4 (Panels A–B–C, columns 1–2).

Moran's I	Mean	Median	N. of quarters (out of 40) with	
			P-value < 0.05	P-value < 0.01
Table 3 Panel A Column 1	0.0906	0.0716	10	3
Table 3 Panel A Column 2	0.0087	0.0060	4	1
Table 3 Panel B Column 1	0.0543	0.0363	5	1
Table 3 Panel B Column 2	0.0124	0.0160	2	0
Table 3 Panel C Column 1	0.1158	0.1091	12	6
Table 3 Panel C Column 2	−0.0015	−0.0055	3	1
Table 4 Panel A Column 1	0.0904	0.0701	8	3
Table 4 Panel A Column 2	0.0091	0.0063	4	1
Table 4 Panel B Column 1	0.0577	0.0333	5	2
Table 4 Panel B Column 2	0.0138	0.0191	2	0
Table 4 Panel C Column 1	0.1168	0.1116	12	6
Table 4 Panel C Column 2	−0.0015	−0.0057	3	1

Moran's I was obtained using a spatial contiguity matrix. Neighbouring districts are identified using geographical contiguity, that is, two HDs are considered neighbours if they share a border.

higher-level organisation, through which hospital services are planned and coordinated. Although the small number of LHAs prevents treating this as a stand-alone inferential framework, the results reported in Table A.7 leave the main IV findings largely unchanged.

Altogether, these checks suggest that the main conclusions are not driven by cross-district dependence in hospital admission outcomes. Although isolated spatial correlation cannot be ruled out, the evidence shows no persistent residual spatial structure, and the main IV results remain robust to higher-level clustering and excluding high-outflow districts.

5.2.2. Heterogeneity by age groups

Cardiovascular risk varies with age; so does the prevalence of statin treatment. Moreover, the proportion of patients with multiple comorbidities increases in older cohorts, and greater clinical complexity may affect adherence to therapies and their effectiveness. Examining the effect of statins across age groups can therefore shed further light on the issue. We consider individuals aged 50–74 and 75+. Table 8 displays the results using DDDs per 1000 inhabitants for statin use. The drop in IHD elective admissions is larger for the 50–74 age group, whereas the impact on emergency CD hospitalisations appears greater for the 75+ age group. However, taken together, the age-specific results confirm most of the main baseline patterns and do not point to substantially different dynamics across age groups.

Although the age-specific results support the overall analysis, they do not fully rule out the possibility that residual changes in age composition within the 50+ population affect the estimates. We add a robustness check using age-standardised hospitalisation rates, computed by keeping the age structure observed at the start of the sample period fixed. Specifically, we compute age-adjusted hospitalisation rates as the weighted average of age-specific hospitalisation rates (for age groups 50–64, 65–74, 75–79, 80–84, 85+) using the 2010 regional population as the standard population to derive the weights for each age group.

The results, reported in Table A.8, closely align with the main IV estimates: the significant associations remain concentrated on elective IHD and emergency CD hospitalisation rates. This indicates that the main diagnosis-by-admission-type pattern is not driven by demographic ageing or by differential changes in age composition across districts.

5.2.3. Treatment dynamics

The baseline specification uses DDDs lagged by four quarters, reflecting the assumption that statins require at least one year before measurable cardiovascular effects can emerge. We assess the sensitivity of the results to treatment timing in two ways. First, we replicate the analysis using DDDs lagged by eight quarters. Second, we replace the single lag with a cumulative exposure measure, defined as the sum of DDDs per 1000 inhabitants per day over the five-quarter window from $t-8$ to $t-4$.[23] The former exercise allows for a longer interval between observed statin use and hospitalisations; the latter preserves the one-year minimum lag while capturing sustained prescribing exposure over a broader pre-outcome window. The evidence reported in Tables A.9 and A.10 in the Appendix confirms the baseline diagnosis-by-admission-type pattern, with significant effects concentrated on elective IHD and emergency CD hospitalisation rates. These timing checks suggest that the hospitalisation pattern is not sensitive to the choice of a specific lag structure.

5.2.4. Population coverage: Fixed-effects IV estimates

As a related analysis of aggregate prescribing, we use the number of patients on statin treatment (per 1000 inhabitants) in Eq. (1) and instrument it with statin prescriptions for individuals under 50. The results in Table 9 show a diagnosis-by-admission-type pattern similar to that observed when using DDDs as the prescribing indicator (Table 4).

In diagnosis-specific regressions, we observe a significant reduction in IHD admissions for elective procedures (larger among men), whereas no effect is observed for emergency cases.[24] For CD-related procedures, the reduction in hospitalisation rates is confined to emergency admissions, with no impact on elective treatments.[25] These results closely mirror the main findings by admission type obtained using total DDDs. This indicates that the coverage-based specification provides an important related analysis and is informative about aggregate prescribing behaviour, although it should not be interpreted as isolating a pure individual-level extensive margin. The estimated associations remain heterogeneous across admission types and diagnostic categories.

5.3. Regression analysis: statin-users

5.3.1. Main analysis

A complementary perspective on the risk-mitigating role of statins in CV prevention comes from focusing on hospitalisations among statin users and relating them to average treatment volume among treated patients. Accordingly, we use admissions for IHD and CD among statin users as outcomes, with DDDs per treated patient as the regressor of

[23] For the corresponding instruments, we use under-50 statin prescribing lagged by eight quarters and the sum of under-50 prescribing measure over the same $t-8$ - $t-4$, respectively.

[24] A 1% increase in patients per 1000 inhabitants is associated with a −1.13% change in IHD elective admissions per 1000 inhabitants (Panel B, column 1).

[25] Here, a 1% increase in patients per 1000 inhabitants is associated with a −0.38% change in CD emergency admissions per 1000 inhabitants (Panel C, column 2).

Table 8
DDDs and hospitalisations for different age subgroups: IV FE estimation.

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)			
	All 50–74		All 75+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)				
DDDs$_{t-4}$	−0.0064***	−0.0023***	−0.0011	−0.0075***
	[0.0018]	[0.0009]	[0.0019]	[0.0027]
1st stage dep. var.	DDDs$_{t-4}$			
DDDs under50$_{t-4}$	15.4217***	15.4217***	23.6031***	23.6031***
F-stat.	152.96	152.96	148.28	148.28
Panel B: pat. codes 410–414 (IHD)				
DDDs$_{t-4}$	−0.0059***	−0.0004	−0.0033**	−0.0018
	[0.0018]	[0.0006]	[0.0016]	[0.0018]
1st stage dep. var.	DDDs$_{t-4}$			
DDDs under50$_{t-4}$	15.4389***	15.4389***	23.6335***	23.6335***
F-stat.	153.98	153.98	149.58	149.58
Panel C: pat. codes 430–438 (CD)				
DDDs$_{t-4}$	−0.0005	−0.0018***	0.0021*	−0.0057**
	[0.0005]	[0.0007]	[0.0012]	[0.0023]
1st stage dep. var.	DDDs$_{t-4}$			
DDDs under50$_{t-4}$	15.4244***	15.4244***	23.6014***	23.6014***
F-stat.	152.83	152.83	148.22	148.22
All controls	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. DDDs = DDDs per 1000 inhabitants per day.

interest. This variable should be interpreted as an aggregate district-level measure of treatment volume among drug users, rather than as a clean measure of individual dosage.

The concerns about potential endogeneity in prescriptions and the resulting threats to consistent estimation of the parameter of interest also apply in this context. Therefore, we focus on the IV estimates that are reported in Table 10. The same instrument is used for coverage and treatment intensity, as under-50 statin prescribing is interpreted as a proxy for local prescribing style. This prescribing style may affect coverage by influencing the share of residents treated with statins, and it may also affect average treatment volume among already-treated users through local practices in the management of ongoing therapy.

In all specifications, the first-stage F-statistic is large, supporting its relevance. For second-stage estimates, when summing IHD and CD admissions, treatment intensity negatively affects hospitalisations mainly for men. When the analysis is disaggregated by disease, the results show marked heterogeneity across conditions. Variation along the intensive margin of treatment yields a significant preventive effect only for IHD elective conditions. By contrast, no significant reduction in hospitalisations for CDs is detected.

Since the statin-user analysis scales hospitalisations by the number of treated patients and uses lagged DDDs per patient as the intensity measure, the estimates may be sensitive to the treated-user denominator. To address this issue, we also estimated IV Poisson models for hospitalisation counts, using the number of statin users as an offset and lagged DDDs per treated patient as the treatment variable. The offset is based on the same denominator employed in the baseline rate specification. The model is estimated by GMM, instrumenting DDDs per treated patient with under-50 statin prescribing, and district-clustered standard errors are computed for the full IV Poisson estimation. Results are reported in the Table A.11. The offset estimates broadly preserve the direction of the baseline estimates, although some differences emerge by diagnosis and gender, and several subgroup coefficients are measured with less precision, especially for the aggregate IHD+CD outcome. When IHD and CD are analysed separately, the offset estimates show a negative association for elective IHD admissions among men, and for emergency CD admissions in the pooled treated-user sample and among women. This reinforces our cautious interpretation of DDDs per treated patient as an aggregate measure of treatment volume among treated users. Taken together, the baseline and offset specifications for the statin user population indicate that the intensity-based estimates are less stable than the coverage-based results. These findings support the idea that a broader coverage of the at-risk population may be more effective than larger average treatment dosage among already-treated users.

5.3.2. *Heterogeneity by recent hospitalised vascular event history*

Statin users differ in their clinical history, which may shape both prescribing patterns and the risk of subsequent CV hospitalisation. Patients with a recent major cardiovascular event are likely to differ from other statin users in underlying risk, clinical monitoring, adherence, and treatment protocols.[26] We examine here whether the district-level associations differ across groups defined by different recent cardiovascular hospitalisation histories. The available data identifies two subgroups of patients: the first comprises those who had a hospitalised MACE event in the previous year; the second, those who did not experience a MACE within the past 3 years.[27] For each group, CVD admissions are monitored in the following year, allowing patients sufficient time to respond to treatment.

Patients who have experienced a recent hospitalised MACE are typically managed within a secondary-prevention clinical pathway. Conversely, the group without a recent hospitalised MACE cannot

[26] Randomised controlled trials and systematic reviews have established the therapeutic effectiveness of statins across both primary and secondary prevention (e.g. Naci et al., 2013; Collins et al., 2016).

[27] Consistently with this definition, earlier MACE events, occurring outside the one-year look-back window, are not used to define the hospitalised-MACE group.

Table 9
Statin cover and hospitalisations for various diagnostic categories: IV FE estimation.

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)	Elective (7)	Emergency (8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
Patients (per 1000 inhab.)$_{t-4}$	−0.0062***	−0.0045**	−0.0059**	−0.0032	−0.0051***	−0.0059***	−0.0042**	−0.0054**
WB 95% CI	[−0.0102, −0.0021]	[−0.0082, −0.0008]	[−0.0113, −0.0007]	[−0.0072, 0.0012]	[−0.0084, −0.0018]	[−0.0102, −0.0017]	[−0.0084, −0.0001]	[−0.0099, −0.0012]
1st stage dep. var.	Patients (per 1000 inhab.)$_{t-4}$							
DDDs under50$_{t-4}$	15.6871***	15.6871***	17.7548***	17.7548***	14.0518***	14.0518***	21.4004***	21.4004***
F-stat.	162.18	162.18	139.86	139.86	184.42	184.42	142.07	142.07
Panel B: pat. codes 410–414 (IHD)								
Patients (per 1000 inhab.)$_{t-4}$	−0.0055***	−0.0008	−0.0067***	0.0001	−0.0035**	−0.0016	−0.0048**	−0.0011
WB 95% CI	[−0.0093, −0.0016]	[−0.0033, 0.0016]	[−0.0115, −0.0022]	[−0.0030, 0.0031]	[−0.0063, −0.0005]	[−0.0041, 0.0007]	[−0.0087, −0.0010]	[−0.0038, 0.0015]
1st stage dep. var.	Patients (per 1000 inhab.)$_{t-4}$							
DDDs under50$_{t-4}$	15.6918***	15.6918***	17.7644***	17.7644***	14.0438***	14.0438***	21.4212***	21.4212***
F-stat.	162.38	162.38	140.07	140.07	184.32	184.32	142.62	142.62
Panel C: pat. codes 430–438 (CD)								
Patients (per 1000 inhab.)$_{t-4}$	−0.0009	−0.0037***	0.0007	−0.0033**	−0.0016	−0.0042***	0.0005	−0.0044**
WB 95% CI	[−0.0035, 0.0014]	[−0.0063, −0.0010]	[−0.0014, 0.0027]	[−0.0063, −0.0004]	[−0.0051, 0.0013]	[−0.0072, −0.0014]	[−0.0018, 0.0025]	[−0.0079, −0.0011]
1st stage dep. var.	Patients (per 1000 inhab.)$_{t-4}$							
DDDs under50$_{t-4}$	15.6904***	15.6904***	17.7575***	17.7575***	14.0523***	14.0523***	21.3970***	21.3970***
F-stat.	162.10	162.10	139.76	139.76	184.57	184.57	141.88	141.88
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

2nd stage: statistical significance is based on district-level wild cluster bootstrap p-values; brackets report 95% confidence intervals. 1st stage: statistical significance is based on conventional district-level cluster p-values. ***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Patients (per 1000 inhab.) = patients per 1000 inhabitants.

Table 10
Statin intensity and hospitalisations among statin-users: IV FE estimation.

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 patients at t−4)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)	Elective (7)	Emergency (8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs (per 1000 pat.)$_{t-4}$	−0.0097**	−0.0052	−0.0104***	−0.0055**	−0.0070*	−0.0051	−0.0078	−0.0069*
WB 95% CI	[−0.0181, −0.0018]	[−0.0119, 0.0009]	[−0.0189, −0.0024]	[−0.0105, −0.0008]	[−0.0147, 0.0006]	[−0.0160, 0.0047]	[−0.0181, 0.0020]	[−0.0150, 0.0009]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$							
DDDs under50$_{t-4}$	29.5427***	29.5427***	35.4067***	35.4067***	23.0644***	23.0644***	27.8100***	27.8100***
F-stat.	61.82	61.82	66.84	66.84	58.26	58.26	63.57	63.57
Panel B: pat. codes 410–414 (IHD)								
DDDs (per 1000 pat.)$_{t-4}$	−0.0098***	−0.0029	−0.0117***	−0.0029	−0.0064**	−0.0030	−0.0095**	−0.0031
WB 95% CI	[−0.0181, −0.0023]	[−0.0071, 0.0014]	[−0.0204, −0.0039]	[−0.0068, 0.0009]	[−0.0128, −0.0003]	[−0.0088, 0.0028]	[−0.0186, −0.0008]	[−0.0088, 0.0026]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$							
DDDs under50$_{t-4}$	29.6213***	29.6213***	35.4848***	35.4848***	23.1337***	23.1337***	27.8698***	27.8698***
F-stat.	62.50	62.50	67.55	67.55	58.83	58.83	64.59	64.59
Panel C: pat. codes 430–438 (CD)								
DDDs (per 1000 pat.)$_{t-4}$	−0.0001	−0.0023	0.0012	−0.0026	−0.0008	−0.0021	0.0016	−0.0038
WB 95% CI	[−0.0027, 0.0026]	[−0.0069, 0.0020]	[−0.0018, 0.0044]	[−0.0070, 0.0015]	[−0.0049, 0.0027]	[−0.0099, 0.0046]	[−0.0018, 0.0047]	[−0.0100, 0.0021]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$							
DDDs under50$_{t-4}$	29.5494***	29.5494***	35.4045***	35.4045***	23.0769***	23.0769***	27.7969***	27.7969***
F-stat.	61.63	61.63	66.65	66.65	58.08	58.08	63.32	63.32
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

2nd stage: statistical significance is based on district-level wild cluster bootstrap p-values; brackets report 95% confidence intervals. 1st stage: statistical significance is based on conventional district-level cluster p-values. ***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. The (2nd stage) dependent variable is the number of hospitalisations at t for 1000 patients treated at t−4; statin users are defined as patients with at least one statin dispensing in the previous calendar year.

be considered a pure primary prevention case. These patients may include individuals with vascular events occurring before the observed three-year lookback window. The analysis should therefore be read as evidence on heterogeneity by recent hospitalised cardiovascular event history, not as evidence on sharply defined clinical prevention categories.

Table 11 presents the IV estimates for the two groups. Among statin users with a recent hospitalised MACE, changes in treatment intensity generally do not show statistically significant associations with subsequent CVD hospitalisations. The only exception is a negative coefficient for elective admissions for CD. For statin users without a recent hospitalised MACE, the district-level associations are slightly more evident: higher treatment intensity correlates with lower elective IHD and (weakly) with emergency IHD hospitalisation rates, while no association is observed for CD.

To examine whether the estimated coefficients differ statistically across the two groups, we estimate a stacked IV model in which district-quarter observations are combined for statin users with and without a recent hospitalised MACE. Treatment intensity is interacted with the subgroup indicator and instrumented by the corresponding interaction between the subgroup indicator and under-50 statin prescribing. The specification includes all control variables interacted with the subgroup indicator, subgroup-specific HD and seasonal and year dummies, ensuring it closely mirrors the two separate subgroup regressions while allowing us to directly test the equality of the coefficients. The results of these tests are reported in Table 11 and qualify the interpretation of the subgroup estimates. Although some point estimates differ in magnitude between the two groups, the null hypothesis of equal coefficients is generally not rejected. The only exception is elective admissions for cerebrovascular disease, for which the difference between the two coefficients is statistically significant at the 5% level.

Several mechanisms may align with the patterns illustrated here, even if our aggregate data do not allow us to distinguish among them. For treated users with a recent hospitalised vascular event, district-level average treatment intensity is likely to reflect prescribing decisions made within more standardised secondary-prevention pathways. This may reduce the scope for additional local variation in intensity to be associated with hospitalisation rates. For treated users without a recent hospitalised MACE, average intensity may instead capture a broader mix of local prescribing practices and cardiovascular-risk management strategies.

Overall, the subgroup analysis suggests that the district-level association between average treatment intensity and hospitalisation rates is more precisely measured among statin users without a recent history of hospitalised vascular events. Nonetheless, this exploratory exercise should be interpreted cautiously as the formal equality tests provide limited support for statistically significant heterogeneity across the two groups.

6. Discussion

The heterogeneous pattern by diagnosis and admission type that characterises our main findings deserves cautious interpretation. IHD and CD episodes have distinct epidemiological origins and follow different care pathways, suggesting that the effects of statin prescribing need not be expected to translate uniformly across different types of hospital admissions. Our main results indicate a significant reduction in elective IHD admissions and emergency CD admissions, while the corresponding effects on emergency IHD and elective CD admissions are not statistically significant.

The significant association observed for IHD elective admissions is consistent with the role of statins in the long-term management of chronic coronary disease. Elective IHD admissions, mainly accounted for by angina and other forms of chronic IHD, largely reflect planned care for chronic coronary conditions. Statin therapy may reduce disease progression, symptom burden, and the need for planned hospital-based coronary care. This interpretation is consistent with clinical guidelines, which include lipid-lowering therapy as part of the broader management of chronic coronary disease, alongside risk-factor control and revascularisation decisions (NICE, 2011). The absence of a significant association with emergency IHD admissions should not be interpreted as evidence that statins do not reduce acute coronary risk at the individual level. Rather, within our ecological analysis, the coronary association appears more clearly through the elective chronic-care pathway than through emergency IHD admissions. Emergency IHD admissions mainly capture acute coronary presentations, such as myocardial infarction or unstable episodes requiring urgent care. These events may be less closely related to gradual district-level differences in prescribing than planned admissions. Thus, the difference between elective and emergency IHD admissions may reflect the distinction between gradual prevention of chronic coronary deterioration and the occurrence of acute coronary events.

For CD, the pattern is different. The population-level effect is marked and significant for emergency admissions, whereas we find no evidence of a reduction in elective admissions. On the one hand, most cerebrovascular events, including cerebral artery occlusion and transient ischaemic events, typically require urgent hospital evaluation and enter via emergency admission pathways. On the other hand, this finding is consistent with substantial heterogeneity in cerebrovascular episodes, both in their genesis and in the hospital pathways for their treatment. In support of this, trial evidence indicates that statins reduce ischaemic stroke and broader vascular events, but cerebrovascular conditions are clinically heterogeneous and may therefore not respond uniformly to lipid-lowering strategies (Heart Protection Study Collaborative Group, 2004; Amarenco and Labreuche, 2009).

In the baseline analysis restricted to the statin-user population, we find that treatment intensity is not significantly associated with cerebrovascular admissions. The relationship between lipid-lowering and cerebrovascular outcomes may be less direct than for coronary outcomes, partly because cerebrovascular disease includes heterogeneous onset mechanisms and partly because cerebrovascular risk depends strongly on several pathways not strictly related to lipid values. Additional variation in DDDs per treated patient among already treated users may therefore be less strongly associated with CD admissions than with IHD admissions. The offset IV Poisson specification provides a partly different picture, showing significant negative associations for emergency CD admissions in the pooled sample and among women. These results reinforce a cautious interpretation of DDDs per treated patient as a measure of treatment intensity.

Overall, we interpret the observed heterogeneous pattern as informative but not definitive. For IHD, the estimates are consistent with an association operating partly through chronic coronary disease management and elective-care pathways. For cerebrovascular disease, the evidence points more clearly to lower emergency admission rates at the population level, with less support for changes in elective admissions or for a role of average treatment volume among statin users. However, our data does not allow us to identify the precise clinical channel, and we therefore present the mechanisms discussed here as plausible interpretations rather than as directly tested explanations.

7. Conclusions

We investigated the relationship between district-level variation in statin use and cardiovascular hospitalisations using quarterly data from Emilia-Romagna (Italy) from 2010 to 2019. We estimated panel fixed-effects models and used an IV strategy that, under the identifying assumptions, yields estimates consistent with causal district-level effects of prescribing variation on hospitalisation rates. By doing so, we address an important limitation of existing ecological research, which has mainly examined correlations between area-level statin prescriptions and population health outcomes. The instrument relies on the idea that prescriptions for very low-risk individuals reflect prescribing

Table 11
Statin intensity and hospitalisations among statin-users: no recent MACE vs recent MACE (IV FE).

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 patients at t−4)			
	Elective		Emergency	
	All 50+ No recent MACE (1)	All 50+ Recent MACE (2)	All 50+ No recent MACE (3)	All 50+ Recent MACE (4)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)				
DDDs (per 1000 pat.)$_{t-4}$	−0.0099**	−0.0096	−0.0061**	0.0021
	[0.0039]	[0.0068]	[0.0027]	[0.0085]
P-value equality test	0.9540		0.3236	
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$			
DDDs under50$_{t-4}$	26.1176***	77.5921***	26.1176***	77.5921***
F-stat.	52.15	100.07	52.15	100.07
Panel B: pat. codes 410–414 (IHD)				
DDDs (per 1000 pat.)$_{t-4}$	−0.0103***	−0.0041	−0.0037*	0.0005
	[0.0037]	[0.0056]	[0.0019]	[0.0072]
P-value equality test	0.2288		0.5608	
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$			
DDDs under50$_{t-4}$	26.1905***	77.6387***	26.1905***	77.6387***
F-stat.	52.81	100.20	52.81	100.20
Panel C: pat. codes 430–438 (CD)				
DDDs (per 1000 pat.)$_{t-4}$	0.0003	−0.0055**	−0.0024	0.0016
	[0.0013]	[0.0025]	[0.0020]	[0.0044]
P-value equality test	0.0390		0.3813	
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$			
DDDs under50$_{t-4}$	26.1255***	77.5962***	26.1255***	77.5962***
F-stat.	52.02	99.49	52.02	99.49
All controls	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. The (2nd stage) dependent variable is the number of hospitalisations at t for 1000 patients treated at t−4; statin users are defined as patients with at least one statin dispensing in the previous calendar year.

styles, which are unrelated to the underlying cardiovascular risk of the higher-risk population targeted for statin treatment.

Our study further provides analyses by gender, diagnosis, and admission type, offering novel evidence on how local prescribing patterns relate to cardiovascular hospitalisation rates across diagnoses and admission types. Additionally, by focusing on the entire resident population and the subgroup of patients receiving statin therapy, we examine related aggregate prescribing indicators based on treatment coverage within the overall population and average treatment volume among statin users. We find heterogeneous district-level effects across diseases and admission types. In the overall population, higher aggregate prescribing volumes are associated with lower elective admission rates for IHD and lower emergency admission rates for CD. The coverage-based specification yields patterns closer to those of the baseline specification and appears more robust. Among statin users, estimates based on DDDs per treated patient are less stable and should be interpreted more cautiously; they indicate a negative association with IHD hospitalisation rates but not with CD.

District-level statin intensity is negatively associated with hospitalisation rates among patients without recent hospitalised MACE, while estimates are less precise for the recent-MACE group. Formal tests, however, do not indicate significant differences between subgroup coefficients.

From a health policy perspective, our findings offer insights relevant to decision-makers, with implications for local prescribing environments and population-level hospitalisation rates. First, they show that, even within ecological studies based on real-world data, prevention through large-scale drug prescription can significantly impact key dimensions of population health. Furthermore, the analysis suggests that even within a relatively homogeneous social and institutional context, variations in the dissemination of prescribing strategies can have a significant impact on health outcomes. This influence seems particularly pronounced for those therapeutic decisions where physicians retain larger professional discretion and where local policies and practices may exert influence. Among these, strategies that shape district-level coverage appear particularly relevant, although our data does not allow us to identify which individual patients should be targeted.

This limitation reflects the ecological nature of our design, which prevents us from accurately mapping district-level IV evidence to individual treatment effects. The data also have limitations: they measure dispensed drugs rather than actual consumption, and in-hospital dispensing is not observed. These features suggest a cautious interpretation of the mechanisms behind the estimated district-level effects.

The analysis was carried out in a setting characterised by a high prevalence of elderly patients, many of whom are likely affected by multimorbidity. Expanding the analysis to include additional chronic conditions and drug classes is a natural direction for future research. This would allow for a more precise assessment of the role of prescription drugs in managing chronic diseases within the same methodological framework. From a complementary perspective, longitudinal analyses based on individual-level data would be needed to identify which patients benefit, distinguish between initiation, adherence,

Table A.1
Avg. annual hospitalisations in the 50+ population for each diagnostic category (2010–2019).

ICD-9 code		Elective		Emergency	
		Men	Women	Men	Women
410	Acute myocardial infarction	484.9	249.3	3884.6	2345.5
411	Other acute and subacute forms of ischaemic heart disease	599.7	219.4	958.4	516.6
412	Old myocardial infarction	40.0	20.4	22.3	11.3
413	Angina pectoris	1349.3	466.8	382.1	218.6
414	Other forms of chronic ischaemic heart disease	1847.8	554.0	447.8	269.1
430	Subarachnoid hemorrhage	19.4	23.6	116.7	169.2
431	Intracerebral hemorrhage	85.9	90.6	672.0	704.9
432	Other and unspecified intracranial hemorrhage	50.1	31.7	243.1	158.4
433	Occlusion and stenosis of precerebral arteries	1104.3	597.2	463.4	367.3
434	Occlusion of cerebral arteries	184.4	246.1	2670.4	3037.5
435	Transient cerebral ischaemia	45.8	68.0	819.0	976.3
436	Acute, but ill-defined, cerebrovascular disease	42.2	83.4	177.9	242.4
437	Other and ill-defined cerebrovascular disease	302.0	566.1	457.8	651.6
438	Late effects of cerebrovascular disease	750.9	801.2	137.1	168.0

persistence, and dosage mechanisms, and translate district-level patterns into patient-level implications. Such analyses would further enhance our understanding of the underlying dynamics driving these associations.

CRediT authorship contribution statement

Alberto Basso: Writing – original draft, Methodology, Formal analysis, Data curation. **Matteo Lippi Bruni:** Writing – original draft, Project administration, Formal analysis, Conceptualization. **Irene Mammi:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT and Grammarly to improve the manuscript's readability and language. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the article's content.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix

A.1. Hospitalisations statistics

See Table A.1.

A.2. Full set of controls

This appendix illustrates the role of contextual factors in shaping hospital admissions.

Demographic indicators come from ISTAT; income and higher-education enrolment from the Ministry of Finance and the Ministry of University and Research; and health data from the Ministry of Health and ISTAT's Health4all dataset.[28] Inpatient days are drawn from discharge records after excluding episodes with a primary diagnosis of CVD. Information on the deployment of Community Healthcare Centres (CHCs) comes from the Health Department.

In Table A.3 we report results for the IV–FE specification, considering CVD hospitalisations in the total (50+) population as the outcome and DDDs per 1000 inhabitants as the main regressor. These specifications correspond to columns 1–2 (Panel A) of Table 4.

Demographic controls mainly indicate the relevance of changes in districts' age profiles. A higher share of older residents is associated with more elective hospitalisations, but not emergency admissions, while nationality composition generally has no significant effect. Socio-economic controls have little explanatory role: income is not associated with hospitalisations, and education displays no clear pattern. Local health-service characteristics likewise do not significantly explain changes in CVD hospitalisations. Proxies for infrastructural resources, hospital-based (beds) and territorial (CHCs), have negligible effects, while hospital days produced are negatively associated with elective admissions. Human-capital measures show a slightly different pattern: cardiology specialists are associated with more emergency cases but not with elective admissions. It appears that contextual factors have a negligible or at most modest impact on hospitalisation trends for CVDs once the time-invariant component of district heterogeneity is controlled for through fixed effects.

A.3. Threats to identification and validation checks

See Tables A.4–A.7.

[28] Missing data on cardiologists for 2010 are imputed using linear predictions. Hospital doctors and cardiologists are aggregated at the LHA level. Cardiologists are assigned to each district within an LHA based on population weights, defined as the district's share of the LHA's population. For hospital doctors, a similar approach is used, employing hospital bed counts to construct the weights.

Table A.2
Descriptive statistics (mean) for DDDs and hospitalisations by age groups.

	All under-50	All 50–64	All 65–74	All 75+
DDDs per 1000 inhab. per day	4.78	78.81	193.06	193.55
IHD's elective hospitalisations per 1000 inhab.	0.03	0.49	1.14	0.96
IHD's emergency hospitalisations per 1000 inhab.	0.06	0.57	1.14	2.19
CD's elective hospitalisations per 1000 inhab.	0.03	0.21	0.66	1.34
CD's emergency hospitalisations per 1000 inhab.	0.06	0.40	1.16	4.03

Note: means are computed using quarterly district-level data over the period 2010–2019.

Table A.3
Full results of the 2nd stage for Table 4 (panel A, columns 1–2).

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)	
	All 50+ Elective (1)	All 50+ Emergency (2)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)		
DDDs$_{t-4}$	−0.0056***	−0.0040***
	[0.0016]	[0.0015]
Share Rosuvast$_t$	0.0064*	0.0112***
	[0.0036]	[0.0042]
Avg age naives$_{t-4}$	0.0135**	−0.0201**
	[0.0068]	[0.0097]
Share 75+$_t$	0.2262***	0.0359
	[0.0533]	[0.0636]
Share age 65–74$_t$	0.2978***	0.0007
	[0.0733]	[0.0528]
(ln)Income cap.$_t$	−0.2542	−0.5953
	[1.4192]	[1.9004]
Higher educ proxy$_t$	−0.0036	0.0502
	[0.0299]	[0.0338]
Share foreign$_t$	0.1022	−0.0640
	[0.0711]	[0.1067]
Hospital days (res)$_t$	−0.0017	0.0008
	[0.0013]	[0.0009]
Hospital days (hosp)$_t$	−0.0031***	0.0011*
	[0.0011]	[0.0006]
CHCs$_t$	0.0985	−2.1376
	[1.3343]	[1.6092]
Hosp. doctors wei$_t$	−0.0003	0.0007
	[0.0009]	[0.0010]
Doctors card. wei$_t$	0.0029	0.0346***
	[0.0079]	[0.0111]
Hosp. beds$_t$	0.0006	−0.0745
	[0.0837]	[0.0729]
Year dummies	Yes	Yes
Seasonal dummies	Yes	Yes
N	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets.

Table A.4
Falsification tests: placebo outcomes (IV FE).

Dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)					
	All 50+		Men 50+		Women 50+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)
Panel A: clean falsification outcomes						
Appendicitis	0.0000 [0.0000]	−0.0001 [0.0001]	−0.0000 [0.0000]	−0.0001 [0.0001]	0.0000 [0.0000]	0.0000 [0.0001]
Kidney stones	0.0003 [0.0002]	−0.0003 [0.0002]	0.0006* [0.0004]	−0.0004* [0.0002]	−0.0000 [0.0003]	−0.0001 [0.0003]
Diseases of the oral cavity DDDs$_{t-4}$	0.0001 [0.0001]	−0.0000 [0.0000]	0.0001 [0.0001]	0.0000 [0.0000]	0.0002 [0.0001]	−0.0001 [0.0001]
Panel B: care-sensitive falsification outcomes						
Pressure ulcers	0.0000 [0.0000]	−0.0000 [0.0001]	0.0000 [0.0001]	−0.0000 [0.0001]	0.0000 [0.0001]	−0.0000 [0.0001]
Infections of the skin and subcutaneous tissue	0.0000 [0.0001]	0.0001 [0.0001]	−0.0001 [0.0001]	0.0001 [0.0001]	0.0001 [0.0001]	0.0002* [0.0001]
Influenza	0.0000** [0.0000]	0.0002 [0.0002]	0.0000* [0.0000]	0.0001 [0.0001]	0.0001* [0.0000]	0.0002 [0.0003]
Dehydration	−0.0001 [0.0001]	0.0001 [0.0003]	−0.0001 [0.0001]	−0.0001 [0.0002]	−0.0001 [0.0001]	0.0005 [0.0005]
Panel C: supplementary analysis						
Osteoarthritis	0.0012 [0.0008]	0.0000 [0.0000]	0.0009 [0.0008]	−0.0001 [0.0000]	0.0021* [0.0012]	0.0002* [0.0001]
Traumatic non-pathological fractures	−0.0007 [0.0005]	−0.0010 [0.0009]	−0.0002 [0.0003]	−0.0016** [0.0007]	−0.0013 [0.0008]	0.0002 [0.0018]
All controls	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. The coefficients reported in the table are those associated to the variable "DDDs$_{t-4}$" (i.e. DDDs per 1000 inhabitants per day at t−4 in the over-50 population). The regressions use the same control variables as in the specification adopted in the analysis for the over-50 population in Table 4 (Panel A).

Table A.5
Admission-setting sensitivity: IV FE estimation.

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)			
	Elective + Day Hospital			
	All 50+ (1)	Men 50+ (2)	Women 50+ (3)	All 65+ (4)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)				
DDDs$_{t-4}$	−0.0057*** [0.0019]	−0.0050** [0.0025]	−0.0050*** [0.0016]	−0.0038* [0.0020]
1st stage dep. var.	DDDs$_{t-4}$			
DDDs under50$_{t-4}$	17.5209***	21.2868***	14.3563***	23.7248***
F-stat.	158.50	146.12	173.46	143.97
Panel B: pat. codes 410–414 (IHD)				
DDDs$_{t-4}$	−0.0055*** [0.0018]	−0.0062*** [0.0022]	−0.0038*** [0.0012]	−0.0047** [0.0018]
1st stage dep. var.	DDDs$_{t-4}$			
DDDs under50$_{t-4}$	17.5340***	21.3080***	14.3569***	23.7536***
F-stat.	159.2	147.00	173.73	145.38
Panel C: pat. codes 430–438 (CD)				
DDDs$_{t-4}$	−0.0003 [0.0010]	0.0011 [0.0009]	−0.0012 [0.0014]	0.0009 [0.0010]
1st stage dep. var.	DDDs$_{t-4}$			
DDDs under50$_{t-4}$	17.5242***	21.2879***	14.3586***	23.7189***
F-stat.	158.20	145.79	173.47	143.54
All controls	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. DDDs = DDDs per 1000 inhabitants per day.

Table A.6
Excluding districts with strong outflows in hospital use (IV FE).

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective	Emergency	Elective	Emergency	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs$_{t-4}$	−0.0058***	−0.0040**	−0.0050**	−0.0018	−0.0056***	−0.0064***	−0.0042**	−0.0047**
	[0.0017]	[0.0017]	[0.0023]	[0.0018]	[0.0015]	[0.0020]	[0.0020]	[0.0021]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	16.6959***	16.6959***	20.3220***	20.3220***	13.8456***	13.8456***	22.5081***	22.5081***
F-stat.	125.42	125.42	118.86	118.86	138.52	138.52	121.90	121.90
Panel B: pat. codes 410–414 (IHD)								
DDDs$_{t-4}$	−0.0048***	−0.0006	−0.0055***	0.0007	−0.0036***	−0.0020*	−0.0041**	−0.0008
	[0.0016]	[0.0011]	[0.0020]	[0.0013]	[0.0012]	[0.0010]	[0.0016]	[0.0012]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	16.7126***	16.7126***	20.3481***	20.3481***	13.8482***	13.8482***	22.5395***	22.5395***
F-stat.	125.49	125.49	119.09	119.09	138.61	138.61	122.61	122.61
Panel C: pat. codes 430–438 (CD)								
DDDs$_{t-4}$	−0.0011	−0.0034***	0.0004	−0.0026**	−0.0020	−0.0044***	−0.0002	−0.0040**
	[0.0010]	[0.0012]	[0.0008]	[0.0013]	[0.0013]	[0.0015]	[0.0011]	[0.0016]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	16.6969***	16.6969***	20.3199***	20.3199***	13.8459***	13.8459***	22.4959***	22.4959***
F-stat.	125.03	125.03	118.51	118.51	138.45	138.45	121.54	121.54
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1400	1400	1400	1400	1400	1400	1400	1400

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. DDDs = DDDs per 1000 inhabitants per day.

Table A.7
Clustering at the LHA level (IV FE).

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective	Emergency	Elective	Emergency	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs$_{t-4}$	−0.0056***	−0.0040***	−0.0049**	−0.0026	−0.0050***	−0.0057***	−0.0038*	−0.0049***
	[0.0021]	[0.0015]	[0.0025]	[0.0018]	[0.0014]	[0.0018]	[0.0020]	[0.0018]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	17.5209***	17.5209***	21.2868***	21.2868***	14.3563***	14.3563***	23.7248***	23.7248***
F-stat.	50.25	50.25	43.62	43.62	68.08	68.08	49.51	49.51
Panel B: pat. codes 410–414 (IHD)								
DDDs$_{t-4}$	−0.0049**	−0.0007	−0.0056**	0.0001	−0.0035*	−0.0016	−0.0043**	−0.0010
	[0.0023]	[0.0008]	[0.0025]	[0.0012]	[0.0019]	[0.0010]	[0.0021]	[0.0010]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	17.5340***	17.5340***	21.3080***	21.3080***	14.3569***	14.3569***	23.7536***	23.7536***
F-stat.	50.40	50.40	43.85	43.85	68.06	68.06	49.89	49.89
Panel C: pat. codes 430–438 (CD)								
DDDs$_{t-4}$	−0.0008	−0.0034***	0.0006	−0.0028**	−0.0016	−0.0041***	0.0005	−0.0040***
	[0.0009]	[0.0011]	[0.0007]	[0.0014]	[0.0015]	[0.0011]	[0.0007]	[0.0014]
1st stage dep. var.	DDDs$_{t-4}$							
DDDs under50$_{t-4}$	17.5242***	17.5242***	21.2879***	21.2879***	14.3586***	14.3586***	23.7189***	23.7189***
F-stat.	50.12	50.12	43.51	43.51	67.99	67.99	49.39	49.39
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the LHA level are reported in square brackets. DDDs = DDDs per 1000 inhabitants per day.

Table A.8
Age-standardised hospitalisations (IV FE).

2nd stage dep. var.	Age-standardised hospitalisations$_t$ (per 1000 inhabitants)					
	All 50+		Men 50+		Women 50+	
	Elective	Emergency	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)						
DDDs$_{t-4}$	−0.0055***	−0.0040***	−0.0049**	−0.0028*	−0.0050***	−0.0054***
	[0.0016]	[0.0015]	[0.0021]	[0.0016]	[0.0014]	[0.0018]
1st stage dep. var.	DDDs$_{t-4}$					
DDDs under50$_{t-4}$	17.5209***	17.5209***	21.2868***	21.2868***	14.3563***	14.3563***
F-stat.	158.50	158.50	146.12	146.12	173.46	173.46
Panel B: pat. codes 410–414 (IHD)						
DDDs$_{t-4}$	−0.0049***	−0.0008	−0.0057***	−0.0001	−0.0035***	−0.0016
	[0.0015]	[0.0010]	[0.0018]	[0.0011]	[0.0011]	[0.0010]
1st stage dep. var.	DDDs$_{t-4}$					
DDDs under50$_{t-4}$	17.5340***	17.5340***	21.3080***	21.3080***	14.3569***	14.3569***
F-stat.	159.20	159.20	147.00	147.00	173.73	173.73
Panel C: pat. codes 430–438 (CD)						
DDDs$_{t-4}$	−0.0007	−0.0032***	0.0006	−0.0027**	−0.0015	−0.0038***
	[0.0009]	[0.0011]	[0.0007]	[0.0012]	[0.0012]	[0.0013]
1st stage dep. var.	DDDs$_{t-4}$					
DDDs under50$_{t-4}$	17.5242***	17.5242***	21.2879***	21.2879***	14.3586***	14.3586***
F-stat.	158.20	158.20	145.79	145.79	173.47	173.47
All controls	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. DDDs = DDDs per 1000 inhabitants per day. Age-adjusted hospitalisation rates are computed as the weighted average of age-specific hospitalisation rates (for age groups 50–64, 65–74, 75–79, 80–84, 85+) using the regional population in 2010 as the standard population to generate the weights for each age-group.

Table A.9
DDDs and hospitalisations: extended lag (IV FE).

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective	Emergency	Elective	Emergency	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs$_{t-8}$	−0.0052***	−0.0049***	−0.0047**	−0.0029**	−0.0043***	−0.0076***	−0.0037**	−0.0058***
	[0.0015]	[0.0013]	[0.0019]	[0.0015]	[0.0013]	[0.0017]	[0.0018]	[0.0015]
1st stage dep. var.	DDDs$_{t-8}$							
DDDs under50$_{t-8}$	17.7984***	17.7984***	21.6072***	21.6072***	14.5145***	14.5145***	23.9535***	23.9535***
F-stat.	154.97	154.97	148.80	148.80	161.72	161.72	143.71	143.71
Panel B: pat. codes 410–414 (IHD)								
DDDs$_{t-8}$	−0.0051***	−0.0011	−0.0062***	−0.0005	−0.0031***	−0.0018*	−0.0048***	−0.0013
	[0.0015]	[0.0007]	[0.0017]	[0.0009]	[0.0011]	[0.0010]	[0.0016]	[0.0009]
1st stage dep. var.	DDDs$_{t-8}$							
DDDs under50$_{t-8}$	17.7809***	17.7809***	21.5954***	21.5954***	14.4911***	14.4911***	23.9496***	23.9496***
F-stat.	156.05	156.05	149.73	149.73	163.08	163.08	144.88	144.88
Panel C: pat. codes 430–438 (CD)								
DDDs$_{t-8}$	−0.0002	−0.0038***	0.0014	−0.0025**	−0.0013	−0.0058***	0.0011	−0.0046***
	[0.0010]	[0.0010]	[0.0010]	[0.0011]	[0.0012]	[0.0012]	[0.0010]	[0.0011]
1st stage dep. var.	DDDs$_{t-8}$							
DDDs under50$_{t-8}$	17.8078***	17.8078***	21.6155***	21.6155***	14.5217***	14.5217***	23.9534***	23.9534***
F-stat.	154.35	154.35	148.21	148.21	161.25	161.25	142.89	142.89
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. DDDs = DDDs per 1000 inhabitants per day.

Table A.10
Cumulative DDDs (IV FE).

2nd stage dep. var.	Hospitalisations$_t$ (per 1000 inhabitants)							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)	Elective (7)	Emergency (8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
cDDDs$_{t-4,t-8}$	−0.0012*** [0.0003]	−0.0010*** [0.0003]	−0.0011*** [0.0004]	−0.0006** [0.0003]	−0.0010*** [0.0003]	−0.0014*** [0.0003]	−0.0008** [0.0004]	−0.0011*** [0.0003]
1st stage dep. var.	cDDDs$_{t-4,t-8}$							
cDDDs under50$_{t-4,t-8}$	19.9950***	19.9950***	24.4041***	24.4041***	16.2975***	16.2975***	26.9148***	26.9148***
F-stat.	257.30	257.30	229.20	229.20	278.71	278.71	225.05	225.05
Panel B: pat. codes 410–414 (IHD)								
cDDDs$_{t-4,t-8}$	−0.0011*** [0.0003]	−0.0002 [0.0002]	−0.0013*** [0.0004]	−0.0000 [0.0002]	−0.0007*** [0.0002]	−0.0003* [0.0002]	−0.0010*** [0.0003]	−0.0002 [0.0002]
1st stage dep. var.	cDDDs$_{t-4,t-8}$							
cDDDs under50$_{t-4,t-8}$	19.9889***	19.9889***	24.4033***	24.4033***	16.2837***	16.2837***	26.9204***	26.9204***
F-stat.	258.61	258.61	230.97	230.97	279.77	279.77	226.97	226.97
Panel C: pat. codes 430–438 (CD)								
cDDDs$_{t-4,t-8}$	−0.0001 [0.0002]	−0.0008*** [0.0002]	0.0002 [0.0002]	−0.0006*** [0.0002]	−0.0003 [0.0003]	−0.0011*** [0.0002]	0.0002 [0.0002]	−0.0009*** [0.0002]
1st stage dep. var.	cDDDs$_{t-4,t-8}$							
cDDDs under50$_{t-4,t-8}$	20.0036***	20.0036***	24.4114***	24.4114***	16.3047***	16.3047***	26.9164***	26.9164***
F-stat.	256.74	256.74	228.80	228.80	278.48	278.48	224.29	224.29
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets. cDDDs = cumulative DDDs per 1000 inhabitants per day (from lag *t–4* to lag *t–8*).

Table A.11
Statin intensity and hospitalisations among statin-users: IV Poisson with offset.

2nd stage dep. var.	HospCount$_t$							
	All 50+		Men 50+		Women 50+		All 65+	
	Elective (1)	Emergency (2)	Elective (3)	Emergency (4)	Elective (5)	Emergency (6)	Elective (7)	Emergency (8)
Panel A: pat. codes 410–414 + 430–438 (IHD+CD)								
DDDs (per 1000 pat.)$_{t-4}$	−0.0014** [0.0006]	−0.0008* [0.0004]	−0.0010* [0.0005]	−0.0005 [0.0004]	−0.0020** [0.0008]	−0.0013* [0.0007]	−0.0009 [0.0007]	−0.0007 [0.0004]
Panel B: pat. codes 410–414 (IHD)								
DDDs (per 1000 pat.)$_{t-4}$	−0.0020** [0.0009]	−0.0003 [0.0006]	−0.0018** [0.0008]	−0.0003 [0.0004]	−0.0021 [0.0014]	−0.0002 [0.0010]	−0.0018* [0.0010]	0.0001 [0.0006]
Panel C: pat. codes 430–438 (CD)								
DDDs (per 1000 pat.)$_{t-4}$	−0.0002 [0.0006]	−0.0013** [0.0006]	0.0006 [0.0006]	−0.0009 [0.0006]	−0.0014 [0.0012]	−0.0020** [0.0009]	0.0005 [0.0008]	−0.0014** [0.0006]
(ln)Patients$_{t-4}$	1	1	1	1	1	1	1	1
All controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Seasonal dummies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	1520	1520	1520	1520	1520	1520	1520	1520

IV Poisson models are estimated by GMM. ***, **, * denotes statistical significance at 1%, 5% and 10% levels, respectively. Robust standard errors clustered at the district level are reported in square brackets.

A.4. Age-standardised hospitalisations (IV FE)

See Table A.8.

A.5. Treatment dynamics

See Tables A.9 and A.10.

A.6. Poisson model with offset

See Table A.11.

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