

SUPPLEMENTAL MATERIAL

Table S1. Non-inclusion criteria

Most criteria were defined based on ICD-10 and ATC codes.

ICD-10 codes: any occurrence in the 5 years preceding inclusion date (February 15, 2020) is used.

ATC codes: having 3 dispensing (or 2 when at least one concerned the dispensing of large pack size) in the year preceding inclusion date is used. For lipid lowering drugs, additional condition was required: having at least one dispensing in the last month (if small pack size) or 3 months (if large pack size) preceding inclusion.

Other codes were also detailed.

Exclusion criteria	Codes
Lipid lowering drugs	
Fibrates	
ATC	C10AB
Bile acid sequestrants	
ATC	C10AC
Nicotinic acid and derivatives	
ATC	C10AD
Other lipid lowering drugs (ezetimibe, PCSK9 inhibitors,* etc.)	
ATC	C10AX
Combinations of lipid lowering drugs	
ATC	C10B
Cardiovascular and neurovascular diseases	
Include following conditions: Acute or chronic coronary artery disease Acute stroke or aftermath Acute or chronic heart failure Peripheral vascular disease Arrhythmia or cardiac conduction disorders Valvular heart disease Acute pulmonary embolism Other cardiovascular conditions	
ICD-10	I50 J81 I11 I13 K761 I20 I21 I22 I23 I24 I25 I48 I05 I06 I07 I08 I34 I35 I36 I37 I38 I39 I44, I45, I47, I48, I49 I702, I26 I739, I74.0, I74.3, I74.4, I74.5, G46 I60 I61 I62 I63 I64 I65 I66 I67 I68 I69 G45 I26 I800 I801 I802 I803 I808 I809 I81 I82 I70, I73, I74 only for those included in the list of long-term diseases
Other comorbidities	
Cancer	
ICD-10	C0x.x-C9x.x D00.x-D09.x Z08, Z51.0, Z51.1
Kidney transplant, dialysis	
ICD-10	N18 (long-term diseases), Z940
CCAM	JAEA003, HNEA002 JVJB001, JVJF004, JVJF008, JVRP004, JVRP007, JVRP008, YYYY007
Diagnosis related group	27C06, 24M39Z, 11M17

	11K02, 28Z01-28Z04
Billing code for dialysis session conducted at home, self-care dialysis, in a dialysis unit under medical supervision	D11-D16, D20-24
Dementia	
ICD-10	F00 F01 F02 F03 F051 G30
ATC	N06DA04 N06DX01

*For PCSK9 inhibitors: any dispensing in the past year.

Table S2. Exposure of interest

Definition (ATC codes): having 3 dispensing (or 2 when at least one concerned the dispensing of large pack size) in the year preceding inclusion date and having at least one dispensing in the last month (if small pack size) or 3 months (if large pack size) preceding inclusion.

Types and statin intensity was defined based on the lastly dispensed statin between November 15, 2019 and February 15, 2020 (index date).

Types of statins

Statins (HMG CoA reductase inhibitors)	ATC codes
Atorvastatin	C10AA05
Fluvastatin	C10AA04
Pravastatin	C10AA03
Rosuvastatin	C10AA07
Simvastatin	C10AA01

Classification of statins according to their intensity

This classification is based on an article published by ACC/AHA, Circulation, 2019.

Intensity (LDL-cholesterol lowering)	Dose 1	Dose 2
Low (< 30%)		
Fluvastatin	20	40
Pravastatin	10	20
Simvastatin	10	
Moderate (30% - 49%)		
Atorvastatin	10	20
Rosuvastatin	5	10
Simvastatin	20	40
Pravastatin	40	
Fluvastatin	80	
High (≥50%)		
Atorvastatin	40	80
Rosuvastatin	20	

Table S3. Matching variables

Most criteria were defined based on ICD-10 and ATC codes.

ICD-10 codes: any occurrence in the 5 years preceding inclusion date (February 15, 2020) is used.

ATC codes: having 3 dispensing (or 2 when at least one concerned the dispensing of large pack size) in the year preceding inclusion date is used.

In addition to year of birth, sex, residence area, other matching variables were:

Covariates	Codes
Hypertension ATC	C02AB02, C02AC01, C02AC02, C02AC05, C02AC06, C02CA01, C02CA06, C02DC01, C02LA01, C03AA01, C03AA03, C03BA04, C03BA10, C03BA11, C03BX03, C03CA01, C03CA02, C03CA03, C03DA01, C03DB01, C03EA, C03EA01, C03EA04, C07AA02, C07AA03, C07AA05, C07AA06, C07AA12, C07AA15, C07AA16, C07AA23, C07AB02, C07AB03, C07AB04, C07AB05, C07AB07, C07AB08, C07AB12, C07AG01, C07BA02, C07BB02, C07BB03, C07BB07, C07BB12, C07CA03, C07DA06, C07FB02, C07FB03, C08CA01, C08CA02, C08CA03, C08CA04, C08CA05, C08CA08, C08CA09, C08CA11, C08CA13, C08CX01, C08DA01, C08DB01, C08GA02, C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA07, C09AA08, C09AA09, C09AA10, C09AA13, C09AA15, C09AA16, C09BA01, C09BA02, C09BA03, C09BA04, C09BA05, C09BA06, C09BA07, C09BA09, C09BA15, C09BB02, C09BB04, C09BB10, C09BX02, C09CA01, C09CA02, C09CA03, C09CA04, C09CA06, C09CA07, C09CA08, C09DA01, C09DA02, C09DA03, C09DA04, C09DA06, C09DA07, C09DA08, C09DB01, C09DB02, C09DB04, C09XA02, C09XA52, C10BX03
Diabetes mellitus	
ICD-10 ATC	E10, E11, E12, E13, E14 G59.0, G63.2, G73.0, G99.0, H28.0, H36.0, I79.2, L97, M14.2, M14.6, N08.3 A10 excluding benfluorex (A10BX06)
Chronic respiratory condition	
ICD-10 ATC	J40, J41, J42, J43, J44, J45, J46, J47, J96 (excluding J96.0, J96.9), J98 R03 (drugs for obstructive airway diseases)

Table S4. Covariates

Most criteria were defined based on ICD-10 and ATC codes.

ICD-10 codes: any occurrence in the 5 years preceding inclusion date (February 15, 2020) is used.

ATC codes: having 3 dispensing (or 2 when at least one concerned the dispensing of large pack size) in the year preceding inclusion date is used.

Other codes were also detailed.

Covariates	Codes
Health behavior characteristics	
Smoking-related condition	
ICD-10	Z716 F17 T652 Z720
ATC	N07BA
Primary care delivery	Tobacco consultation service (9566, 9526, 9527) in the 5 years preceding index date (at least once)
Alcohol-related condition	
ICD-10	E244, E512, F10, G312, G621, G721, I426, K292, K70, K860, R780, T51, X45, X65, Y15, Y90, Y91, Y573, Z502, Z714, or Z721
ATC	N07BB01, N07BB03, N07BB04, N07BB05 at least 2 dispensing in the 5 years preceding index date M03BX01 (baclofen) without following neurological disease (ICD-10): C70, C71, C793, C794, D32, D33, D42, D43, G04, G05, G06, G09, G12, G13, G24, G25, G26, G31, G32, G35, G36, G37, G46, G80, G81, G82, G83, G91, G93, G95
Laboratory test (NABM)	516, 517, 519 (gamma-GT)
Obesity-related condition	
ICD-10	E66 excluding E66.03, E66.13, E66.83, E66.93 (since 2006)
CCAM	HFCA001, HFCC003, HFFA001, HFFA011, HFFC004, HFFC018, HFGC900, HFKA001, HFKA002, HFKC001, HFLC900, HFLE002, HFMA009, HFMA010, HFMA011, HFMC006, HFMC007, HFMC008, HGCA009, HGCC027 (bariatric surgery)
Comorbidities or comedications	
Liver and pancreas disorder	
ICD-10	B18, I85, K70, K71, K72, K73, K74, K75, K76 K85, K86
ATC/UCD/CIP	Treatment for chronic hepatitis B: J05AF08, J05AF10, J05AF11 9212525, 9212531 (UCD, Zeffix®) 3519671, 3519694 (CIP, Zeffix®) Treatment for chronic hepatitis B: L03AB05, L03AB09, L03AB10, L03AB11 J05AB04 J05AP08, J05AP51, J05AP55, J05AP56, J05AX (3400930108765 (CIP), 3400894287391 (UCD)), J05AX14, J05AX15, J05AX16, J05AX65, J05AX67, J05AX68
Laboratory test (NABM)	4125: hepatitis C genotype 4124: hepatitis C viral load 1000 to 1002 (Fibrotest®, Fibromètre®V, Hépascore®)
CCAM	HLQM002, HLHB001, HLHH001, HLHH005, HLHJ003 (liver biopsy, etc.)
Medications (ATC)	

Non-steroidal anti-inflammatory drugs (ATC)	M01AE09, M01AE11, M01AE01, M01AE02, M01AB01, M01AE03, M01AB05, M01AB16, M01AH01, M01AH05, M01AC01, M01AC02, M01AC06, M01AX01, M01AX17, M01AB08, M01AE16, M01AX02, M01AX22, M01AX21
Low-dose aspirin (CIP)	18 CIP codes: 3400934744198 3400933247379 3400931893639 3400932703616 3400926939939 3400938206371 3400933226558 3400934323492 3400934300141 3400930013953 3400930013984 3400930014035 3400930014066 3400935902269 3400935984814 3400926940188 3400930182543 3400930195697
Antiplatelet	B01AC04-B01AC07 B01AC22-B01AC24 B01AC30
Heparin	B01AB,B01AX
Anticoagulant	B01AA,B01AE,B01AF,B01AX
Oral corticosteroid	H02A
Anxiolytic	N05BA01, N05BA04, N05BA05, N05BA06, N05BA08, N05BA09, N05BA11, N05BA12, N05BA16, N05BA18, N05BA21, N05BA23, N05BB01, N05BB02, N05BC01, N05BE01, N05BX03
Hypnotic	N05BC51, N05CD02, N05CD03, N05CD04, N05CD05, N05CD06, N05CD07, N05CD11, N05CF01, N05CF02, N05CM11, N05CM16, N05CX
Antidepressant	N06A, N05AN01, N03AG02 3400934876233, 3400934876691, 3400935444271 (CIP)
Antipsychotic	N05A (excluding N05AN01 and N05AL06) 3400932896332 (CIP)

NABM: *nomenclature des actes de biologie médicale.*

Table S5. Population distribution by geographical region

	In metropolitan France		In the present study	
	January 1, 2021*		No exposure	Statin exposure
Auvergne-Rhône-Alpes	8,092,598	(12,4)	213,640 (10.4)	213,640 (10.4)
Bourgogne-Franche-Comté	2,786,205	(4,3)	98,693 (4.8)	98,693 (4.8)
Bretagne	3,371,297	(5,2)	104,714 (5.1)	104,714 (5.1)
Centre-Val de Loire	2,562,431	(3,9)	95,625 (4.6)	95,625 (4.6)
Corse	349,273	(0,5)	8,697 (0.4)	8,697 (0.4)
Grand Est	5,524,817	(8,5)	192,826 (9.4)	192,826 (9.4)
Hauts-de-France	5,977,46	(9,2)	234,718 (11.4)	234,718 (11.4)
Île-de-France	12,326,429	(18,9)	317,010 (15.4)	317,010 (15.4)
Normandie	3,306,092	(5,1)	121,260 (5.9)	121,260 (5.9)
Nouvelle Aquitaine	6,039,767	(9,3)	199,285 (9.7)	199,285 (9.7)
Occitanie	5,985,751	(9,2)	164,959 (8.0)	164,959 (8.0)
Pays de la Loire	3,838,060	(5,9)	125,184 (6.1)	125,184 (6.1)
Provence-Alpes-Côte d'Azur	5,089,661	(7,8)	133,389 (6.5)	133,389 (6.5)
Total	65,249,843		2,058,249	2,058,249

*Source: INSEE, Population census. Data available on the French Institute for Demographic Studies website (INED: <https://www.ined.fr>).

Table S6. Association between statin exposure and hospitalization for COVID-19

	Hospitalization N=9396	IPTW*		IPTW further adjusted model†	
		HR [95%CI]	P-value	HR [95%CI]	P-value
Statin exposure					
No exposure	5,024 (0.24)	1	.	1	.
Statin exposure	4,372 (0.21)	0.85 [0.82-0.89]	<.0001	0.84 [0.80-0.87]	<.0001
Type of statin					
No exposure	5,024 (0.24)	1	.	1	.
Atorvastatin	1,944 (0.23)	0.91 [0.85-0.97]	0.0035	0.88 [0.83-0.94]	0.0002
Fluvastatin	92 (0.17)	0.69 [0.52-0.92]	0.0114	0.71 [0.53-0.95]	0.0212
Pravastatin	730 (0.19)	0.86 [0.77-0.95]	0.0038	0.84 [0.76-0.93]	0.0012
Rosuvastatin	794 (0.21)	0.82 [0.75-0.91]	<.0001	0.80 [0.72-0.88]	<.0001
Simvastatin	812 (0.20)	0.79 [0.72-0.87]	<.0001	0.78 [0.71-0.87]	<.0001
Statin intensity					
No exposure	5,024 (0.24)	1	.	1	.
Low	778 (0.18)	0.79 [0.71-0.87]	<.0001	0.78 [0.71-0.87]	<.0001
Moderate	3,231 (0.22)	0.85 [0.81-0.89]	<.0001	0.83 [0.79-0.88]	<.0001
High	363 (0.28)	1.12 [0.95-1.31]	0.1756	1.04 [0.88-1.23]	0.6193
Statin intensity and its type					
No exposure	5,024 (0.24)	1	.	1	.
<u>Low</u>					
Fluvastatin 20/40	58 (0.17)	0.71 [0.50-1.01]	0.0595	0.74 [0.51-1.06]	0.0973
Pravastatin 10/20	537 (0.19)	0.82 [0.73-0.93]	0.0015	0.81 [0.72-0.92]	0.0007
Simvastatin 10	183 (0.17)	0.71 [0.59-0.87]	0.0009	0.72 [0.59-0.89]	0.0018
<u>Moderate</u>					
Atorvastatin 10/20	1,638 (0.23)	0.88 [0.82-0.95]	0.0004	0.86 [0.80-0.93]	<.0001
Fluvastatin 80	34 (0.16)	0.66 [0.41-1.06]	0.0886	0.67 [0.42-1.09]	0.1048
Pravastatin 40	193 (0.22)	0.97 [0.79-1.20]	0.8066	0.94 [0.76-1.17]	0.5806
Rosuvastatin 5/10	737 (0.20)	0.80 [0.72-0.88]	<.0001	0.78 [0.71-0.87]	<.0001
Simvastatin 20/40	629 (0.21)	0.82 [0.73-0.91]	0.0003	0.81 [0.72-0.90]	0.0001
<u>High</u>					
Atorvastatin 40/80	306 (0.28)	1.09 [0.91-1.29]	0.3393	1.02 [0.85-1.22]	0.8238
Rosuvastatin 20	57 (0.28)	1.29 [0.85-1.95]	0.2252	1.18 [0.78-1.80]	0.4359

HR for hazard ratio; 95%CI for 95% confidence interval; IPTW for inverse probability of treatment weighting.

*Conditional Cox proportional hazards model with IPTW.

†Conditional Cox proportional hazards model with IPTW further adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, low-dose aspirin, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic).

Table S7. Association between statin exposure and hospital outcomes after excluding participants with low-dose aspirin

	Fully adjusted model [*]	
	HR [95%CI]	P-value
Hospitalization for COVID-19		
Statin exposure		
No	1	-
Yes	0.84 [0.79-0.89]	<.0001
Statin intensity		
No exposition	1	-
Low	0.79 [0.70-0.89]	0.0002
Moderate	0.84 [0.79-0.90]	0.0000
High	1.04 [0.83-1.31]	0.7330
In-hospital deaths for COVID-19		
Statin exposure		
No	1	-
Yes	0.80 [0.68-0.92]	0.0028
Statin intensity		
No exposition	1	-
Low	0.74 [0.54-1.02]	0.0639
Moderate	0.78 [0.66-0.93]	0.0061
High	1.36 [0.73-2.54]	0.3352

HR for hazard ratio; 95%CI for 95% confidence interval.

^{*}Conditional Cox proportional hazards model adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic).

Table S8. Characteristics of the study population according to statin intensity

	Before IPTW				After IPTW			
	No exposure (n=2,058,249)	Low (n=431,167)	Moderate (n=1,496,809)	High (n=130,273)	No exposure (n=2,059,865)	Low (n=430,877)	Moderate (n=1,497,236)	High (n=129,810)
Matching variables								
Age (years)								
Mean (SD)	68.65 (10.36)	70.03 (10.39)	68.41 (10.31)	66.84 (10.40)	68.77 (10.45)	68.66 (10.43)	68.68 (10.25)	68.76 (10.25)
Age categories								
40-59	395,018 (19.2)	68,576 (15.9)	294,549 (19.7)	31,893 (24.5)	393,908 (19.1)	83,290 (19.3)	281,126 (18.8)	24,167 (18.6)
60-69	683,378 (33.2)	133,583 (31.0)	504,099 (33.7)	45,696 (35.1)	675,066 (32.8)	141,375 (32.8)	501,607 (33.5)	43,582 (33.5)
70-79	660,264 (32.1)	146,141 (33.9)	476,803 (31.9)	37,320 (28.6)	659,763 (32.1)	138,366 (32.1)	486,325 (32.5)	41,898 (32.2)
>=80	319,589 (15.5)	82,867 (19.2)	221,358 (14.8)	15,364 (11.8)	331,128 (16.1)	67,846 (15.7)	228,178 (15.2)	20,163 (15.5)
Sex								
Men	958,989 (46.6)	180,842 (41.9)	705,247 (47.1)	72,900 (56.0)	953,716 (46.3)	200,817 (46.6)	695,127 (46.4)	59,735 (45.9)
Women	1,099,260 (53.4)	250,325 (58.1)	791,562 (52.9)	57,373 (44.0)	1,106,151 (53.7)	230,062 (53.4)	802,109 (53.6)	70,076 (53.8)
Residence area								
Auvergne-Rhône-Alpes	213,640 (10.4)	46,402 (10.8)	153,759 (10.3)	13,479 (10.3)	211,820 (10.3)	46,107 (10.7)	153,836 (10.3)	13,630 (10.5)
Bourgogne-Franche-Comté	98,693 (4.8)	20,662 (4.8)	71,392 (4.8)	6,639 (5.1)	98,760 (4.8)	20,419 (4.7)	71,484 (4.8)	6,894 (5.3)
Bretagne	104,714 (5.1)	26,632 (6.2)	71,362 (4.8)	6,720 (5.2)	103,224 (5.0)	25,991 (6.0)	72,537 (4.8)	6,891 (5.3)
Centre-Val de Loire	95,625 (4.6)	21,013 (4.9)	69,118 (4.6)	5,494 (4.2)	94,986 (4.6)	20,878 (4.8)	70,104 (4.7)	5,898 (4.5)
Corse	8,697 (0.4)	1,859 (0.4)	6,499 (0.4)	339 (0.3)	9,048 (0.4)	1,789 (0.4)	6,347 (0.4)	302 (0.2)
Grand Est	192,826 (9.4)	37,524 (8.7)	144,291 (9.6)	11,011 (8.5)	196,157 (9.5)	37,416 (8.7)	142,586 (9.5)	11,074 (8.5)
Hauts-de-France	234,718 (11.4)	41,586 (9.6)	176,315 (11.8)	16,817 (12.9)	241,077 (11.7)	41,848 (9.7)	173,364 (11.6)	16,086 (12.3)
Ile-de-France	317,010 (15.4)	57,879 (13.4)	239,199 (16.0)	19,932 (15.3)	313,047 (15.2)	59,433 (13.8)	239,784 (16.0)	19,816 (15.2)
Normandie	121,260 (5.9)	27,880 (6.5)	86,616 (5.8)	6,764 (5.2)	122,824 (6.0)	27,751 (6.4)	86,127 (5.8)	6,725 (5.2)
Nouvelle-Aquitaine	199,285 (9.7)	47,489 (11.0)	139,229 (9.3)	12,567 (9.6)	198,574 (9.6)	47,079 (10.9)	141,019 (9.4)	13,143 (10.1)
Occitanie	164,959 (8.0)	37,273 (8.6)	118,545 (7.9)	9,141 (7.0)	163,733 (8.0)	37,101 (8.6)	119,146 (8.0)	9,074 (7.0)
Overseas departments	47,939 (2.3)	7,349 (1.7)	35,138 (2.3)	5,452 (4.2)	48,232 (2.3)	7,851 (1.8)	34,777 (2.3)	4,708 (3.6)
Overseas territories	310 (0.0)	65 (0.0)	207 (0.0)	38 (0.0)	315 (0.0)	74 (0.0)	206 (0.0)	36 (0.0)
Pays de la Loire	125,184 (6.1)	30,893 (7.2)	85,542 (5.7)	8,749 (6.7)	124,445 (6.0)	30,582 (7.1)	86,012 (5.7)	8,234 (6.3)
Provence-Alpes-Côte d'Azur	133,389 (6.5)	26,661 (6.2)	99,597 (6.7)	7,131 (5.5)	133,618 (6.5)	26,552 (6.2)	99,899 (6.7)	7,293 (5.6)
Covariates								
Hypertension								
No	1,198,186 (58.2)	237,112 (55.0)	878,869 (58.7)	82,205 (63.1)	1,194,456 (58.0)	249,811 (57.9)	870,240 (58.1)	78,250 (60.1)
Yes	860,063 (41.8)	194,055 (45.0)	617,940 (41.3)	48,068 (36.9)	865,410 (42.0)	181,067 (42.0)	626,997 (41.9)	51,561 (39.6)
Diabetes mellitus								

No	1,364,924 (66.3)	307,159 (71.2)	983,960 (65.7)	73,805 (56.7)	1,357,640 (66.0)	286,008 (66.3)	989,815 (66.1)	80,966 (62.2)
Yes	693,325 (33.7)	124,008 (28.8)	512,849 (34.3)	56,468 (43.3)	702,226 (34.1)	144,871 (33.6)	507,421 (33.9)	48,845 (37.5)
Chronic respiratory condition								
No	1,872,316 (91.0)	394,499 (91.5)	1,361,260 (90.9)	116,557 (89.5)	1,872,250 (91.0)	391,818 (90.9)	1,361,593 (91.0)	117,580 (90.3)
Yes	185,933 (9.0)	36,668 (8.5)	135,549 (9.1)	13,716 (10.5)	187,617 (9.1)	39,060 (9.1)	135,644 (9.1)	12,231 (9.4)
Social deprivation index (quintiles)								
1 (least deprived)	343,795 (16.7)	66,309 (15.4)	244,750 (16.4)	19,149 (14.7)	338,101 (16.4)	66,521 (15.4)	246,129 (16.4)	20,596 (15.8)
2	366,832 (17.8)	77,603 (18.0)	264,559 (17.7)	22,214 (17.1)	362,894 (17.6)	78,132 (18.1)	266,239 (17.8)	23,306 (17.9)
3	393,467 (19.1)	85,186 (19.8)	283,928 (19.0)	24,197 (18.6)	392,651 (19.1)	84,848 (19.7)	284,438 (19.0)	24,495 (18.8)
4	422,536 (20.5)	94,334 (21.9)	306,801 (20.5)	26,949 (20.7)	425,373 (20.7)	93,683 (21.7)	306,602 (20.5)	26,327 (20.2)
5 (most deprived)	449,430 (21.8)	92,908 (21.5)	336,361 (22.5)	30,443 (23.4)	457,832 (22.2)	92,534 (21.5)	333,883 (22.3)	28,688 (22.0)
Unknown	82,189 (4.0)	14,827 (3.4)	60,410 (4.0)	7,321 (5.6)	83,015 (4.0)	15,158 (3.5)	59,943 (4.0)	6,398 (4.9)
Smoking-related condition								
No	2,001,677 (97.3)	417,468 (96.8)	1,436,216 (96.0)	122,283 (93.9)	1,990,894 (96.7)	416,274 (96.5)	1,446,959 (96.7)	125,253 (96.1)
Yes	56,572 (2.7)	13,699 (3.2)	60,593 (4.0)	7,990 (6.1)	68,973 (3.4)	14,605 (3.4)	50,278 (3.4)	4,558 (3.5)
Alcohol-related condition								
No	2,025,242 (98.4)	426,071 (98.8)	1,474,072 (98.5)	127,232 (97.7)	2,028,053 (98.5)	424,201 (98.4)	1,474,250 (98.5)	127,614 (98.0)
Yes	33,007 (1.6)	5,096 (1.2)	22,737 (1.5)	3,041 (2.3)	31,814 (1.5)	6,677 (1.5)	22,987 (1.5)	2,197 (1.7)
Obesity-related condition								
No	2,015,058 (97.9)	424,354 (98.4)	1,464,716 (97.9)	126,523 (97.1)	2,016,463 (98.0)	421,848 (97.8)	1,465,808 (97.9)	126,805 (97.3)
Yes	43,191 (2.1)	6,813 (1.6)	32,093 (2.1)	3,750 (2.9)	43,404 (2.1)	9,030 (2.1)	31,429 (2.1)	3,006 (2.3)
Liver and pancreas disorder								
No	2,030,710 (98.7)	428,432 (99.4)	1,485,005 (99.2)	128,971 (99.0)	2,038,195 (99.0)	426,312 (98.9)	1,481,631 (99.0)	128,335 (98.5)
Yes	27,539 (1.3)	2,735 (0.6)	11,804 (0.8)	1,302 (1.0)	21,672 (1.1)	4,566 (1.1)	15,606 (1.0)	1,476 (1.1)
Non-steroidal anti-inflammatory								
No	1,732,982 (84.2)	364,847 (84.6)	1,245,484 (83.2)	109,615 (84.1)	1,725,349 (83.8)	361,483 (83.8)	1,255,350 (83.9)	107,885 (82.8)
Yes	325,267 (15.8)	66,320 (15.4)	251,325 (16.8)	20,658 (15.9)	334,517 (16.3)	69,396 (16.1)	241,887 (16.2)	21,927 (16.8)
Low-dose aspirin								
No	1,827,030 (88.8)	328,902 (76.3)	1,108,038 (74.0)	77,365 (59.4)	1,669,681 (81.1)	348,232 (80.8)	1,215,634 (81.2)	105,230 (80.8)
Yes	231,219 (11.2)	102,265 (23.7)	388,771 (26.0)	52,908 (40.6)	390,186 (19.0)	82,646 (19.2)	281,602 (18.8)	24,581 (18.9)
Antiplatelet agent								
No	2,042,260 (99.2)	423,613 (98.2)	1,459,937 (97.5)	122,258 (93.8)	2,021,734 (98.2)	423,714 (98.3)	1,472,331 (98.4)	127,585 (97.9)
Yes	15,989 (0.8)	7,554 (1.8)	36,872 (2.5)	8,015 (6.2)	38,133 (1.9)	7,164 (1.7)	24,906 (1.7)	2,226 (1.7)
Heparin								
No	2,044,349 (99.3)	428,538 (99.4)	1,487,559 (99.4)	129,411 (99.3)	2,046,403 (99.4)	428,086 (99.3)	1,487,529 (99.4)	128,922 (99.0)
Yes	13,900 (0.7)	2,629 (0.6)	9,250 (0.6)	862 (0.7)	13,463 (0.7)	2,792 (0.6)	9,708 (0.6)	889 (0.7)

Anticoagulant

No	2,010,491 (97.7)	419,361 (97.3)	1,455,088 (97.2)	125,388 (96.3)	2,005,242 (97.4)	419,692 (97.3)	1,458,442 (97.4)	126,253 (96.9)
Yes	47,758 (2.3)	11,806 (2.7)	41,721 (2.8)	4,885 (3.7)	54,624 (2.7)	11,187 (2.6)	38,794 (2.6)	3,558 (2.7)

Oral corticosteroid

No	1,944,371 (94.5)	409,134 (94.9)	1,416,044 (94.6)	123,291 (94.6)	1,947,198 (94.6)	407,439 (94.5)	1,415,769 (94.6)	122,676 (94.2)
Yes	113,878 (5.5)	22,033 (5.1)	80,765 (5.4)	6,982 (5.4)	112,668 (5.5)	23,439 (5.4)	81,468 (5.4)	7,135 (5.5)

Anxiolytic

No	1,872,500 (91.0)	381,414 (88.5)	1,326,948 (88.7)	115,006 (88.3)	1,844,824 (89.6)	386,921 (89.7)	1,343,356 (89.7)	116,067 (89.1)
Yes	185,749 (9.0)	49,753 (11.5)	169,861 (11.3)	15,267 (11.7)	215,043 (10.4)	43,958 (10.2)	153,881 (10.3)	13,744 (10.6)

Hypnotic

No	1,975,317 (96.0)	409,748 (95.0)	1,419,181 (94.8)	123,358 (94.7)	1,962,836 (95.4)	411,091 (95.3)	1,427,986 (95.4)	123,565 (94.9)
Yes	82,932 (4.0)	21,419 (5.0)	77,628 (5.2)	6,915 (5.3)	97,031 (4.7)	19,787 (4.6)	69,250 (4.6)	6,246 (4.8)

Antidepressant

No	1,902,683 (92.4)	386,729 (89.7)	1,344,623 (89.8)	116,320 (89.3)	1,873,144 (91.0)	392,469 (91.0)	1,363,551 (91.1)	117,950 (90.5)
Yes	155,566 (7.6)	44,438 (10.3)	152,186 (10.2)	13,953 (10.7)	186,722 (9.1)	38,410 (8.9)	133,686 (8.9)	11,861 (9.1)

Antipsychotic

No	2,044,795 (99.3)	427,542 (99.2)	1,484,359 (99.2)	129,004 (99.0)	2,044,152 (99.3)	427,614 (99.2)	1,486,009 (99.3)	128,817 (98.9)
Yes	13,454 (0.7)	3,625 (0.8)	12,450 (0.8)	1,269 (1.0)	15,715 (0.8)	3,265 (0.8)	11,227 (0.8)	995 (0.8)

Table S9. Association between covariates and hospitalization for COVID-19 examined in a fully adjusted model

	Fully adjusted model*			P-value
	HR	95%CI		
Statin exposure				
No exposure	1.00	.	.	.
Statin exposure	0.84	0.81	0.88	<.0001
Social deprivation index (quintiles)				
1 (least deprived)	1.00	.	.	.
2	1.18	1.07	1.31	0.0014
3	1.38	1.23	1.54	<.0001
4	1.42	1.27	1.59	<.0001
5 (most deprived)	1.58	1.42	1.75	<.0001
Unknown	1.34	0.98	1.82	0.0631
Smoking-related condition				
No	1.00	.	.	.
Yes	0.50	0.41	0.63	<.0001
Alcohol-related condition				
No	1.00	.	.	.
Yes	1.31	1.02	1.67	0.0322
Obesity-related condition				
No	1.00	.	.	.
Yes	1.49	1.25	1.79	<.0001
Liver failure				
No	1.00	.	.	.
Yes	1.69	1.34	2.12	<.0001
Non-steroidal anti-inflammatory				
No	1.00	.	.	.
Yes	1.11	1.03	1.21	0.0084
Low-dose aspirin				
No	1.00	.	.	.
Yes	1.13	1.06	1.22	0.0006
Antiplatelet agent				
No	1.00	.	.	.
Yes	1.58	1.29	1.93	<.0001
Heparin				
No	1.00	.	.	.
Yes	1.14	0.81	1.60	0.4629
Anticoagulant				
No	1.00	.	.	.
Yes	1.35	1.16	1.57	<.0001
Oral corticosteroid				
No	1.00	.	.	.
Yes	1.55	1.37	1.75	<.0001
Anxiolytic				
No	1.00	.	.	.
Yes	1.06	0.96	1.18	0.2398
Hypnotic				
No	1.00	.	.	.

	Fully adjusted model [*]			
	HR	95%CI		P-value
Yes	0.94	0.82	1.09	0.4046
Antidepressant				
No	1.00	.	.	.
Yes	1.10	0.98	1.22	0.0984
Antipsychotic				
No	1.00	.	.	.
Yes	1.91	1.40	2.60	<.0001

HR for hazard ratio; 95%CI for 95% confidence interval.

^{*}Conditional Cox proportional hazards model adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, low-dose aspirin, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic).

Table S10. Association between statin exposure and in-hospital COVID-19 deaths

	Death N=1648	IPTW*		IPTW further adjusted model†	
		HR [95%CI]	P-value	HR [95%CI]	P-value
Statin exposure					
No exposure	914 (0.044)	1	.	1	.
Statin exposure	734 (0.036)	0.77 [0.69-0.85]	<.0001	0.76 [0.68-0.85]	<.0001
Type of statin					
No exposure	914 (0.044)	1	.	1	.
Atorvastatin	329 (0.040)	0.86 [0.73-1.01]	0.0584	0.83 [0.70-0.98]	0.0280
Fluvastatin	22 (0.040)	0.87 [0.48-1.57]	0.6457	0.88 [0.47-1.65]	0.6970
Pravastatin	118 (0.031)	0.66 [0.52-0.84]	0.0009	0.66 [0.51-0.85]	0.0014
Rosuvastatin	126 (0.033)	0.73 [0.58-0.93]	0.0093	0.72 [0.56-0.92]	0.0084
Simvastatin	139 (0.034)	0.73 [0.58-0.91]	0.0065	0.75 [0.59-0.96]	0.0212
Statin intensity					
No exposure	914 (0.044)	1	.	1	.
Low	142 (0.033)	0.72 [0.58-0.90]	0.0038	0.74 [0.59-0.94]	0.0116
Moderate	527 (0.035)	0.76 [0.68-0.86]	<.0001	0.75 [0.66-0.85]	<.0001
High	65 (0.050)	1.05 [0.71-1.55]	0.8103	1.00 [0.66-1.51]	0.9977
Statin intensity and its type					
No exposure	914 (0.044)	1	.	1	.
<u>Low</u>					
Fluvastatin 20/40	14 (0.040)	0.78 [0.39-1.56]	0.4890	0.82 [0.39-1.72]	0.6016
Pravastatin 10/20	91 (0.032)	0.65 [0.49-0.85]	0.0019	0.66 [0.50-0.88]	0.0041
Simvastatin 10	37 (0.034)	0.94 [0.59-1.50]	0.8084	1.01 [0.62-1.64]	0.9769
<u>Moderate</u>					
Atorvastatin 10/20	273 (0.038)	0.82 [0.69-0.98]	0.0278	0.80 [0.67-0.96]	0.0169
Fluvastatin 80	8 (0.038)	1.17 [0.37-3.73]	0.7888	1.08 [0.33-3.55]	0.9052
Pravastatin 40	27 (0.031)	0.72 [0.42-1.24]	0.2379	0.67 [0.38-1.17]	0.1628
Rosuvastatin 5/10	117 (0.032)	0.72 [0.57-0.92]	0.0093	0.71 [0.55-0.91]	0.0072
Simvastatin 20/40	102 (0.033)	0.67 [0.51-0.87]	0.0029	0.68 [0.52-0.91]	0.0079
<u>High</u>					
Atorvastatin 40/80	56 (0.051)	1.10 [0.71-1.71]	0.6626	1.02 [0.65-1.61]	0.9380
Rosuvastatin 20	9 (0.044)	0.85 [0.35-2.10]	0.7307	0.93 [0.37-2.34]	0.8697

HR for hazard ratio; 95%CI for 95% confidence interval; IPTW for inverse probability of treatment weighting.

*Conditional Cox proportional hazards model with IPTW.

†Conditional Cox proportional hazards model with IPTW further adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, low-dose aspirin, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic).

Table S11. Association between statin exposure and in-hospital deaths in COVID-19-related hospitalized individuals (N=9,396)

	Death* N = 1529	Unadjusted model†		Fully adjusted model‡		IPTW further adjusted model§	
		HR [95% CI]¶	P-value	HR [95% CI]¶	P-value	HR [95% CI]¶	P-value
Statin exposure							
No exposure	839 (16.70)	1	.	1	.	1	.
Statin exposure	690 (15.78)	0.94 [0.85-1.04]	0.2597	0.84 [0.76-0.93]	0.0012	0.87 [0.79-0.96]	0.0083
Type of statin							
No exposure	839 (16.70)	1	.	1	.	1	.
Atorvastatin	309 (15.90)	0.95 [0.83-1.08]	0.4297	0.85 [0.74-0.97]	0.0141	0.85 [0.74-0.97]	0.0191
Fluvastatin	21 (22.83)	1.44 [0.93-2.22]	0.0998	1.23 [0.80-1.90]	0.3445	1.33 [0.86-2.08]	0.2017
Pravastatin	113 (15.48)	0.93 [0.76-1.13]	0.4650	0.81 [0.67-0.99]	0.0402	0.84 [0.68-1.03]	0.0868
Rosuvastatin	121 (15.24)	0.91 [0.75-1.10]	0.3185	0.83 [0.68-1.00]	0.0515	0.88 [0.73-1.07]	0.1981
Simvastatin	126 (15.52)	0.93 [0.77-1.12]	0.4214	0.83 [0.69-1.00]	0.0553	0.89 [0.73-1.07]	0.2098
Statin intensity							
No exposure	839 (16.70)	1	.	1	.	1	.
Low	133 (17.10)	1.03 [0.86-1.24]	0.7353	0.91 [0.76-1.10]	0.3452	0.96 [0.80-1.16]	0.6716
Moderate	494 (15.29)	0.91 [0.82-1.02]	0.1034	0.82 [0.73-0.92]	0.0007	0.85 [0.76-0.95]	0.0050
High	63 (17.36)	1.04 [0.81-1.34]	0.7635	0.87 [0.67-1.13]	0.3038	0.85 [0.64-1.14]	0.2830
Statin intensity and its type							
No exposure	839 (16.70)	1	.	1	.	1	.
Fluvastatin 20/40	13 (22.41)	1.42 [0.82-2.45]	0.2102	1.27 [0.73-2.19]	0.3974	1.44 [0.84-2.45]	0.1813
Pravastatin 10/20	87 (16.20)	0.97 [0.78-1.21]	0.8087	0.86 [0.68-1.07]	0.1674	0.88 [0.70-1.10]	0.2616
Simvastatin 10	33 (18.03)	1.09 [0.77-1.54]	0.6311	0.99 [0.70-1.40]	0.9481	1.06 [0.75-1.51]	0.7270
Atorvastatin 10/20	255 (15.57)	0.93 [0.81-1.07]	0.2969	0.84 [0.73-0.97]	0.0151	0.85 [0.74-0.98]	0.0286
Fluvastatin 80	8 (23.53)	1.47 [0.73-2.95]	0.2775	1.18 [0.59-2.38]	0.6418	1.15 [0.53-2.53]	0.7223
Pravastatin 40	26 (13.47)	0.81 [0.55-1.19]	0.2842	0.70 [0.47-1.03]	0.0699	0.72 [0.47-1.09]	0.1162
Rosuvastatin 5/10	112 (15.20)	0.91 [0.74-1.10]	0.3240	0.83 [0.68-1.01]	0.0626	0.88 [0.72-1.07]	0.2051
Simvastatin 20/40	93 (14.79)	0.88 [0.71-1.09]	0.2396	0.79 [0.63-0.98]	0.0293	0.84 [0.67-1.04]	0.1054
Atorvastatin 40/80	54 (17.65)	1.06 [0.81-1.40]	0.6765	0.89 [0.67-1.17]	0.3935	0.84 [0.62-1.16]	0.2907
Rosuvastatin 20	9 (15.79)	0.93 [0.48-1.80]	0.8366	0.80 [0.41-1.55]	0.5091	0.91 [0.46-1.78]	0.7755

HR for hazard ratio; 95% CI for 95% confidence interval; IPTW for inverse probability of treatment weighting.

^{*}There is a lower number of 119 individuals (44 in statin group and 75 in unexposed group) compared with the total number of deaths reported in Table 3 (n=1648). These individuals were not included in the present table as they died of COVID-19 but were hospitalized for other reasons than COVID-19.

[†]Cox proportional hazards model.

[‡]Cox proportional hazards model adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, low-dose aspirin, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic), and influenza vaccination.

[§]Cox proportional hazards model with IPTW and further adjustment with the same variables as those in the full adjusted model.

^{||}The strength of the association between statins and in-hospital death for COVID-19 was less strong than that of Table 3. This may be due to the difference in the used designs: conventional Cox proportional hazards model in this table vs conditional Cox proportional hazards model on Table 3. The latter model could not be used here as the number of paired statin users and their matched controls was small (n=17) in this sub-sample of hospitalized individuals for COVID-19.

Table S12. Impact of history of influenza vaccination on the association between statin exposure and severe COVID-19 outcomes

a. Description of influenza vaccination according to statin exposure

	No exposure (n = 2,058,249)	Statin exposure (n = 2,058,249)	Standardized difference
Influenza vaccination since November 15, 2017*			
No	1,235,041 (60.0)	1,058,253 (51.4)	0.17357
Yes	823,208 (40.0)	999,996 (48.6)	

*Variable defined from ATC codes J07BB (at least one dispensing since November 15, 2017).

b. Association between statin exposure and hospitalization for COVID-19 in a fully adjusted conditional Cox proportional hazards model with further adjustment for history of influenza vaccination

	Hospitalization N = 9396	Unadjusted model*		Fully adjusted model†		IPTW further adjusted model‡	
		HR [95% CI]	P-value	HR [95% CI]	P-value	HR [95% CI]	P-value
Statin exposure No	5,024 (0.24)	1	.	1	.	1	.
Yes	4,372 (0.21)	0.87 [0.83-0.90]	<.0001	0.84 [0.80-0.87]	<.0001	0.83 [0.79-0.87]	<.0001

HR for hazard ratio; 95% CI for 95% confidence interval; IPTW for inverse probability of treatment weighting.

*Conditional Cox proportional hazards model.

†Conditional Cox proportional hazards model adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, low-dose aspirin, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic), and influenza vaccination.

‡Conditional Cox proportional hazards model with IPTW and further adjustment with the same variables as those in the full adjusted model.

c. Association between statin exposure and in-hospital death for COVID-19 in a fully adjusted conditional Cox proportional hazards model with further adjustment for history of influenza vaccination

	Death N= 1648	Unadjusted model*		Fully adjusted model†		IPTW further adjusted model‡	
		HR [95% CI]	P-value	HR [95% CI]	P-value	HR [95% CI]	P-value
Statin exposure No	914 (0.044)	1	.	1	.	1	.
Yes	734 (0.036)	0.80 [0.73-0.88]	<.0001	0.77 [0.69-0.86]	<.0001	0.76 [0.68-0.85]	<.0001

HR for hazard ratio; 95% CI for 95% confidence interval; IPTW for inverse probability of treatment weighting.

*Conditional Cox proportional hazards model.

†Conditional Cox proportional hazards model adjusted for the following covariates: social deprivation index, smoking-, alcohol-, and obesity-related conditions, liver failure, and concomitant medications (non-steroidal anti-inflammatory, low-dose aspirin, antiplatelet agent, heparin, anticoagulant, oral corticosteroid, anxiolytic, hypnotic, antidepressant, antipsychotic), and influenza vaccination.

‡Conditional Cox proportional hazards model with IPTW and further adjustment with the same variables as those in the full adjusted model.

Figure S1. Standardized differences before and after inverse probability of treatment weighting (IPTW)

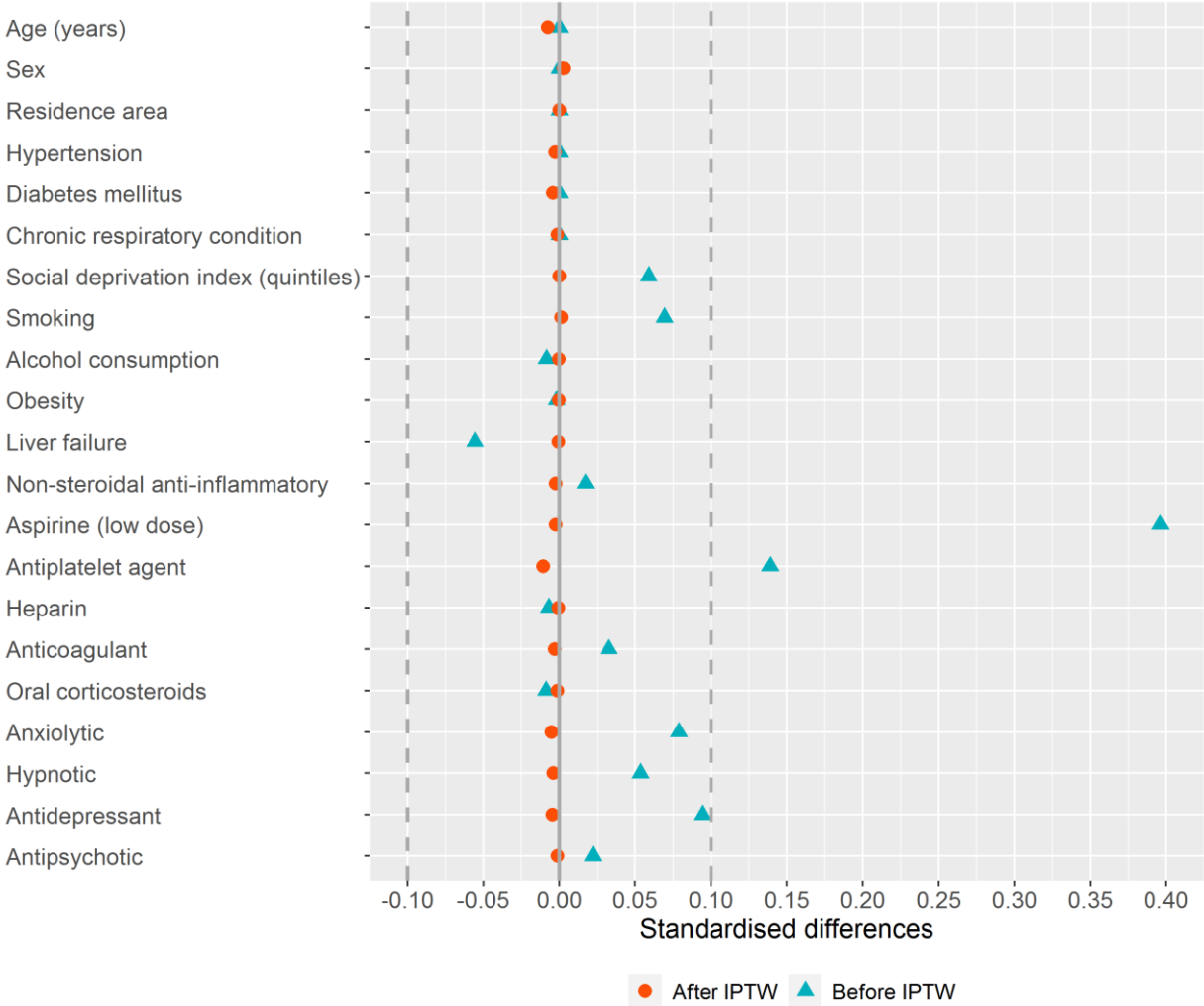
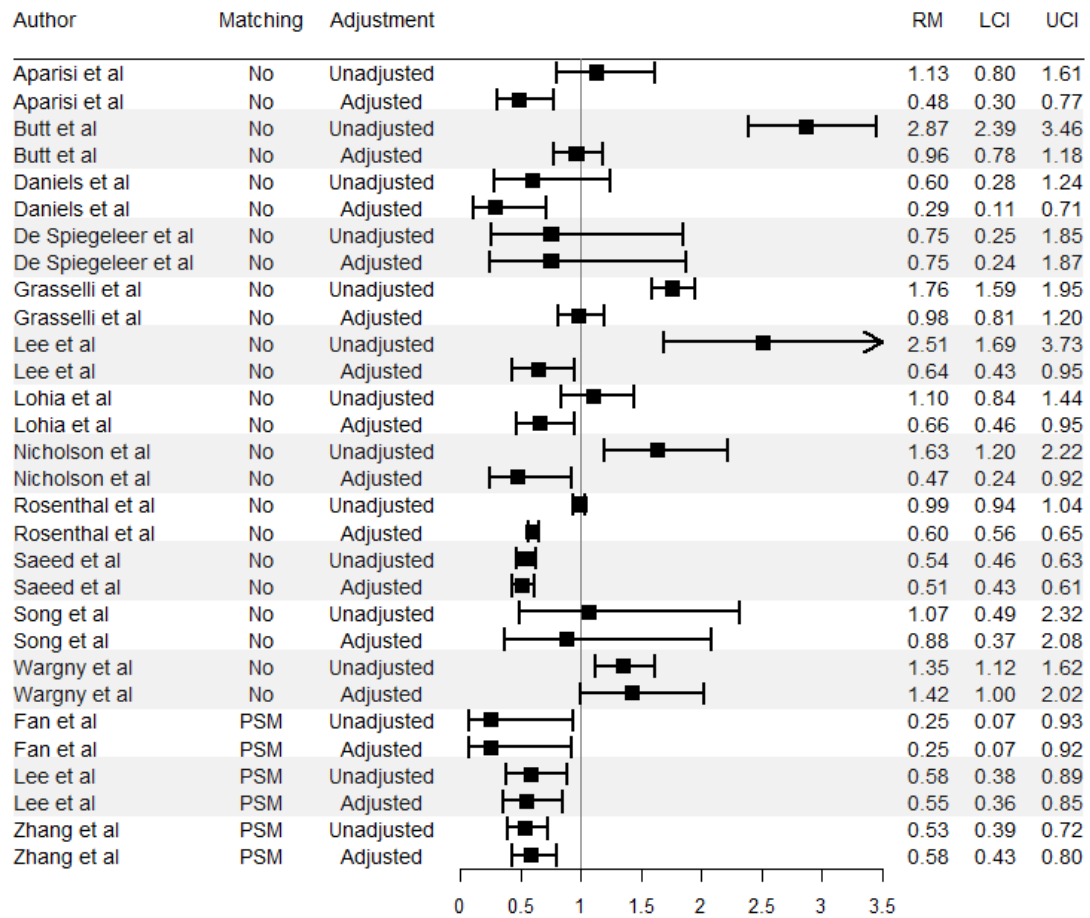


Figure S2. Association between statin exposure and in-hospital deaths from COVID-19: results from literature review



RM for ratio measures referring to effect measures such as odds ratio and hazard ratio; LCI for 95% lower limit of the confidence interval; UCI for 95% upper limit of the confidence interval; PSM for propensity score matching.