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KEYWORDS

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We identify exogenous variation in statin consumption unrelated to unobserved cardiovascular risk by leveraging observed variation in pre- scribing patterns and physicians' preferences. 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). Our findings indicate that statins significantly reduce hospitalisations for cardiovascular disease, with effects differing by diagnosis, admission type, and gender. Additionally, when analysing two aspects of statin use—coverage and treatment intensity—we find that coverage appears to be more influential across different types of cardiovascular events.
We also find that the reduction in the risk of adverse episodes predominantly involves medium- to low-risk groups, rather than individuals who have already experi- enced major cardiovascular events. From a policy perspective, our findings emphasise the importance of tailoring prevention measures to medium- and low-risk groups and the effectiveness of prevention strategies based on prescription drugs, beyond individual risk assessment.

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Alberto Basso* Matteo Lippi Bruni* Irene Mammi†

This version: March 20, 2026

Abstract

Managing cardiovascular risk is a vital concern for healthcare systems. Statins are lipid-lowering drugs used to prevent adverse cardiovascular events. Using an instrumental variables approach, this study investigates the causal effect of statin use on hospitalisations for cardiovascular disease, moving beyond the correlational evidence from existing ecological studies. We identify exogenous variation in statin consumption unrelated to unobserved cardiovascular risk by leveraging observed variation in prescribing patterns and physicians' preferences. 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). Our findings indicate that statins significantly reduce hospitalisations for cardiovascular disease, with effects differing by diagnosis, admission type, and gender. Additionally, when analysing two aspects of statin use—coverage and treatment intensity—we find that coverage appears to be more influential across different types of cardiovascular events. We also find that the reduction in the risk of adverse episodes predominantly involves medium- to low-risk groups, rather than individuals who have already experienced major cardiovascular events. From a policy perspective, our findings emphasise the importance of tailoring prevention measures to medium- and low-risk groups and the effectiveness of prevention strategies based on prescription drugs, beyond individual risk assessment.

Keywords: cardiovascular disease; hospitalisations; statins; panel data; prevention.

JEL Codes: I11; I18; H51

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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).[1] In addition to direct medical costs, CVDs also undermine productivity and economic growth.[2] While poor lifestyle factors such as smoking, unhealthy diets, and lack of physical activity contribute to increased cardiovascular (CV) risk, medical treatments nonetheless play a significant role in tackling these adverse events (Vancheri et al., 2022).[3] As prescription drugs targeting CVDs are a key instrument to contain disease prevalence and progression, there is an interest in evaluating their contribution to population health, particularly in the context of the rising burden of 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 and Pettersson, 2014), including whether newer drugs reduce CVD hospitalisations (Lichtenberg, 2009) and increase longevity (Lichtenberg, 2017). Other studies have examined the impact of adherence. Higher adherence is associated with reduced ischemic heart disease mortality (Haukka et al., 2012), improved post-infarction survival (Rasmussen et al., 2007), and fewer 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.

[1] In Italy, the costs associated with CVDs exceed the EU average, accounting for an estimated 14.9% of total health expenditure in 2021.

[2] The overall economic burden in Italy has been estimated at 726 euros per inhabitant, above the EU average of 630 euros (Luengo-Fernandez et al., 2023).

[3] According to Palmieri et al. (2010), in Italy between 1980 and 2000, 40% of the drop in mortality rates for ischemic heart disease can be attributed to advancements in medical therapies. However, in some circumstances, drugs may act as substitutes rather than complements to better lifestyles, as when statins are used in place of a healthy diet (Kaestner et al., 2014).

Among drugs targeting CV risk, statins hold a prominent position and include several blockbuster molecules (Feng and Maini, 2024). By lowering low-density lipoprotein cholesterol (LDL-C), they mitigate the risk of adverse CV events. Randomised controlled trials substantiate the clinical efficacy of these molecules, with benefits typically emerging within one to two years following treatment initiation (Shepherd et al., 1995; Baigent et al., 2005).

Physicians play a pivotal role in the diffusion of statin therapy. As gatekeepers to treatment, they determine whether the level of CV risk warrants initiating therapy, then set the individual dosage and adjust it in response to changes in clinical conditions. Prescribers, therefore, shape both the extent of population coverage (the extensive margin) and the intensity of therapy for patients under treatment (the intensive margin).[4]

Despite its policy relevance, real-world evidence on the impact of statin utilisation on CVDs in large populations remains limited. By linking prescriptions to health outcomes at the local 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. However, to date, only a relatively small number of ecological studies have examined the relationship between statins and CVD outcomes, and the evidence has yielded mixed, context-specific findings. Moreover, the 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, municipality-level 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 significant reduction in mortality for ischemic heart disease (IHD) (Merlo et al., 1999). Also, Vancheri et al. (2016) do not find significant relationships between levels (nor changes) of statin use and IHD mortality rates

[4]In deciding which patients to treat and at what intensity, prescribers, who act as double agents for both their patients and the payer, typically weigh the expected health gains from pharmaceutical prevention against the responsible use of healthcare resources. See Blomqvist (1991) for a seminal model of double agency, and Crea et al. (2019) for an empirical application to the statin market using individual data.

using cross-sectional country-level data for 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 statin use was negatively associated with IHD hospitalisations in the Spanish population between 1996 and 2006. More recently, using country-level data from 2000 to 2020, Treciokienė et al. (2024) find an inverse association between statin use and IHD mortality in Sweden, but not in Lithuania.

Existing studies rely mainly on either cross-sectional variation or time-series data. While the former lacks a longitudinal dimension, the latter does not capture heterogeneity across jurisdictions, which is relevant in decentralised health systems. Furthermore, empirical work often focuses on a single condition or homogeneous episodes, whereas preventive effects may differ across conditions and types of acute events (e.g., elective versus emergency cases). As a result, accounting for these heterogeneous effects carries important implications for resource allocation and hospital organisation.

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.

To the best of our knowledge, this is the first ecological study to examine the causal effect of statin use on CVD hospitalisations. We do so by leveraging prescribing patterns in very low–risk groups to capture physicians' prescribing styles that would otherwise go unobserved. By isolating exogenous variation in statin consumption unrelated to contemporaneous cardiovascular risk, our instrumental variable (IV) strategy enables causal interpretation of the estimated effects, going beyond correlational evidence from existing ecological studies.

A second contribution to the literature is the provision of more comprehensive evidence on the preventive role of prescription drugs against CVDs than is commonly available, by

accounting for variation across jurisdictions and over time, and by distinguishing between conditions (ischemic heart diseases-IHDs and cerebrovascular diseases-CDs) and types of admissions (elective and emergency episodes).

A further distinctive feature of our study, with relevance for healthcare policy, lies in the separate investigation of how changes in the extensive and intensive margins of prescriptions affect CVD hospitalisations. This issue has important implications, as prescribers exercise relatively greater discretion in determining the prevalence of statin treatment in the population than in choosing individual dosages. Indeed, preventive drug therapy is initiated based on both clinical and lifestyle considerations, especially in non–very high-risk patients, whereas dosage is dictated mainly by stricter therapeutic indications. We also conduct further analysis, classifying patients as being in "secondary" or "primary" prevention based on whether they experienced hospitalisations for vascular events in the preceding three years. We thereby provide insight into how drug prescribing may affect outcomes differently across populations with varying levels of CV risk.

The institutional context and available data are well-suited to our purposes, as the region is homogeneous with respect to lifestyle, socioeconomic, and environmental conditions. At the same time, local health jurisdictions enjoy significant autonomy and can influence prescribing behaviour through locally defined policies.

We find that the impact of statins on CVD hospitalisations varies across diseases and admission types. In the overall population, higher volumes lead to fewer elective admissions for IHDs and emergency admissions for CDs, largely reflecting the role of expanded treatment coverage. Among treated patients, variation in average area-level dosage is linked to lower hospitalisation rates for IHDs, but shows no measurable impact on cerebrovascular outcomes. This effect is concentrated among individuals without prior vascular hospitalisations in the past three years, rather than among higher-risk patients.

2 Institutional background and the statin market

The Italian National Health Service (NHS) is funded through general taxation and provides hospital and primary care services, mostly free at the point of need. Local Health Authorities (LHAs) are funded using an adjusted capitation formula that covers the costs of health services in the national benefit package ("Essential Levels of Care"). Community care policies are managed by Health Districts (HDs), which are territorial sub-units of LHAs and serve a population of around 100,000–120,000 inhabitants. HDs set local priorities and targets for community and primary care, including decisions on funding for ad-hoc programs that support local initiatives. As a result, policies can vary substantially across districts.

Medications are prescribed by specialists and general practitioners (GPs), with the latter being self-employed physicians contracted with the NHS and primarily compensated through a capitation scheme. GPs receive additional remuneration through their HDs to undertake activities promoted locally (Iezzi et al., 2014). This design leaves room for heterogeneity in prescription strategies at the local level, with greater variability where decisions are not strictly dictated by medical guidelines, but instead reflect nuanced judgments about patient risk and the relative 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. This is the case for statins, for which 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 expen-

[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.

diture in 2023 (13.7% of the total), with per capita expenditure of 60.43 euros (AIFA - Italian Medicines Agency, 2024). Within this group, statins display the highest utilisation rate (82.0 Defined Daily Doses (DDDs) per 1,000 inhabitants per day) and the highest expenditure per capita (8.09 euros). They absorb more than 6% of retail pharmaceutical expenses, and nearly 20% in the cardiovascular area.

The family of 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), whereas the other molecules account for small market shares. Simvastatin is the earliest compound, atorvastatin belongs to a later generation, and rosuvastatin is the most recently introduced and highest-potency option. Decisions regarding therapy initiation, compound choice, and dosage depend on the prescriber's judgment and are typically based on cholesterol levels, cardiovascular risk, individual patient characteristics and clinical history. A certain degree of substitutability among active ingredients remains, particularly between the first two. Rosuvastatin is different, as AIFA recommends limiting its use as a second-line treatment to patients at the highest CV risk who do not respond to lower-intensity therapies or for whom they are contraindicated (Fiorentini et al., 2022).[7]

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

[7]Our aggregate prescription data does not account for the distribution of different active ingredients across districts, although we do control for the share of rosuvastatin.

3 Data

3.1 Population of interest

The population of interest comprises residents aged 50 and above, as cardiovascular risk is negligible at younger ages. Prevention policies based on large-scale prescription drugs are expected to influence CVD hospitalisations primarily by targeting at-risk populations and by determining which patients initiate therapy. They may vary with local physicians' practice style, leading to differences in population coverage across areas. Therefore, 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 decisions influences outcomes, reflecting local strategies for therapy coverage.

Subsequently, we restrict the analysis to statin users. Linking prescriptions to hospitalisations among the treated population, we focus on treatment intensity. Heterogeneity in this context also arises from the fact that among statin users, some are in primary and others in secondary prevention. Although we cannot determine from full medical histories whether statin use indicates primary or secondary prevention, we can distinguish patients who have experienced a major adverse cardiovascular event (MACE) in the preceding three years from those who have not. A recent MACE shifts patients into secondary prevention, where statin therapy is strongly recommended and routinely adopted. In contrast, statin prescriptions among individuals without a recent MACE reflect preventive treatment in response to CV risk assessment rather than following an adverse CV event.

3.2 Variables description

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

3.2.1 Hospital admissions

To measure adverse events related to CVDs, we consider inpatient hospitalisations of residents of Emilia-Romagna, occurring both within and outside the region. Hospitalisations are grouped by the patient's district of residence, irrespective of where treatment is provided.

Hospital admissions are identified by primary diagnosis, classified according to 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.[9] Furthermore, we distinguish between elective admissions and those initiated through the emergency department (ED). We exclude day cases and ED visits that do not lead to hospital admission.

AMI is the most prevalent diagnosis (21.6% of the total). For cardiac diseases, the other conditions contributing most to hospital admissions are angina and other forms of chronic IHD, whereas within the CD category, the main drivers are arterial occlusions and intracerebral haemorrhages. The distribution between elective and emergency episodes reflects clinical

[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.

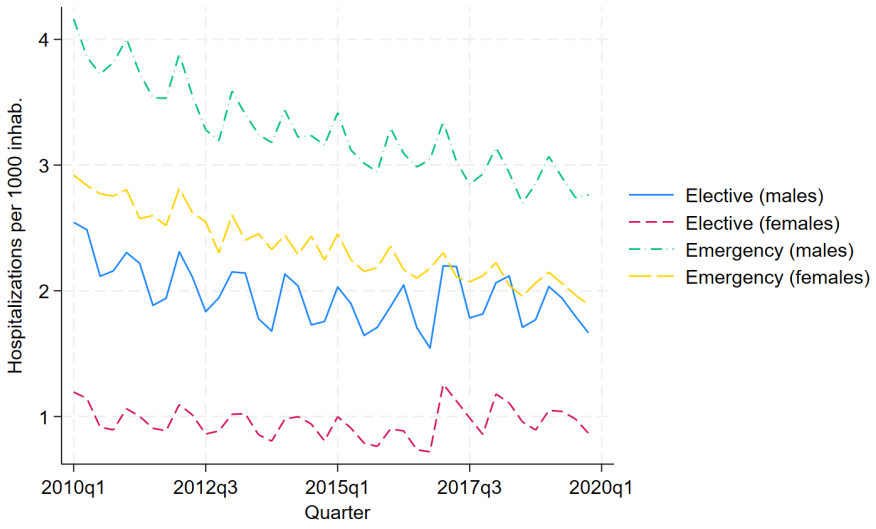
[9] Among the cases of AMI (ICD-9 410), we include only the initial episode of care.

characteristics. AMI is predominantly associated with emergencies (89.5%), whereas elective cardiovascular hospitalisations are less frequent and mainly due to angina. Emergency admissions exceed elective ones in cerebrovascular diseases (70.6% vs. 29.4%), particularly for occlusions of cerebral arteries and intracerebral haemorrhages. Elective cases are primarily associated with occlusions of the precerebral arteries and the late effects of disease.[10]

The indicators for hospital admissions are expressed as the number of CVD hospitalisations per 1,000 inhabitants, when we consider the entire population, and the number of CVD hospitalisations for 1,000 patients treated, when we focus on statin-users.[11] These measures are recorded quarterly for each HD, diagnosis group, and type of admission.

Figure 1 displays the patterns of CVD hospitalisations in the population aged 50+ years at the regional level. We observe a pronounced seasonal component together with a declining trend in emergency admissions, whereas elective cases are fairly stable over time. Moreover, hospitalisations are consistently higher for men compared to women.

Figure 1: CVDs hospital admissions in Emilia-Romagna (2010-2019)



[10] A detailed breakdown by ICD-9 code and gender is reported in Appendix in Table A-1.
[11] In the latter case, hospitalisations refer to patients who have been under treatment for at least one year.

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 DDDs per 1,000 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.

The volume indicator combines two components: population coverage rate and average dosage per 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 the role of population coverage *per se* on CVD hospitalisations by considering the number of patients receiving statin treatment (per 1,000 inhabitants), rather than DDDs, as an alternative measure of treatment extent.

Finally, when the population of interest is represented by patients under therapy, statin use is measured as the number of DDDs per 1,000 patients per day, which captures treatment intensity.

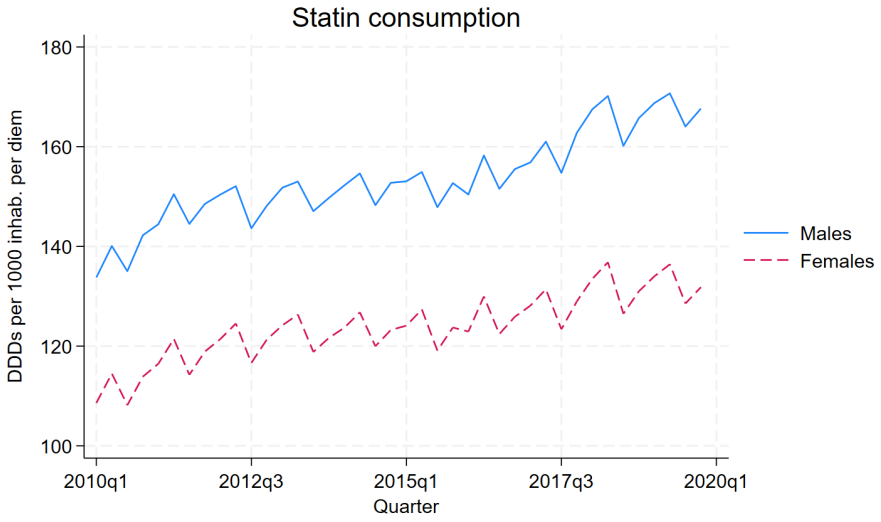
Variations in prescribing patterns may also reflect differences in patient case mix. To address this issue, we utilise indicators that capture underlying population characteristics, including the share of rosuvastatin consumption relative to total statin use, and the average age of

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

patients newly prescribed statins (i.e., treatment-naïve patients).[13]

Figure 2 displays DDDs per 1,000 inhabitants per day, 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.

Figure 2: Statin consumption in Emilia-Romagna (2010-2019)



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.[14]

[13] Patients are classified as naïves in the quarter they receive statins for the first time.

[14] As for Italy, lower education and income are associated with higher IHD risk (e.g. Giampaoli et al., 2015; Bonaccio et al., 2012) while higher education is linked to better preventive behaviours (e.g. Damiani et al., 2011).

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 1,000 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 1,000 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 Community Healthcare Centres (CHCs) per 1,000 inhabitants operating in each quarter within the HD.

Table 1 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.

TABLE 1 HERE

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. Then, to capture potential heterogeneous effects of medication use on specific medical conditions, 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:

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

where $i = 1, ..., 38$ identifies the HDs, $t = 1, ..., 40$ represents the quarters, $\boldsymbol{\delta}_i$ is a district fixed effect, $\boldsymbol{\tau}_t$ is a vector of seasonal $(q_1, ...q_4)_t$ and year $(y_1...y_9)_t$ 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.

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 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 seasonal patterns in cardiovascular hospitalisations

and statin consumption.[15]

We also control for the average age of statin initiators (naïve patients) at the district-quarter level. This variable acts as a proxy for time-varying underlying cardiovascular 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 cardiovascular risk becomes clinically significant. The variable helps account for remaining within-district variation in cardiovascular risk that could be related to both statin use and hospitalisations.[16] 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 as an additional control for high-risk cases.

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 establishing a causal link 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' judgment, and local clinical

[15] Accounting for seasonality is relevant because cardiovascular risk changes depending on the season, as also statin purchases do. In Italy, for example, AMI events are characterised by a winter peak (e.g. Stewart et al., 2017), and there is evidence of drug stockpiling ahead of holiday seasons (e.g. Fiorentini et al., 2022). Our specification assumes that seasonal patterns remain stable over time, which is supported by an inspection of our data. In practice, combining year and quarter fixed effects is equivalent to more flexible quarter-year fixed effects, while also allowing for a more parsimonious model.

[16] This measure is particularly 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.

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.

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 ensure 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 exogenous variation in aggregate statin purchases 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 1,000 inhabitants per day.

We estimate the model in Equation 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 $i = 1, ..., 38$ identifies the HDs, $t = 1, ..., 40$ represents the quarters, $\boldsymbol{\mu}_i$ is a district fixed effect, $\boldsymbol{t}_t$ is a vector of seasonal $(q_1, ...q_4)_t$ and year $(y_1...y_9)_t$ 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 Equation 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 instrumental variable, both in terms of relevance and validity.

The under-50 age group has a minimal risk of cardiovascular hospitalisation and accounts for a small proportion 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 or guidelines, 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 toward 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 any feedback effect on statin

prescriptions for younger people, given the very different risk levels for the two groups; that is, there is no concern of reverse causality here. 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 statins prescribed to younger individuals could reflect unobserved cardiovascular risk or early disease onset. However, the fact that individuals under 50 are genuinely at very low risk is corroborated by the negligible proportion of cardiovascular hospitalisations they account for.[17] Furthermore, any time-invariant differences in underlying risk are captured by district fixed effects and identification hinges on within-district variability in prescribing behaviour towards low-risk groups, rather than on risk differences across districts. We measure the outcome and the IV on separate groups of individuals. However, given the longitudinal structure of our data, we cannot exclude that some younger statin patients may contribute to hospitalisations among patients aged 50+ in the coming years. This is not particularly worrisome as long as we work with aggregated data and the

[17]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.

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.

5 Results

5.1 Regression analysis: general population

5.1.1 Statin volumes (DDDs): Fixed-effects estimates

We first examine the association between statin use and CVD hospital admissions in the general population aged 50 years and older. In panel A of Table 2, 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 Equation 1 for all residents aged 50 and above, while the following columns display the results separately by gender.

TABLE 2 HERE

The primary variable of interest is the volume of drug prescriptions, expressed as DDDs per 1,000 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 hospitalisations for IHD and CD. However, this association cannot be interpreted in a causal way, as drug volumes may be endogenous.

Regarding the contribution of high-risk patients, a larger share of rosuvastatin prescriptions in the HD is positively linked with emergency admissions. The effect is smaller and less statistically significant for elective conditions. The other indicator capturing underlying population characteristics - 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 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 Equation 1 separately for IHDs and CDs. The results reveal strikingly different patterns between emergency and elective episodes. Table 2 (Panel B) shows the estimates for IHD hospitalisations. Volume coefficients indicate a negative, significant association between DDDs and elective admissions, with a larger effect among men. In contrast to all-case admissions, however, higher drug use does not reduce 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 to estimate the causal impact of drug volumes on hospitalisations. Table 3 presents the IV estimates based on Equations 2 and 3. The results are reported following the same structure as in Table 2.

TABLE 3 HERE

The first-stage coefficient on the instrument is statistically significant across all specifications and is positively associated with the endogenous variable. Furthermore, the F-statistic is well above the conventional threshold of 10. Taken together, these results support 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 and above. The absolute values of the estimated coefficients are generally 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 preventive effect of statin use. Furthermore, the IV approach identifies a LATE for districts 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 hospitalisations than the average variation across all districts.

As before, no marked gender differences are observed, except for emergency admissions, which decline relatively more for women in response to statin use.[18] A 1% increase in DDDs per 1,000 inhabitants per diem leads to a -0.53% change in total elective admissions per 1,000 inhabitants and a -0.20% change in total emergency admissions per 1,000 inhabitants.[19]

Disaggregating the analysis by diagnostic category confirms substantial heterogeneity across

[18] We report in Table 3 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).

[19] Elasticities are calculated at mean values for all covariates and refer to the coefficients estimated in Panel A, column 1 and 2, respectively.

clinical conditions in the effect of statins on hospitalisations, with DDD coefficients differing sharply by admission type. For IHD, no effect is observed on emergency conditions, whereas elective admissions decline. A 1% increase in DDDs per 1,000 inhabitants per diem is associated with a -0.84% change in IHD elective admissions per 1,000 inhabitants (Panel B, column 1). Instead, for CD-related events, statin volumes lower emergency episodes, with no significant impact on elective episodes. For the former, a 1% increase in DDDs per 1,000 inhabitants per diem corresponds to a -0.28% change in CD emergency admissions per 1,000 inhabitants (Panel C, column 2).

Finally, in Columns 7-8, we carry out a robustness check to further support the validity of our instrument, 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 above) and the low-risk group on which the instrument is constructed (individuals younger than 50). Excluding individuals aged 50-64 eliminates any possible 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.

Adopting a more conservative approach, implying leaving an age-*donut* when constructing the outcome, strengthens the validity of the instrument, but comes at the cost of excluding an important segment of patients, which is responsible for a sizeable share of CVD admissions. As such, individuals aged 50–64 constitute a relevant target for policy interventions aimed at influencing preventive treatment. Still, the empirical findings are consistent with those for the population aged 50 and above in terms of the sign, statistical significance, and magnitude of the volume coefficients across all three panels. Overall, such evidence supports the empirical strategy and corroborates the conclusions of the preceding analyses.

5.1.3 Extensions: heterogeneity by age groups and two-year lag

In this subsection, we further explore statin prescribing to characterise the phenomenon and the sensitivity of our results more thoroughly.

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 4 displays the results using DDDs per 1,000 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.

TABLE 4 HERE

Thus far, our analysis has been based on the conjecture that statins require approximately 12 months to begin exerting measurable effects, which motivates the use of DDDs lagged by four quarters. In the medical literature, this is considered the minimum interval for clinical efficacy to emerge, with effects materialising within one to two years. To ensure that our results are not driven by the choice of one year time horizon, we replicate the analysis considering an extended two-year window between observed statin consumption and CVD hospitalisations. The results are reported in Table A-4 in the Appendix. Overall, the results are consistent with, and qualitatively similar to, the previous ones, showing no sensitivity to the choice of time window.[20]

[20]Both the endogenous variable and the instrument are specified with a two-year lag.

5.1.4 Population coverage: Fixed-Effects IV estimates

To investigate the role of population coverage alone, we use the number of patients on statin treatment (per 1,000 inhabitants) in Equation 1 and instrument it with statin prescriptions for individuals under 50. The results in Table 5 suggest that coverage affects hospitalisations across diagnostic categories and admission types in a way that is similar to that observed when using the volumes of statin consumption as a regressor (Table 3). As for the size of the impact, a 1% increase in patients per 1,000 inhabitants is associated with a -0.67% change in total elective admissions per 1,000 inhabitants (Panel A, column 1) and a -0.25% change in total emergency admissions per 1,000 inhabitants (Panel A, column 2).

TABLE 5 HERE

When we consider 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. A 1% increase in patients per 1,000 inhabitants is associated with a -1.07% change in IHD elective admissions per 1,000 inhabitants (Panel B, column 1). For CD-related procedures, the reduction in hospitalisations is again confined to emergency admissions, with no impact on elective treatments. Here, a 1% increase in patients per 1,000 inhabitants is associated with a -0.36% change in CD emergency admissions per 1,000 inhabitants (Panel C, column 2).

Overall, the results suggest that population coverage, in itself, plays a central role in preventing hospital admissions for CVDs. HDs where treatment has been expanded to a larger audience achieve some beneficial effects, in terms of reduced hospitalisations. However, these effects cannot be generalised across admission types and diagnostic categories.

5.2 Regression analysis: statin-users

5.2.1 Main analysis

A complementary perspective on the risk-mitigating role of statins in CV prevention comes from shifting the focus from the extensive to the intensive margin of treatment. In this case, the research question concerns the impact of changes in dosage on CVD hospitalisation among patients receiving statin therapy. Accordingly, we use admissions for IHD and CD among statin users as outcomes, with the DDDs per treated patient as the regressor of interest.

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 6. The instrument is the same as discussed in previous sections.

In all specifications, the IV is statistically significant, and the first-stage F-statistic is large, supporting its relevance. For the second-stage estimates, when summing IHD and CD admissions, treatment intensity negatively affects hospitalisations, except for female emergency admissions. The aggregate evidence suggests that higher average doses reduce the risk of CVD hospitalisations. The effect is relatively large as a 1% increase in DDDs per 1,000 patients per diem reduces elective admissions per 1,000 patients by 2.13% (Panel A, column 1) and emergency admissions per 1,000 patients by 0.93% (Panel A, column 2).

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, and the impact is larger for elective conditions. By contrast, no significant reduction in hospitalisations for CDs is detected. The latter finding marks a difference also with the case covering the general population, where an expansion in the scope of drug prescription significantly contributed to the containment of CD emergency admissions.

TABLE 6 HERE

5.2.2 Primary vs secondary prevention

One concern with the previous analysis is that the population of statin users is heterogeneous with respect to clinical history. This heterogeneity can influence both prescribing decisions and the risk of cardiovascular hospitalisation, underscoring the importance of distinguishing between patients in primary and secondary prevention.[21]

Secondary prevention refers to patients who have experienced a major adverse cardiovascular event at some point in their lives. By contrast, primary prevention refers to patients who receive treatment based on risk factor assessment but have not experienced any MACE.[22] A proper identification of the two patient groups would require observation of complete clinical histories, which is not available in our data. To further pursue this line of analysis, however, we use district-level data on statin use among patients who experienced a MACE in the previous three years and classify them as being under secondary prevention. We track CVD admissions in the following year, again allowing patients sufficient time to respond to treatment. This approach distinguishes prescriptions and associated hospitalisations among individuals who, having previously been admitted for a MACE, can be unambiguously classified as secondary-prevention cases, from those of patients receiving statin therapy who have not experienced a vascular event over a short- to medium-term horizon.

The results shown in Table 7 indicate that, in most cases, variations in treatment intensity do not yield significant effects for patients in secondary prevention following a MACE. The only partial exception is a reduction in elective admissions for cerebrovascular conditions.

[21] Randomised controlled trials 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).

[22] MACEs are defined as myocardial infarctions and strokes. Because our data do not record the occurrence of these events, we measure them using hospital admissions with the corresponding diagnoses.

By contrast, among patients who did not experience a MACE in the preceding three years, statins were associated with a widespread and statistically significant preventive effect on hospitalisations for IHD, but not for CD. Overall, the evidence suggests that the effects identified without distinguishing between primary and secondary prevention are driven by the impact of statin therapy on individuals at comparatively lower cardiovascular risk.

In the absence of individual-level data, we can only speculate about the mechanisms underlying these findings. The limited effectiveness of changes in treatment intensity in secondary prevention may reflect the fact that, following a MACE, clinical guidelines, monitoring practices, and adherence tend to be more stringent, at least in the early post-event period. This is likely to reduce the scope for variation in individual prescribing strategies relative to what is observed among patients who are, on average, at lower cardiovascular risk. By contrast, the preventive effect of higher prescription intensity on IHD hospitalisations among patients with no recent history of MACE is consistent with evidence from randomised controlled trials suggesting that the proportional risk reductions associated with statin therapy can also be large for lower-risk individuals (Collins et al., 2016). This finding underscores the importance of paying attention also to medium- and low-risk groups in the design and implementation of risk-mitigating strategies based on prescription drugs.

TABLE 7 HERE

6 Conclusions

We investigated the impact of district-level variation in statin use on cardiovascular hospitalisations using quarterly data from Emilia-Romagna (Italy) from 2010 to 2019. We estimated panel fixed-effects models and employed an IV strategy to address the limitations of existing research, which has not established the causal relationship between prescriptions and popu-

lation health outcomes. The instrument relies on the idea that prescriptions for very low-risk individuals reflect prescribing 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 and multifaceted evidence on the effectiveness of prescription drugs in preventing adverse cardiovascular events. Additionally, by alternatively focusing on the entire resident population and the subgroup of patients receiving statin therapy, we examine the impact of variations in treatment coverage and intensity, respectively. We detect heterogeneous effects across diseases and types of admission. In the overall population, larger volumes decrease elective admissions for ischaemic heart disease and emergency admissions for cerebrovascular disease. Coverage plays a key role in driving these results. Among treated patients, area-level variation in dosage reduces hospitalisations for ischaemic heart disease, but not for cerebrovascular disease: the effect mainly arises from patients who have not experienced hospitalisations for vascular events in the previous three years, rather than from higher-risk groups.

From a health policy perspective, these findings offer important insights for decision-makers. First, they show that, even within ecological studies based on real-world data, prevention through widespread prescription of pharmaceuticals 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, patient recruitment decisions are especially crucial, as they determine the extent of therapeutic coverage. These findings highlight the importance of supporting, at the local level, strategies focused on the timely identification of individuals at medium to low cardiovascular risk.

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 could provide deeper insights into the mechanisms behind the results observed in aggregated data, thereby enhancing our understanding of the fundamental dynamics that drive these phenomena.

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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.

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7 Tables

Table 1: 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.	6.87	3.52	0	26.54	2.13	1.54	0	11.54
Emergency IHD Admissions per 1000 pat.	7.10	3.04	0	22.92	3.51	1.83	0	10.92
Elective CD Admissions per 1000 pat.	3.48	1.95	0	16.31	2.47	1.83	0	15.98
Emergency CD Admissions per 1000 pat.	5.63	2.14	0	13.60	5.18	2.11	0	17.47
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	1766.10	178.86	1374.48	2258.20	1529.96	116.03	1228.06	1855.64
Patients per 1000 inhab.	87.89	15.50	34.91	121.89	81.57	14.48	35.30	119.27
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	15527.39	1651.02	11980.95	20039.02
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 specialized 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.

Table 2: DDDs and hospitalisations for various diagnostic categories: FE estimation

Dep. var.	Hospitalizations$_t$ (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***
	[0.0012]	[0.0012]	[0.0014]	[0.0013]	[0.0011]	[0.0015]
Share Rosuvast$_t$	0.0067*	0.0112**	0.0091*	0.0119**	0.0024	0.0094**
	[0.0035]	[0.0042]	[0.0046]	[0.0049]	[0.0038]	[0.0042]
Avg age naives$_{t-4}$	0.0141**	-0.0202**	0.0217**	-0.0215**	0.0027	-0.0071
	[0.0069]	[0.0099]	[0.0104]	[0.0085]	[0.0049]	[0.0084]
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**
	[0.0012]	[0.0006]	[0.0013]	[0.0008]	[0.0009]	[0.0006]
Share Rosuvast$_t$	0.0025	0.0009	0.0047	0.0025	-0.0004	-0.0013
	[0.0031]	[0.0022]	[0.0042]	[0.0033]	[0.0023]	[0.0019]
Avg age naives$_{t-4}$	0.0188***	-0.0052	0.0249***	-0.0033	0.0002	-0.0098**
	[0.0063]	[0.0049]	[0.0090]	[0.0056]	[0.0030]	[0.0042]
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**
	[0.0008]	[0.0009]	[0.0007]	[0.0008]	[0.0012]	[0.0013]
Share Rosuvast$_t$	0.0044*	0.0103***	0.0046**	0.0095***	0.0029	0.0106**
	[0.0022]	[0.0035]	[0.0018]	[0.0031]	[0.0030]	[0.0039]
Avg age naives$_{t-4}$	-0.0048	-0.0150*	-0.0032	-0.0181***	0.0026	0.0027
	[0.0042]	[0.0077]	[0.0047]	[0.0066]	[0.0038]	[0.0077]
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

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

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

2nd stage dep. var.	Hospitalizations$_t$ (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***
	[0.0016]	[0.0015]	[0.0020]	[0.0016]	[0.0015]	[0.0018]	[0.0017]	[0.0018]
Share Rosuvast$_t$	0.0064*	0.0112***	0.0086*	0.0124**	0.0021	0.0090**	0.0036	0.0166**
	[0.0036]	[0.0042]	[0.0047]	[0.0055]	[0.0038]	[0.0041]	[0.0066]	[0.0065]
Avg age naives$_{t-4}$	0.0135**	-0.0201**	0.0211**	-0.0210**	0.0026	-0.0072	0.0197*	-0.0314**
	[0.0068]	[0.0097]	[0.0100]	[0.0084]	[0.0049]	[0.0082]	[0.0110]	[0.0153]
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
	[0.0015]	[0.0010]	[0.0018]	[0.0011]	[0.0011]	[0.0010]	[0.0015]	[0.0011]
Share Rosuvast$_t$	0.0020	0.0010	0.0040	0.0028	-0.0009	-0.0013	-0.0017	0.0007
	[0.0030]	[0.0022]	[0.0043]	[0.0036]	[0.0023]	[0.0019]	[0.0049]	[0.0037]
Avg age naives$_{t-4}$	0.0180***	-0.0050	0.0242***	-0.0030	0.0000	-0.0098**	0.0281***	-0.0095
	[0.0061]	[0.0048]	[0.0086]	[0.0055]	[0.0030]	[0.0041]	[0.0088]	[0.0084]
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	159.2	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***
	[0.0009]	[0.0011]	[0.0007]	[0.0011]	[0.0013]	[0.0013]	[0.0009]	[0.0014]
Share Rosuvast$_t$	0.0044**	0.0103***	0.0047***	0.0097***	0.0030	0.0103***	0.0053	0.0160***
	[0.0021]	[0.0034]	[0.0017]	[0.0032]	[0.0028]	[0.0038]	[0.0042]	[0.0054]
Avg age naives$_{t-4}$	-0.0047	-0.0151**	-0.0031	-0.0180***	0.0026	0.0027	-0.0085	-0.0219*
	[0.0041]	[0.0075]	[0.0046]	[0.0065]	[0.0037]	[0.0075]	[0.0072]	[0.0128]
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

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

Table 4: DDDs and hospitalisations for different age subgroups: IV FE estimation

2nd stage dep. var.	Hospitalizations$_t$ (per 1000 inhabitants)			
	All 50-74		All 75+	
	Elective	Emergency	Elective	Emergency
	(1)	(2)	(3)	(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]
Share Rosuvast$_t$	0.0067**	0.0057**	0.0033	0.0193*
	[0.0027]	[0.0027]	[0.0084]	[0.0100]
Avg age naives$_{t-4}$	0.0177**	-0.0113	-0.0018	-0.0360*
	[0.0071]	[0.0083]	[0.0159]	[0.0216]
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]
Share Rosuvast$_t$	0.0045**	0.0005	-0.0039	0.0015
	[0.0023]	[0.0016]	[0.0057]	[0.0058]
Avg age naives$_{t-4}$	0.0186***	-0.0019	0.0181	-0.0109
	[0.0069]	[0.0055]	[0.0115]	[0.0141]
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]
Share Rosuvast$_t$	0.0022*	0.0052***	0.0071	0.0179**
	[0.0012]	[0.0017]	[0.0072]	[0.0088]
Avg age naives$_{t-4}$	-0.0010	-0.0094*	-0.0201*	-0.0250
	[0.0034]	[0.0048]	[0.0110]	[0.0175]
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
Other 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 squared brackets. DDDs= DDDs per 1000 inhabitants per day.

Table 5: Statin cover and hospitalisations for various diagnostic categories: IV FE estimation

2nd stage dep. var.	Hospitalizations$_t$ (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)							
Pat. (per 1000 inhab.)$_{t-4}$	-0.0116***	-0.0084***	-0.0110**	-0.0059*	-0.0094***	-0.0108***	-0.0077**	-0.0101***
	[0.0034]	[0.0030]	[0.0047]	[0.0035]	[0.0028]	[0.0033]	[0.0036]	[0.0035]
Share Rosuvast$_t$	0.0060	0.0109***	0.0086*	0.0124**	0.0014	0.0082**	[0.0067]	[0.0063]
	[0.0037]	[0.0040]	[0.0049]	[0.0054]	[0.0038]	[0.0039]	0.0031	0.0159**
Avg age naives$_{t-4}$	0.0136**	-0.0201**	0.0213**	-0.0209**	0.0027	-0.0072	0.0200*	-0.0310**
	[0.0068]	[0.0096]	[0.0101]	[0.0084]	[0.0048]	[0.0080]	[0.0112]	[0.0152]
1st stage dep. var.	Patients (per 1000 inhab.)$_{t-4}$							
DDDs under50$_{t-4}$	8.4490***	8.4490***	9.4606***	9.4606***	7.6521***	7.6521***	11.5981***	11.5981***
F-stat.	170.52	170.52	143.17	143.17	197.98	197.98	153.67	153.67
	Panel B: pat. codes 410-414 (IHD)							
Pat. (per 1000 inhab.)$_{t-4}$	-0.0102***	-0.0014	-0.0126***	0.0002	-0.0065***	-0.0030	-0.0088***	-0.0020
	[0.0031]	[0.0020]	[0.0041]	[0.0026]	[0.0021]	[0.0018]	[0.0031]	[0.0022]
Share Rosuvast$_t$	0.0017	0.0009	0.0041	0.0028	-0.0014	- 0.0016	-0.0023	0.0005
	[0.0032]	[0.0023]	[0.0045]	[0.0036]	[0.0025]	[0.0019]	[0.0051]	[0.0038]
Avg age naives$_{t-4}$	0.0181***	-0.0050	0.0244***	-0.0030	0.0000	-0.0098**	0.0285***	-0.0094
	[0.0060]	[0.0048]	[0.0087]	[0.0055]	[0.0029]	[0.0040]	[0.0088]	[0.0084]
1st stage dep. var.	Patients (per 1000 inhab.)$_{t-4}$							
DDDs under50$_{t-4}$	8.4526***	8.4526***	9.4653***	9.4653***	7.6500***	7.6500***	11.6078***	11.6078***
F-stat.	170.13	170.13	142.89	142.89	197.52	197.52	153.72	153.72
	Panel C: pat. codes 430-438 (CD)							
Pat. (per 1000 inhab.)$_{t-4}$	-0.0016	-0.0070***	0.0014	-0.0063**	-0.0030	-0.0077***	0.0010	-0.0081***
	[0.0019]	[0.0022]	[0.0016]	[0.0025]	[0.0024]	[0.0024]	[0.0019]	[0.0027]
Share Rosuvast$_t$	0.0044**	0.0101***	0.0047***	0.0097***	0.0028	0.0097***	0.0054	0.0155***
	[0.0021]	[0.0031]	[0.0017]	[0.0031]	[0.0028]	[0.0036]	[0.0042]	[0.0051]
Avg age naives$_{t-4}$	-0.0047	-0.0150**	-0.0032	-0.0179***	0.0026	0.0027	-0.0085	-0.0215*
	[0.0041]	[0.0075]	[0.0046]	[0.0066]	[0.0037]	[0.0074]	[0.0072]	[0.0127]
1st stage dep. var.	Patients (per 1000 inhab.)$_{t-4}$							
DDDs under50$_{t-4}$	8.4520***	8.4520***	9.4635***	9.4635***	7.6529***	7.6529***	11.5976***	11.5976***
F-stat.	170.41	170.41	143.01	143.01	198.18	198.18	153.46	153.46
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 squared brackets. Pat. (per 1000 inhab.)=patients per 1000 inhabitants.

Table 6: Statin intensity and hospitalisations among statin-users: IV FE estimation

2nd stage dep. var.	Hospitalizations$_t$ (per 1000 patients at t-4)							
	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 (per 1000 pat.)$_{t-4}$	-0.0109***	-0.0061**	-0.0111***	-0.0061**	-0.0087**	-0.0070	-0.0094**	-0.0088**
	[0.0036]	[0.0030]	[0.0037]	[0.0024]	[0.0034]	[0.0049]	[0.0047]	[0.0039]
Share Rosuvast$_t$	-0.0118	-0.0002	-0.0214	-0.0075	-0.0048	0.0095	-0.0181	0.0058
	[0.0202]	[0.0192]	[0.0273]	[0.0252]	[0.0188]	[0.0203]	[0.0270]	[0.0249]
Avg age naives$_{t-4}$	0.1203*	-0.1000*	0.2237***	0.0235	-0.0189	-0.1279**	0.1590**	-0.1258*
	[0.0671]	[0.0600]	[0.0795]	[0.0699]	[0.0329]	[0.0499]	[0.0752]	[0.0688]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$							
DDDs under50$_{t-4}$	52.7704***	52.7704***	65.4939***	65.4939***	38.5327***	38.5327***	47.9089***	47.9089***
F-stat.	51.51	51.51	57.17	57.17	43.15	43.15	53.99	53.99
	Panel B: pat. codes 410-414 (IHD)							
DDDs (per 1000 pat.)$_{t-4}$	-0.0108***	-0.0035*	-0.0124***	-0.0033*	-0.0077***	-0.0040	-0.0111***	-0.0042
	[0.0034]	[0.0020]	[0.0036]	[0.0019]	[0.0027]	[0.0028]	[0.0041]	[0.0028]
Share Rosuvast$_t$	-0.0323	-0.0244*	-0.0450*	-0.0306*	-0.0202	-0.0121	-0.0404	-0.0314
	[0.0198]	[0.0143]	[0.0264]	[0.0180]	[0.0124]	[0.0137]	[0.0252]	[0.0208]
Avg age naives$_{t-4}$	0.1081*	-0.0060	0.1635**	0.0372	0.0000	-0.0257	0.1388**	0.0037
	[0.0575]	[0.0415]	[0.0659]	[0.0470]	[0.0249]	[0.0365]	[0.0616]	[0.0523]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$							
DDDs under50$_{t-4}$	52.9095***	52.9095***	65.6535***	65.6535***	38.6314***	38.6314***	48.0220***	48.0220***
F-stat.	51.94	51.94	57.57	57.57	43.38	43.38	54.66	54.66
	Panel C: pat. codes 430-438 (CD)							
DDDs (per 1000 pat.)$_{t-4}$	-0.0001	-0.0027	0.0013	-0.0028	-0.0011	-0.0029	0.0015	-0.0046
	[0.0012]	[0.0021]	[0.0013]	[0.0020]	[0.0020]	[0.0035]	[0.0015]	[0.0029]
Share Rosuvast$_t$	0.0208**	0.0245**	0.0242*	0.0238	0.0158	0.0214	0.0226*	0.0377**
	[0.0089]	[0.0119]	[0.0126]	[0.0177]	[0.0134]	[0.0140]	[0.0117]	[0.0175]
Avg age naives$_{t-4}$	0.0122	-0.0934***	0.0600*	-0.0132	-0.0184	-0.1014***	0.0207	-0.1291***
	[0.0393]	[0.0339]	[0.0362]	[0.0450]	[0.0293]	[0.0283]	[0.0488]	[0.0392]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$							
DDDs under50$_{t-4}$	52.7510***	52.7510***	65.4569***	65.4569***	38.5368***	38.5368***	47.8681***	47.8681***
F-stat.	51.25	51.25	56.88	56.88	43.00	43.00	53.72	52.72
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 squared brackets.

Table 7: Statin intensity and hospitalisations among statin-users: primary vs secondary prevention IV FE estimation

2nd stage dep. var.	Hospitalizations$_t$ (per 1000 patients at t-4)			
	"Primary prevention"		"Secondary prevention"	
	All 50+ Elective	All 50+ Emergency	All 50+ Elective	All 50+ Emergency
	(1)	(2)	(3)	(4)
	Panel A: pat. codes 410-414 + 430-438 (IHD+CD)			
DDDs (per 1000 pat.)$_{t-4}$	-0.0112***	-0.0072**	-0.0113	0.0016
	[0.0039]	[0.0029]	[0.0077]	[0.0094]
Share Rosuvast$_t$	-0.0080	0.0195	0.0480	-0.1200
	[0.0194]	[0.0179]	[0.1304]	[0.2223]
Avg age naives$_{t-4}$	0.1102	-0.0701	0.3897	-1.1708
	[0.0677]	[0.0599]	[0.5782]	[0.7592]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$			
DDDs under50$_{t-4}$	46.4871***	46.4871***	134.4209***	134.4209***
F-stat.	43.06	43.06	67.00	67.00
	Panel B: pat. codes 410-414 (IHD)			
DDDs (per 1000 pat.)$_{t-4}$	-0.0116***	-0.0044**	-0.0052	-0.0002
	[0.0037]	[0.0021]	[0.0063]	[0.0080]
Share Rosuvast$_t$	-0.0257	-0.0088	-0.1747	-0.2769*
	[0.0178]	[0.0127]	[0.1393]	[0.1503]
Avg age naives$_{t-4}$	0.1126**	0.0155	-0.0790	-0.9282
	[0.0530]	[0.0430]	[0.3662]	[0.5749]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$			
DDDs under50$_{t-4}$	46.6232***	46.6232***	134.513***	134.513***
F-stat.	43.55	43.55	66.68	66.68
	Panel C: pat. codes 430-438 (CD)			
DDDs (per 1000 pat.)$_{t-4}$	0.0002	-0.0028	-0.0061**	0.0019
	[0.0014]	[0.0022]	[0.0028]	[0.0048]
Share Rosuvast$_t$	0.0182*	0.0286**	0.2199**	0.1572
	[0.0096]	[0.0112]	[0.0921]	[0.1813]
Avg age naives$_{t-4}$	-0.0024	-0.0851**	0.4663	-0.2420
	[0.0392]	[0.0375]	[0.4869]	[0.3463]
1st stage dep. var.	DDDs (per 1000 pat.)$_{t-4}$			
DDDs under50$_{t-4}$	46.4720***	46.4720***	134.3499***	134.3499***
F-stat.	42.86	42.86	66.53	66.53
Other 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 squared brackets.

A Appendix

A.1 Hospitalisations statistics

Table A-1: Avg. annual hospitalizations in the 50+ population for each diagnostic category (2010-2019)

		Elective		Emergency	
ICD-9 code		Men	Women	Men	Women
410	Acute myocardial infarction	484.9	249.3	3884.6	2345.5
411	Other acute and subacute forms of ischemic 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 ischemic 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 ischemia	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

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.

A.2 Full set of controls

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

The sources of the data are the following: demographic indicators are drawn from ISTAT population data; per capita taxable income and the share of individuals enrolled in higher education from the Ministry of Finance and the Ministry of University and Research, respectively; health data comes from the Ministry of Health and the "Health4all" dataset by ISTAT. [23] Data on the total number of inpatient days are drawn from regional hospital discharge records and, to prevent endogeneity, hospital days for episodes with a primary diagnosis of CVD are excluded. Finally, information on the deployment of Community Healthcare Centres (CHCs) is obtained from the Regional Health Department.

In Table A-3 we report results only for the IV–FE specification, considering: (i) CVD hospitalisations in the total population as the outcome and DDDs per 1,000 inhabitants as the main regressor of interest (columns 1–2); and (ii) hospitalisations among statin users as the outcome and DDDs per treated patient as the main regressor of interest (columns 3–4). These specifications correspond to columns 1–2 of Table 3 and Table 6, respectively.

With respect to demographic controls, there is some evidence of the importance of accounting for changes in the age profile of health districts over time, whereas other factors exert only a minor influence. Specifically, a higher proportion of older residents is associated with increased elective hospitalisations, while no effect is observed for emergency admissions. The population composition by nationality generally shows no significant impact. Regarding socio-economic indicators, income shows no effect on hospitalisations, and the impact of education levels likewise does not reveal a clear pattern. Similarly, the controls capturing the

[23] Missing data on cardiology-specialised doctors for 2010 are imputed using linear predictions. Both indicators, related to hospital doctors and cardiology-specialised doctors, are aggregated at the LHA level. Cardiology-specialised doctors are assigned to each district within an LHA based on population weights, defined as each district's share of the LHA's total population. For hospital doctors, a similar approach is used, employing hospital bed counts to construct the weights.

Table A-3: Full results of 2nd stage for Tables 3 and 6 (panel A, columns 1-2)

	General population		Statin users	
2nd stage dep. var.	Hospitalizations$_t$ (per 1000 inhabitants)		Hospitalizations$_t$ (per 1000 patients at t-4)	
	All 50+ Elective	All 50+ Emergency	All 50+ Elective	All 50+ Emergency
	(1)	(2)	(3)	(4)
	Panel A: pat. codes 410-414 + 430-438 (IHD+CD)			
DDDs$_{t-4}$	-0.0056***	-0.0040***		
	[0.0016]	[0.0015]		
DDDs (per 1000 pat.)$_{t-4}$			-0.0109***	-0.0061**
			[0.0036]	[0.0030]
Share Rosuvast$_t$	0.0064*	0.0112***	-0.0118	-0.0002
	[0.0036]	[0.0042]	[0.0202]	[0.0192]
Avg age naives$_{t-4}$	0.0135**	-0.0201**	0.1203*	-0.1000*
	[0.0068]	[0.0097]	[0.0671]	[0.0600]
Share 75+$_t$	0.2262***	0.0359	0.9813***	-0.3312
	[0.0533]	[0.0636]	[0.1955]	[0.3736]
Share age 65-74$_t$	0.2978***	0.0007	0.5640*	-0.6221**
	[0.0733]	[0.0528]	[0.3198]	[0.2596]
(ln)Income cap.$_t$	-0.2542	-0.5953	0.9470	-3.0521
	[1.4192]	[1.9004]	[7.1540]	[10.5160]
Higher educ proxy$_t$	-0.0036	0.0502	-0.1062	0.0087
	[0.0299]	[0.0338]	[0.1817]	[0.1364]
Share foreign$_t$	0.1022	-0.0640	0.3069	-0.8351
	[0.0711]	[0.1067]	[0.4845]	[0.6221]
Hospital days (res)$_t$	-0.0017	0.0008	-0.0020	0.0100*
	[0.0013]	[0.0009]	[0.0085]	[0.0060]
Hospital days (hosp)$_t$	-0.0031***	0.0011*	-0.0163***	0.0028
	[0.0011]	[0.0006]	[0.0054]	[0.0035]
CHCs$_t$	0.0985	-2.1376	8.8818	2.1921
	[1.3343]	[1.6092]	[10.3015]	[9.0870]
Hosp. doctors wei$_t$	-0.0003	0.0007	0.0014	0.0063
	[0.0009]	[0.0010]	[0.0040]	[0.0047]
Doctors card. wei$_t$	0.0029	0.0346***	0.0991	0.1299
	[0.0079]	[0.0111]	[0.0701]	[0.0801]
Hosp. beds$_t$	0.0006	-0.0745	-0.2581	-0.5575
	[0.0837]	[0.0729]	[0.3819]	[0.3438]
Other 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 squared brackets.

characteristics of health service provision at the local level do not show a significant influence in explaining the evolution of CVD hospitalisations. For example, proxies for infrastructural

resources, both hospital-based (such as beds) and territorial (the deployment of CHCs), have only a negligible impact. An exception is the indicator measuring hospital days produced within the district, which is negatively associated with elective admissions. Slightly different evidence emerges from measures of human capital availability: the presence of cardiology specialists is associated with a higher incidence of emergency cases in the general population, whereas no association is observed for elective admissions. Overall, it appears that contextual factors, capturing local socio-demographic and healthcare supply characteristics, 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 Extended lag analysis

Table A-4: DDDs and hospitalisations: extended lag. IV FE estimation

2nd stage dep. var.	Hospitalizations$_t$ (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]
Share Rosuvast$_t$	0.0041	0.0084*	0.0062	0.0105*	0.0007	0.0055	0.0017	0.0124*
	[0.0032]	[0.0044]	[0.0045]	[0.0054]	[0.0033]	[0.0043]	[0.0063]	[0.0071]
Avg age naives$_{t-8}$	-0.0022	0.0052	0.0151	0.0173*	0.0029	0.0039	-0.0059	0.0130
	[0.0094]	[0.0095]	[0.0117]	[0.0098]	[0.0060]	[0.0093]	[0.0157]	[0.0171]
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]
Share Rosuvast$_t$	-0.0004	0.0002	0.0006	0.0023	-0.0019	- 0.0021	-0.0048	-0.0004
	[0.0030]	[0.0023]	[0.0043]	[0.0035]	[0.0023]	[0.0019]	[0.0049]	[0.0039]
Avg age naives$_{t-8}$	0.0085	0.0010	0.0246**	0.0071	0.0050	-0.0018	0.0112	0.0084
	[0.0068]	[0.0080]	[0.0098]	[0.0077]	[0.0037]	[0.0049]	[0.0107]	[0.0128]
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]
Share Rosuvast$_t$	0.0046**	0.0082**	0.0057***	0.0084**	0.0027	0.0075*	0.0065	0.0129**
	[0.0020]	[0.0036]	[0.0017]	[0.0034]	[0.0027]	[0.0040]	[0.0042]	[0.0059]
Avg age naives$_{t-8}$	-0.0108*	0.0041	-0.0097*	0.0100	-0.0021	0.0058	-0.0169*	0.0043
	[0.0061]	[0.0046]	[0.0057]	[0.0067]	[0.0050]	[0.0079]	[0.0095]	[0.0088]
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
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 squared brackets. DDDs= DDDs per 1000 inhabitants per day.