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Impact of Long-Term Statin Therapy on Influenza Incidence and Overall Mortality: A Real-World Data Analysis

Diana Toledo [1,2], Àurea Cartanyà-Hueso [3,4], Constança Pagès-Fernández [5], Rosa Morros [3,4,6], Maria Giner-Soriano [3,4], Àngela Domínguez [1,2], Carles Vilaplana-Carnerero [1,7], Alba Tor-Roca [1,3,4,8] and María Grau [1,2,9,*]

1 Department of Medicine, School of Medicine and Health Sciences, University of Barcelona, 08036 Barcelona, Spain; dtoledo@ub.edu (D.T.); angela.dominguez@ub.edu (À.D.); carles_vilaplana@ub.edu (C.V.-C.); albator@ub.edu (A.T.-R.)
2 Biomedical Research Consortium in Epidemiology and Public Health (CIBERESP), 28029 Madrid, Spain
3 Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina (IDIAPJGol), 08007 Barcelona, Spain; acartanya@idiapjgol.org (À.C.-H.); rmorros@idiapjgol.org (R.M.); mginer@idiapjgol.info (M.G.-S.)
4 School of Medicine, Universitat Autònoma de Barcelona, 08193 Bellaterra (Cerdanyola del Vallès), Spain
5 School of Pharmacy, University of Barcelona, 08028 Barcelona, Spain; constancapages@gmail.com
6 Biomedical Research Consortium in Infectious Diseases (CIBERINFEC), 28029 Madrid, Spain
7 Service for the Promotion of Quality and Bioethics, General Directorate of Health Planning and Regulation, Department of Health, Government of Catalonia, 08028 Barcelona, Spain
8 Research Institute for Nutrition and Food Safety (INSA-UB), 08921 Santa Coloma de Gramenet, Spain
9 Instituto de Salud Global de Barcelona (ISGlobal), 08003 Barcelona, Spain
* Correspondence: mariagrau@ub.edu

Abstract

Background/Objectives: The study's goal is to assess the association between long-term statin therapy and influenza incidence, influenza severity, and all-cause mortality. **Methods**: Two population-based dynamic cohorts (exposed and unexposed to statins) were followed from 2010 to 2019. Participants were 60 years or older; frail patients were excluded. The primary outcomes were influenza incidence, influenza-related intensive care unit (ICU) admission as a proxy for severity, and all-cause mortality. The exposed cohort comprised new statin users with a minimum of two pharmacy invoices within 90 days of enrollment. Adjusted risk ratios (aRRs) for influenza incidence, ICU admission, and mortality rate were calculated using Poisson regression. **Results**: The initial study population of 639,564 individuals was evenly split into exposed (319,782) and unexposed (319,782) cohorts; mean age was 71 years (standard deviation: 8 years), and 57% were women. Compared to non-users, new statin users showed a higher influenza incidence [9.39 (95% confidence interval: 9.36–9.42) vs. 7.64 (7.61–7.66) per 1000 person-years], ICU admission [1.65 (1.65–1.66) vs. 1.36 (1.35–1.36) per 1000 person-years], and overall mortality rate [97.09 (96.75–97.43) vs. 94.15 (93.82–94.47) per 1000 person-years]. Adjusted analysis revealed no significant association between statin use and influenza incidence [aRR: 1.04 (0.98–1.10)] or influenza-related ICU admission [aRR: 1.03 (0.89–1.19)] and shifted the effect on mortality from harmful to beneficial [aRR: 0.88 (0.87–0.89)]. **Conclusions**: Despite new users' greater vulnerability at the start of treatment, our findings indicate that statins do not influence influenza incidence or severity but reduce all-cause mortality, warranting further exploration of their anti-inflammatory properties.

Keywords: hydroxymethylglutaryl-coA reductase inhibitors; pleiotropic effects; influenza morbidity; all-cause mortality; electronic health records; cohort studies; pharmacoepidemiology

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1. Introduction

Influenza remains a major public health challenge in Europe, causing substantial morbidity and mortality each winter season. Globally, seasonal influenza infects up to 1 billion people annually, with 3–5 million cases of severe illness and an estimated 290,000–650,000 respiratory deaths worldwide [1]. In Europe, annual incidence varies by season but typically affects 5–10% of adults and up to 20–30% of children. Older adults (≥65 years), individuals with chronic conditions, and pregnant women are at the highest risk of complications [2]. Hospitalization burden is significant: during recent seasons, peak influenza-associated hospitalization rates in European countries reached up to 18 per 100,000 population in England, with weekly peaks of 0–366 confirmed cases in sentinel hospitals across the European Union (EU) [2]. In Europe, age-standardized influenza mortality rates among older adults can reach 31 deaths per 100,000 annually [3]. Although most infections are mild, influenza can lead to severe complications such as pneumonia, cardiovascular events, and exacerbation of chronic diseases, driving intensive care admissions and excess winter mortality [2]. Vaccination remains the cornerstone of prevention, yet coverage and effectiveness vary by country and season, underscoring the need for robust surveillance and targeted interventions [4].

Statins, as 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-coA) inhibitors, are widely recognized as lipid-lowering agents and are routinely prescribed for cardiovascular disease prevention [5]. Beyond their cholesterol-lowering properties, numerous studies have documented the pleiotropic effects of statins [6–8]. These include anti-inflammatory actions observed in healthy individuals, such as reductions in TNF-α, C-reactive protein, and metalloproteinase levels following lipopolysaccharide exposure [9]. Indeed, the potential immunomodulatory effects of statins in respiratory infections have been extensively investigated. Some clinical studies suggest that chronic statin treatment exerts protective effects on infectious respiratory diseases [10–14], while others have found no association between the two [15–17].

Analyzing real-world data from electronic health record (EHR) databases provides important insights into the association between chronic statin therapy and both influenza risk and disease severity. These resources capture longitudinal health records across large, diverse populations, permit prolonged follow-up, and document a wide array of outcomes, including influenza diagnoses and intensive care unit admissions [18]. The database used in this study has supported previous research on influenza epidemiology [19] and the anti-inflammatory properties of statins [20]. By leveraging this comprehensive dataset, we aim to produce new evidence on whether long-term statin use influences influenza incidence, thereby addressing a clinically pertinent question.

The goal of this study was to assess whether prior chronic statin therapy influences influenza incidence, intensive care unit (ICU) admission rate, and overall mortality.

2. Results

2.1. Recruitment

Between 1 January 2010 and 31 December 2019, a total of 1,779,709 individuals were recruited. Following the application of exclusion criteria, 394,014 new statin users formed the exposed group, and 773,713 statin non-users formed the unexposed group. Propensity score matching produced a final sample of 639,564 individuals—319,782 in the exposed cohort and 319,782 in the unexposed cohort (Figure 1).

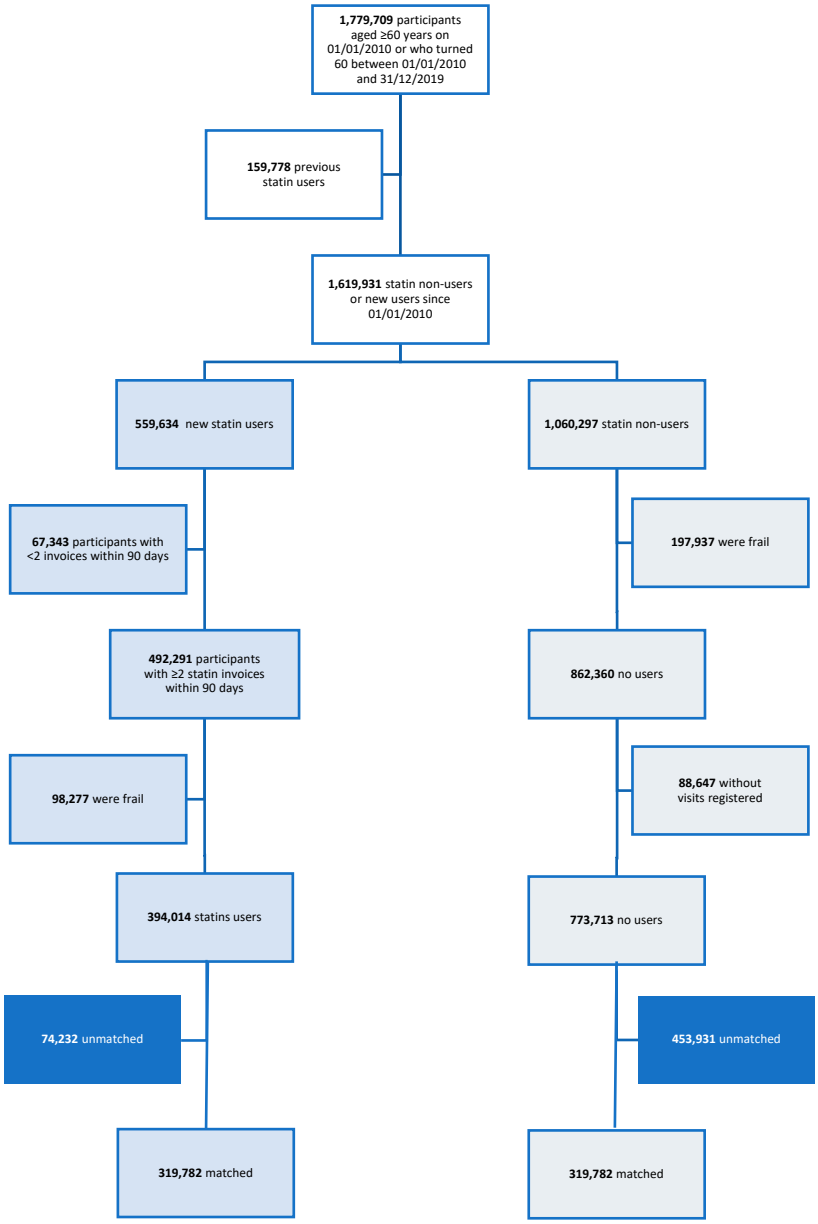


Figure 1. Flowchart of participant selection.

Median follow-up was 8.9 years (Q1 = 5.2; Q3 = 9.9). The mean age was 71 years (SD = 8 years), and the sample included 56.7% women. Comorbidities and risk factors at baseline included diabetes (prevalence = 10.3%), hypertension (33.5%), current smoking (11.4%), and dyslipidemia (24.9%). Baseline characteristics for new users and non-users can be found in Table 1.

Table 1. Baseline characteristics of participants according to statin exposure.

	New Statin Users ***n*** **= 319,782**	**Statin Non-Users** ***n*** **= 319,782**	***p*-Value ***	**SMD**
Sex, *n* (%) (women)	180,405 (56.4)	182,112 (56.9)	<0.001	0.011
Age, mean (SD)	71.09 (7.55)	71.09 (7.55)	0.963	<0.001
Smoking *n* (%)			<0.001	0.078
Smoker	33,532 (10.5)	39,519 (12.4)		
Former smoker	47,249 (14.8)	40,761 (12.7)		

Table 1. *Cont.*

	New Statin Users *n* = 319,782	Statin Non-Users *n* = 319,782	*p*-Value *	SMD
Hypertension, *n* (%)	119,638 (37.4)	94,498 (29.6)	<0.001	0.167
Diabetes, *n* (%)	46,093 (14.4)	19,932 (6.2)	<0.001	0.271
Hypercholesterolemia, *n* (%)	98,696 (30.9)	60,454 (18.9)	<0.001	0.279
Obesity, *n* (%)	44,892 (14.0)	30,983 (9.7)	<0.001	0.135
Charlson index, median [IQR]	2.00 [1.00, 3.00]	2.00 [1.00, 2.00]	<0.001	0.167
MEDEA deprivation index, *n* (%)			<0.001	0.072
Rural	21,629 (6.8)	23,662 (7.4)		
Semi-rural	17,726 (5.5)	18,944 (5.9)		
Urban with low deprivation	62,725 (19.6)	68,602 (21.5)		
Semi-urban	39,256 (12.3)	38,647 (12.1)		
Urban with medium–low deprivation	50,357 (15.7)	51,499 (16.1)		
Urban with medium–high deprivation	68,173 (21.3)	62,318 (19.5)		
Urban with high deprivation	59,478 (18.6)	55,542 (17.4)		
Influenza vaccination, *n* (%)	658 (0.2)	448 (0.1)	<0.001	0.018

IQR: Interquartile range. SD: Standard deviation. SMD: Standard mean difference. * Chi-square test for categorical variables, Student's *t*-test for age, and Wilcoxon rank-sum test for the Charlson index. Table 1 presents baseline characteristics of the same matched cohort used in our previously published study on community-acquired pneumonia [10], although the outcomes analyzed in the present study differ (influenza-related endpoints and all-cause mortality).

2.2. Outcomes According to Statin Use

Between 2010 and 2019, new statin users exhibited a higher influenza incidence than non-users, with rates of 9.39 versus 7.64 per 1000 person-years (95% CI: 9.36–9.42 and 7.61–7.66, respectively). ICU admission was more frequently required for statin users (1.65 per 1000 person-years, 95% CI: 1.65–1.66) compared to non-users (1.36 per 1000 person-years, 95% CI: 1.35–1.36), suggesting a higher severity of the disease among exposed individuals. Additionally, overall mortality was slightly higher for statin users, at 97.09 per 1000 person-years (95% CI: 96.75–97.43), compared to 94.15 per 1000 person-years (95% CI: 93.82–94.47) in non-users. Cumulative incidence curves and log-rank tests for influenza incidence, severity, and all-cause mortality are displayed in Figures 2–4. It should be noted that adjusted analyses found no significant differences in influenza incidence or severity of the episode in new users vs. non-users. Nevertheless, long-term statin use reduced the overall mortality rate by 12% [adjusted RR: 0.88 (95% CI: 0.87–0.89)] (Table 2).

Table 2. Incidence rate of influenza, ICU admission, and overall mortality rate per 1000 person-years for new statin users and non-users.

	New Statin Users		Statin Non-Users		
	Events	Incidence Rate (95% CI)	Events	Incidence Rate (95% CI)	Adjusted Risk Ratio * (95% CI)
Influenza incidence	3003	9.39 (9.36; 9.42)	2442	7.64 (7.61; 7.66)	1.04 (0.98; 1.1)
Influenza severity (ICU admission)	528	1.65 (1.65; 1.66)	434	1.36 (1.35; 1.36)	1.03 (0.89; 1.19)
Overall mortality	31,048	97.09 (96.75; 97.43)	30,107	94.15 (93.82; 94.47)	0.88 (0.87; 0.89)

CI: confidence interval. ICU: intensive care unit. * Model adjusted for Charlson index, influenza vaccination, diabetes, hypercholesterolemia, obesity, hypertension, and smoking.

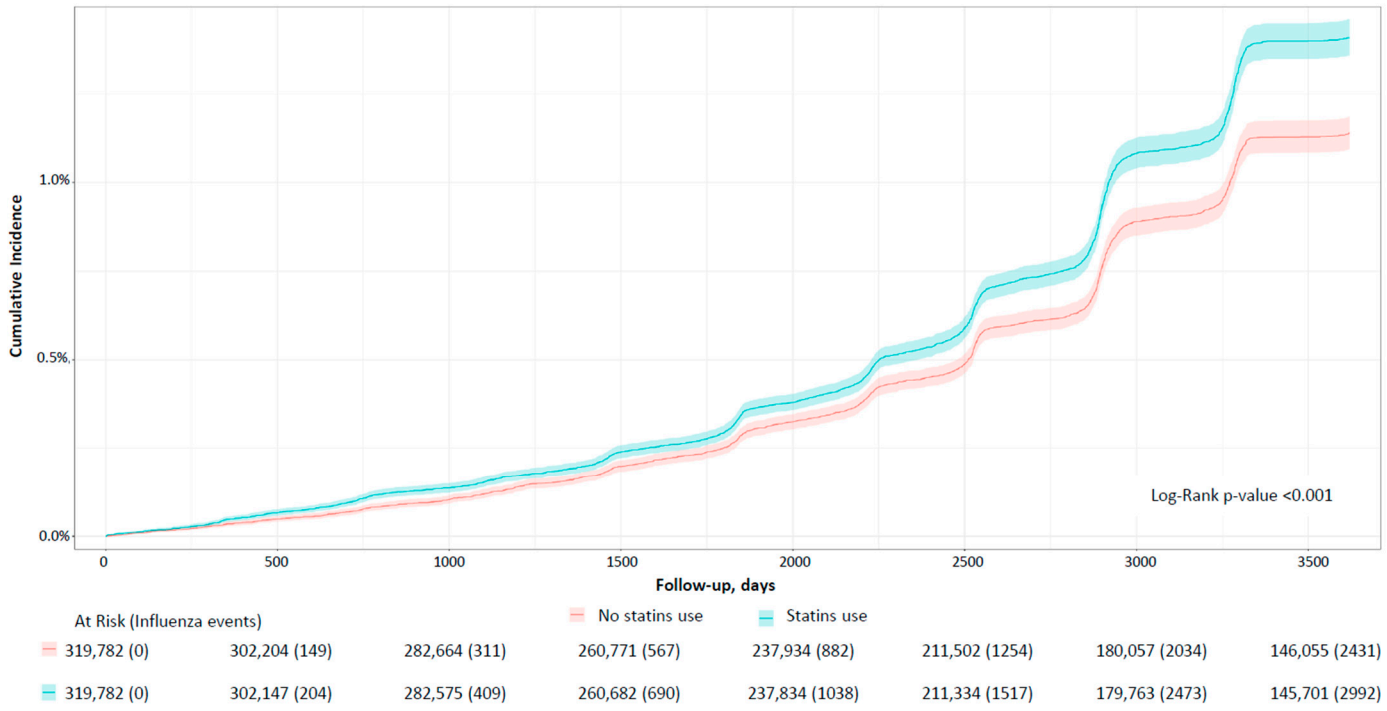


Figure 2. Unadjusted cumulative incidence curve of influenza over a ten-year period.

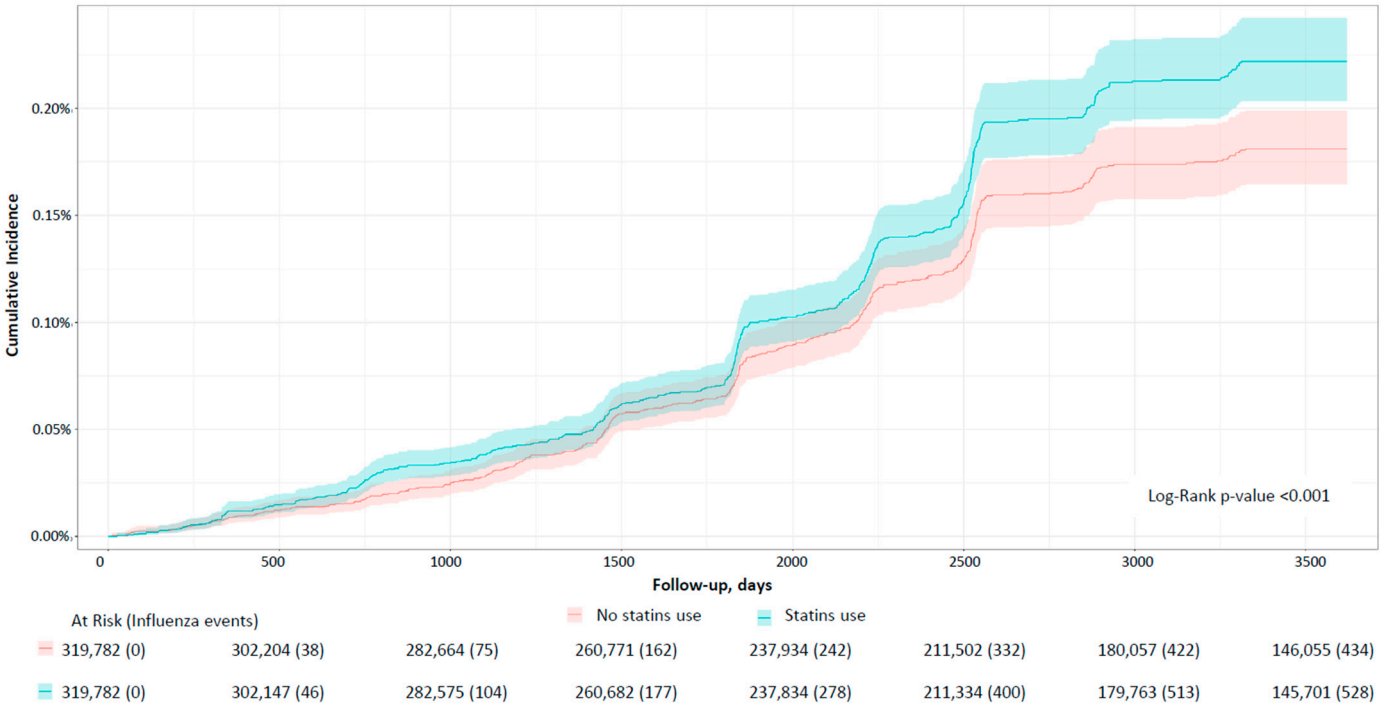


Figure 3. Unadjusted cumulative incidence curve of ICU admission over ten years among patients diagnosed with influenza.

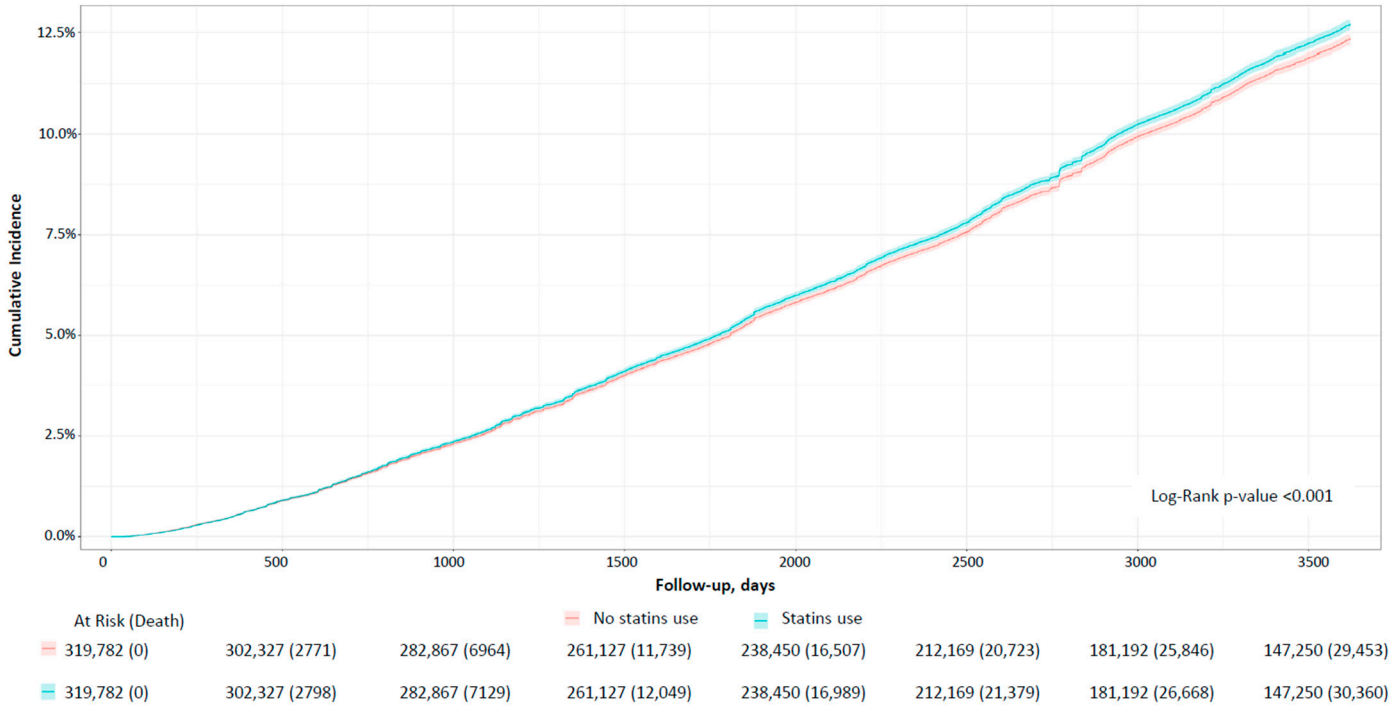


Figure 4. Unadjusted cumulative incidence curve of all-cause mortality over a ten-year period.

3. Discussion

This study utilized a comprehensive database from a real-world clinical setting, conducting a retrospective propensity score-matched cohort analysis of 639,564 participants to explore the impacts of statin treatment on three outcomes: influenza incidence, severity, and overall mortality. Statin users exhibited higher rates of influenza incidence, ICU influenza-related admission, and mortality rate for all causes.

After adjusting for patient complexity, no statistical difference was found in influenza incidence or severity between statin users versus non-users. These findings support statin safety for individuals aged 60 or older, who are particularly vulnerable to influenza [21].

For the remaining outcome, patients on statin treatment showed a 12% lower adjusted risk of overall mortality compared to those not receiving statins. Such results might derive from statins' pleiotropic effects, which extend beyond their primary role as lipid-lowering drugs.

3.1. Chronic Statin Use on Influenza Incidence and Severity

Statins have shown immunomodulatory properties that could affect susceptibility to influenza infection [22,23]. Given the higher risk of severe influenza outcomes among older individuals [21], it is necessary to explore the possible association between statin use and influenza incidence in this population group.

Statins have shown promising antiviral in vitro effects by blocking several steps of the virus life cycle and decreasing the expression of proinflammatory cytokines in influenza-infected cells [24,25]. Numerous preclinical studies have found statins to possess antiviral properties against RSV, HIV-1, and HCV [25]. When it comes to influenza, Liu and colleagues [26] found that a combination of lovastatin and caffeine had therapeutic and preventative effects against H5N1-, H3N2-, and H1N1-infected mice. However, conflicting evidence precludes a consensus. For example, no significant improvements were found in mice treated with either rosuvastatin [27] or simvastatin [28].

Considering the promising but inconclusive preclinical evidence, the use of epidemiological research methodology to analyze EHR databases is particularly suitable for in-

vestigating the impacts of chronic statin treatment on influenza incidence and severity. Still, evidence from observational studies utilizing real-world data remains equally contradictory. Several studies indicate a harmful role of statins on influenza morbidity and mortality [29–32]. For instance, a post hoc analysis using data from a prospective case–control study [30] reported an increased risk of contracting influenza among statin users aged ≥40 years. A recent Canadian study [32] on a population aged ≥66 years similarly found that statin users were 15% more likely to have an influenza infection. Other studies point in the opposite direction [11,14,33]. As an example, Kwong and colleagues [33] found a small yet statistically significant protective role of statins on influenza morbidity and mortality but suggested that the inconsistency of the association could imply it was due to unknown confounders.

Building on these findings, our unadjusted results seem to indicate a harmful effect of statins, but further adjustment reveals it to be null. The absence of association between statin therapy and influenza outcomes is consistent with several population-based studies [17,34–36], and suggests that previously observed differences based on statin use [30] may be attributed to hidden confounders. The highly contrasting results in the literature underscore the relevance of rigorous adjustment for baseline differences, as unadjusted analyses may reflect hidden biases (e.g., healthy user bias or indication bias) rather than true treatment effects. By including numerous variables in our propensity score and adjustment, this study provides a more accurate view of the impact of statins on influenza outcomes. Based on our results, statins have no effect on influenza incidence or severity in patients aged 60 years or older, and their discontinuation should not be recommended as a measure to prevent infection among this population group.

3.2. Statin Therapy and Its Protective Role in All-Cause Mortality

Our results, consistent with previous studies [33,37–40], indicate a protective association between long-term statin therapy and all-cause mortality. Importantly, this beneficial relationship was observed after adjusting for hypercholesterolemia. This aligns with a recent meta-analysis [37], which found the decrease in all-cause mortality risk among statin users to be similar in patients with and without cardiovascular disease, suggesting statins reduce mortality risk through non-cardiovascular mediated mechanisms. As mentioned in Section 4.1, Kwong et al. [33] found a slightly significant protective effect of statins against all-cause mortality after adjusting for relevant covariates. Similarly, Liang et al. [39] described a 20% lower 30-day and 90-day overall mortality among patients receiving long-term statin treatment. Other studies have described a beneficial association between statin treatment after admission and lower overall mortality among ICU patients [40] or patients hospitalized with sepsis [38], which further supports our findings. In contrast, Leung et al. [41] found that the apparent protective effect of statins on 90-day all-cause mortality disappeared after propensity matching, although it should be noted that their sample size was remarkably smaller.

An increasing body of clinical and experimental evidence suggests the existence of certain health benefits of statins unexplained by their primary mechanism as HMG-coA reductase inhibitors [42,43]. These supposed pleiotropic effects include anti-inflammatory, anti-thrombotic, anti-tumoral, and immunomodulatory properties, as well as a reduction in oxidative stress, improved endothelial function, and plaque stabilization [42,44]. In clinical settings, statin therapy has been associated with both a decrease in and therapeutic effects on inflammation-mediated conditions (e.g., cardiovascular events or rheumatoid arthritis) [42,45,46]. With chronic inflammation being at the root of various diseases that collectively represent the leading causes of mortality worldwide [47], our findings, alluding to a positive effect of statins on overall mortality, could be explained by statins' anti-

inflammatory activities. This anti-inflammatory role could improve outcomes for patients on chronic statin therapy, leaving the door open to potential clinical applications of statins beyond their current indication as cholesterol-lowering drugs. However, the mechanisms of statin pleiotropy are yet to be fully elucidated, and further research is needed to understand their real-life implications.

3.3. Strengths and Limitations

A key strength of this study is its large sample obtained from an internally validated, high-quality EHR database. Given the characteristics of Spain's National Health System, such databases provide highly representative real-world data and enable cross-referencing of individual-level information between primary and hospital care. The possibility of reconstructing individual paths within the healthcare system [18] makes EHR databases a remarkably valuable source for epidemiological research. Additionally, these datasets offer high external validity and capture clinical information from groups often underrepresented in trials, including women, older adults, and people with diabetes. As another strength, propensity score matching accounted for several baseline imbalances between the two cohorts, increasing the robustness of the estimates of statin treatment impact.

Limitations inherent to observational studies that rely on medical records must also be recognized. Such studies are susceptible to residual confounding, notably by indication. Individuals with cancer, dementia, paralysis, or organ transplants; those on dialysis; and those who were institutionalized were excluded to mitigate frailty bias. Selection bias cannot be ruled out, as our study population exclusively comprised users of primary care services. Given that the database is based on EHR, observation bias is also possible. Additional nonclinical factors that may influence prescription patterns and treatment adherence include healthcare providers' perceptions of patient risk, prescribers' experiences, unreported side effects, and patients' risk perceptions and willingness to adhere to their treatment [48]. These were unaccounted for in the EHR, potentially leading to interaction bias and/or confounding.

Another important limitation relates to the definition of statin exposure. Following the standard approach in pharmacoepidemiological research, individuals with at least two statin invoices within a 90-day period were classified as statin users at baseline—an exposure definition consistently applied in previous real-world studies assessing statin effects [5,49]. However, our data do not allow us to verify whether participants maintained long-term statin therapy throughout the nearly nine years of median follow-up. Consequently, changes in statin use over time cannot be fully ascertained, which introduces uncertainty in the interpretation of long-term exposure effects.

It must be acknowledged that the adjusted models did not consider influenza vaccination as a covariate. Although recent studies have found statins' effects to be independent of vaccination status [30,32], there is no consensus on the existence of an interaction between statin therapy and influenza vaccination [23,50]. As a possible explanation, McLean et al. [51] found that statin treatment only interacted with vaccination for influenza A(H3N2), but not for influenza A(H1N1) or B, suggesting the degree of interference with statins depends on the virulence of the variant [31]. Because of the seasonal nature of influenza vaccination campaigns and the lack of precise temporal data, accurately portraying vaccination status over time proves particularly challenging. This variability complicates cumulative exposure assessment and the alignment of time of vaccination with influenza episodes. With the objective of avoiding misclassification bias and a reduction in the adjusted estimates' validity, vaccination status was excluded from the current analysis. Further investigation into the interaction between vaccination status and chronic statin treatment could provide valuable insights for future research.

Under-recording or incomplete diagnostic coding in routine clinical practice is another common limitation of real-world datasets. In the present study, approximately 70% of statin patients' medical history did not contain any formally coded hypercholesterolemia diagnosis, revealing that treatment based on laboratory results or cardiovascular risk assessments is not adequately reflected in diagnostic codes. This underscores the need to ensure cohesion between clinical decision-making and administrative records to facilitate observational research and improve the quality of real-world data. Similarly, the absence of cause-of-death information in the SIDIAP database precludes a more granular assessment of statins' association with any cause-specific mortality.

In this study, statin potency or type was not considered. Although reaching contradictory conclusions, prior publications have reported differences among individual statins regarding all-cause mortality [31,39,40]. Lastly, possible variations in statin effect depending on influenza type were not accounted for in the current analysis. Future studies could expand upon previously explored differences in pleiotropic effects according to statin molecular structure [31], dosage [32], or influenza variant [32,51].

4. Materials and Methods

4.1. Study Design and Data Source

Two population-based dynamic cohorts—exposed and unexposed to statins—were followed from 2010 to 2019. Participant data were sourced from the Information System for Research in Primary Care (SIDIAP, from the Spanish *Sistema de Información para el Desarrollo de la Investigación en Atención Primaria*). This study uses the same matched cohort and underlying source population previously described in our published analysis on community-acquired pneumonia [10]. Although the cohort and matching framework are shared, the present manuscript evaluates different outcomes: influenza incidence, influenza-related ICU admission, and all-cause mortality.

The SIDIAP database comprises pseudonymized longitudinal health records routinely collected by over 30,000 healthcare professionals within the Catalan Institute of Health. This data, covering approximately 6 million individuals, encompasses roughly 80% of Catalonia's population and 10.2% of Spain's population. Recorded elements include demographic and lifestyle variables, clinical diagnoses, outcomes, events, referrals, and hospital discharges coded using the International Classification of Diseases (ICD-10), together with laboratory results and prescriptions dispensed through community pharmacies [18]. The study protocol received approval from the ethics committees of the two participating institutions (IDIAP Jordi Gol [23/094-EOM] on 10 July 2023, and the University of Barcelona [IRB00003099]) on 2 February 2024.

4.2. Participants and Exposure Assessment

Participants were enrolled in the cohort upon turning 60 years old, or on 1 January 2010 for those who had already reached that age at the start of the recruitment period. Individuals considered frail—defined as those with a diagnosis of cancer, dementia, or paralysis; those who had undergone an organ transplant; those receiving dialysis; or those living in institutional care—were excluded from the study.

Exposure to statins was defined as the use of medications classified under the ATC code C10AA. This category comprises ATC C10 drugs containing, either as monotherapy or in combination, C10AA01–05 (simvastatin, lovastatin, pravastatin, fluvastatin, and atorvastatin) and C10AA07 (rosuvastatin). The exposed cohort comprised new statin users, identified through health records, who had at least two pharmacy invoices within a 90-day window during the recruitment period. The index date corresponded to the first statin pharmacy invoice. Eligible individuals could not have been exposed to statins prior to

cohort entry (years 2006–2010). Other exclusion criteria for the exposure cohort were the use of non-statin lipid-lowering agents (ATC codes other than C10AA, including C10AB, C10AC, C10AD, and C10AX) not combined with C10AA, as well as less than two statin invoices or more than 90 days between the first and second invoice. Non-users included in the non-exposure cohort were described as individuals with a minimum of one healthcare visit within the 18 months preceding the index date of their matched counterpart.

4.3. Outcomes

The codes assigned to influenza diagnoses in the SIDIAP database were identified for both primary care and hospital discharge records. The assessed outcomes were: (1) the incidence of influenza, determined by influenza diagnosis; (2) ICU admission linked to influenza, serving as a proxy for complicated cases; and (3) overall mortality, described as death from any cause.

4.4. Baseline Covariates

The baseline period was established as the two years prior to the index date. The covariates considered to influence prescription decisions and study outcomes, and which were therefore accounted for, were sex, age, MEDEA index [52], and Charlson Comorbidity Index, along with dichotomous (yes/no) variables for diabetes or use of antidiabetic medication, hypertension or use of antihypertensive medication, dyslipidemia, obesity (defined as BMI > 30 kg/m^2), and influenza vaccination prior to initiation of statin treatment. Lastly, smoking was portrayed in three categories (current, former, and never a smoker).

4.5. Statistical Analysis

To assess the association between statin use and influenza incidence or ICU admission, we used 1:1 nearest neighbor propensity score matching without replacement. The propensity score was estimated using logistic regression of statin use on birth year, sex, MEDEA index [52], smoking status (current, former, or non-smoker), and cohort entry and exit dates. Using the corresponding functions in the MatchIt R package version 4.7.2 [53], the caliper was restricted to 0.1, and individuals were matched by exact year of birth, as well as cohort entry and exit year [54]. The matching process was evaluated through standardized mean differences (SMDs), which measure the discrepancy in covariate means between the two cohorts (exposed and non-exposed), standardized by the pooled standard deviation across both groups. SMDs nearing zero are indicative of good covariate balance between the cohorts [55].

Clinical and sociodemographic characteristics were summarized by statin exposure using absolute frequencies and percentages for categorical variables and means with standard deviations (SDs) or medians with interquartile ranges (IQR; first and third quartiles) for continuous variables. Differences by statin use were assessed using the chi-square test for categorical variables and either Student's *t*-test or the Wilcoxon rank-sum test for continuous variables. Incidence rates per 1000 individuals, with 95% confidence intervals (CIs), were calculated for influenza, influenza-related ICU admission, and all-cause mortality among exposed and unexposed participants. Adjusted risk ratios with 95% CIs for each outcome were estimated by applying g-computation on the matched sample via the avg comparison function from the marginaleffects R package, after fitting the outcome models with the generalized linear model (glm) function. Standard errors were derived using cluster-robust variance estimation, with matching stratum membership specified as the clustering variable [56]. Adjustment covariates included the Charlson index as an indicator of patient complexity, cardiovascular risk factors (diabetes, hypercholesterolemia, obesity, hypertension, and smoking), and influenza vaccination. Cumulative incidence curves with 95% CIs for influenza and influenza-associated ICU admission were plotted

considering death as a competing risk, using cuminc from the tidycmprsk R package [57] and visualization functions from the ggsurvfit R package [58]. Differences in influenza and influenza severity survival distributions between statin users and non-users were assessed using the log-rank test (significance level 0.05) [58]. The R statistical package (R Core Team; version 4.4.3) [59] was used for all calculations.

5. Conclusions

Prior statin therapy showed no association with the adjusted incidence of influenza and related ICU admissions but was associated with a decreased risk of all-cause mortality. These findings reaffirm the safety of statins in older adults and support existing evidence on their pleiotropic anti-inflammatory effects, suggesting that the clinical implications of these properties extend beyond dyslipidemia management.

This study benefits from a very large sample and a high-quality, population-representative EHR database, enabling robust and consistent estimates. As with all observational designs, however, our results remain subject to residual confounding and other inherent limitations. For this reason, while our findings provide strong and methodologically sound real-world evidence, further research—whether through additional observational studies with refined exposure measurements, quasi-experimental designs, or other appropriate methodological approaches—is warranted to clarify statins' pleiotropic effects and their potential clinical and public health applications.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committees of the two involved institutions: IDIAP Jordi Gol [23/094-EOM] on 10 July 2023, and the University of Barcelona [IRB00003099]) on 2 February 2024.

Informed Consent Statement: Patient consent was waived because this manuscript is based on an electronic medical records review.

Data Availability Statement: The data presented in this study are available on request from the corresponding author due to privacy and ethical restrictions.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ATC	Anatomical Therapeutic Chemical
CI	Confidence interval
EHR	Electronic health records
HMG-coA	3-hydroxy-3-methylglutaryl-coenzyme A
ICU	Intensive care unit
SIDIAP	Information System for Research in Primary Care

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