## Supplementary

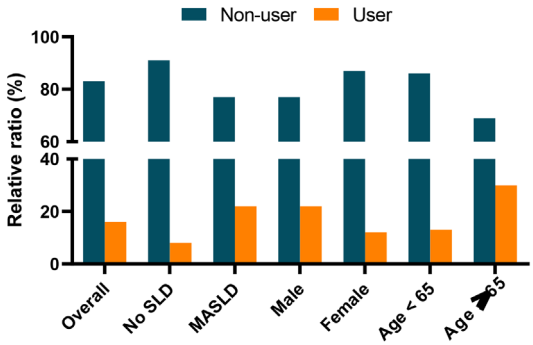


**Figure S1** Distribution of participants of statin users and non-users in each study cohort. Distribution of statin non-users and users in the entire cohort, No SLD cohort, MASLD cohort, male cohort, female cohort, age <65 cohort, and age ≥65 cohort. Data are presented as percentages in the cohorts. SLD, steatotic liver disease; MASLD, metabolic dysfunction associated steatotic liver disease.

**Table S1** Relative ratios based on statin use

| Group | Statin | Number of participants | Relative ratio (%) |
|---|---|---|---|
| Overall | Non-user | 335,316 | 83.3 |
| | User | 67,160 | 16.7 |
| No SLD | Non-user | 151,824 | 91.6 |
| | User | 13,994 | 8.4 |
| MASLD | Non-user | 183,492 | 77.5 |
| | User | 53,166 | 22.5 |
| Male | Non-user | 129,174 | 77.1 |
| | User | 38,313 | 22.9 |
| Female | Non-user | 206,142 | 87.7 |
| | User | 28,847 | 12.3 |
| Age <65 | Non-user | 283,956 | 86.4 |
| | User | 44,527 | 13.6 |
| Age ≥65 | Non-user | 51,360 | 69.4 |
| | User | 22,633 | 30.6 |

SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease.


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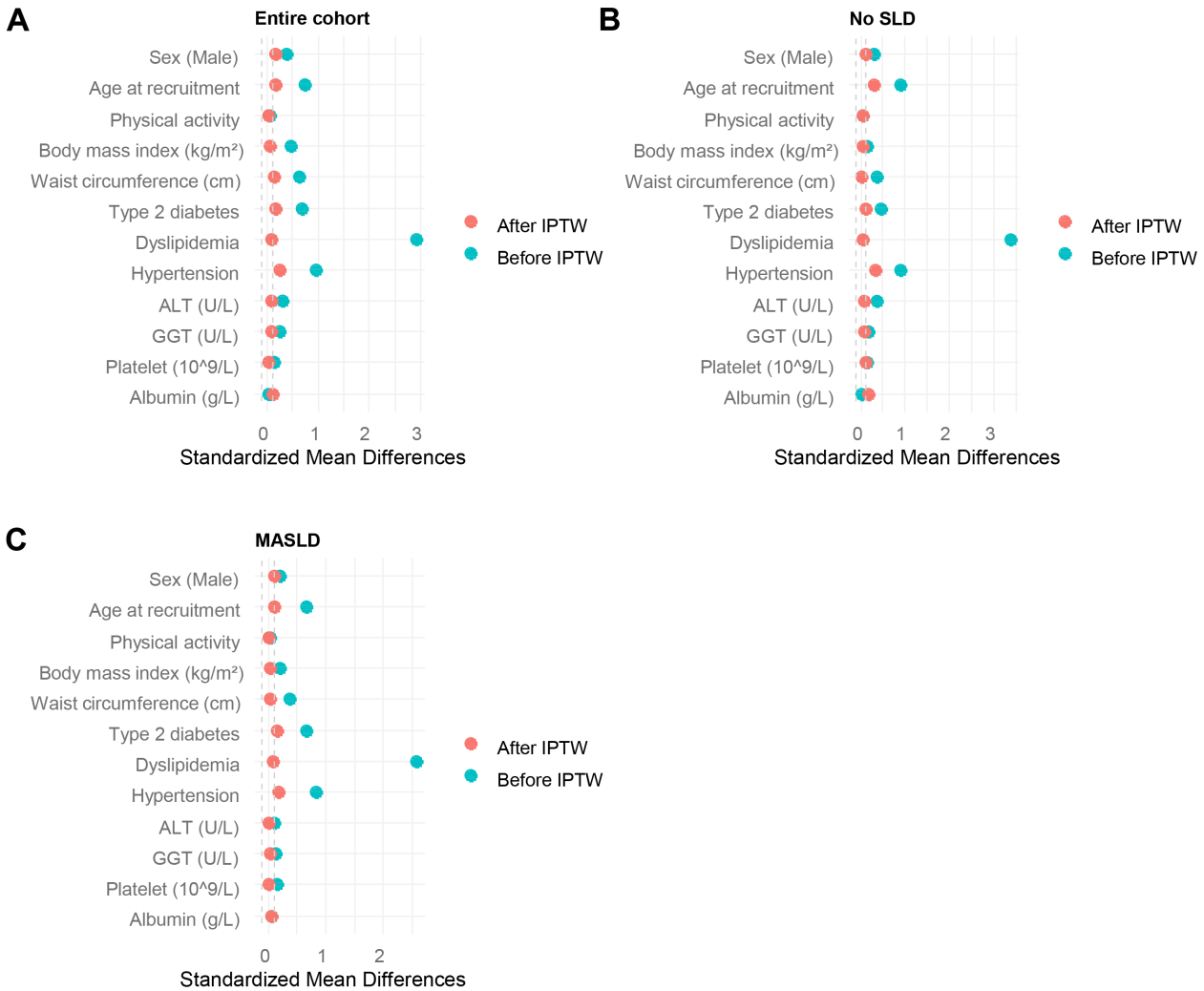


**Figure S2** SMD reduction after IPTW in the entire cohort, No SLD cohort and MASLD cohort. (A) Entire cohort. (B) No SLD cohort. (C) MASLD. IPTW, inverse probability of treatment weighting; SMD, standardized mean difference; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease.


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**Table S2** Baseline clinical characteristics of the entire cohort before and after IPTW

| Clinical characteristics | Before IPTW | | | After IPTW | | |
|---|---|---|---|---|---|---|
| | Statin | | SMD | Statin | | SMD |
| | Non-user, N=335,316 | User, N=67,160 | | Non-user, N=369,626 | User, N=63,802 | |
| Sex (Male) | 135,033 (40.3%) | 40,163 (59.8%) | 0.377 | 165,040 (43.2%) | 133,254 (41.8%) | 0.161 |
| Age at recruitment | 55.32±8.14 | 60.76±6.38 | 0.749 | 56.50±8.04 | 56.27±8.18 | 0.175 |
| Physical activity | | | 0.053 | | | 0.033 |
| More than 4 times | 274,975 (82.0%) | 53,962 (80.3%) | | 303,898 (79.5%) | 253,896 (79.7%) | |
| Under 4 times | 60,341 (18.0%) | 13,198 (19.7%) | | 78,454 (20.5%) | 64,655 (20.3%) | |
| Body mass index (kg/m$^2$) | 26.89±4.74 | 29.19±5.14 | 0.467 | 27.34±4.93 | 27.29±4.95 | 0.062 |
| Waist circumference (cm) | 88.01±13.16 | 96.36±13.68 | 0.624 | 89.61±13.72 | 89.33±13.74 | 0.123 |
| Type 2 diabetes | 21,146 (6.3%) | 21,601 (32.2%) | 0.683 | 44,870 (11.7%) | 34,496 (10.8%) | 0.159 |
| Dyslipidemia | 46,864 (14.0%) | 66,362 (98.8%) | 2.931 | 108,260 (28.3%) | 87,914 (27.6%) | 0.094 |
| Hypertension | 112,765 (33.6%) | 52,511 (78.2%) | 0.957 | 161,769 (42.3%) | 128,097 (40.2%) | 0.254 |
| ALT (U/L) | 22.29±13.47 | 26.36±14.17 | 0.301 | 23.07±13.98 | 22.91±14.26 | 0.072 |
| GGT (U/L) | 33.28±36.81 | 43.00±44.38 | 0.253 | 34.55±35.83 | 34.07±35.39 | 0.079 |
| Platelet ($10^9$/L) | 255.43±59.17 | 246.52±60.11 | 0.148 | 254.42±59.50 | 254.25±59.13 | 0.017 |
| Albumin (g/L) | 4.52±0.25 | 4.53±0.26 | 0.030 | 4.51±0.25 | 4.52±0.25 | 0.101 |

Data are described as mean ± standard deviation or n (%). IPTW, inverse probability of treatment weighting; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; SMD, standardized mean difference.


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**Table S3** Baseline clinical characteristics of the No SLD and MASLD cohort before IPTW

| Clinical characteristics | No SLD | | | MASLD | | |
|---|---|---|---|---|---|---|
| | Statin | | SMD | Statin | | SMD |
| | Non-user, N=151,824 | User, N=13,994 | | Non-user, N=183,492 | User, N=53,166 | |
| Sex (Male) | 32,950 (21.7%) | 4,964 (35.5%) | 0.308 | 96,224 (52.4%) | 33,349 (62.7%) | 0.209 |
| Age at recruitment | 54.58±8.18 | 61.17±6.22 | 0.906 | 55.94±8.09 | 60.72±6.42 | 0.654 |
| Physical activity | | | 0.039 | | | 0.037 |
| More than 4 times | 125,920 (82.9%) | 11,809 (84.4%) | | 142,783 (77.8%) | 40,548 (76.3%) | |
| Under 4 times | 25,904 (17.1%) | 2,185 (15.6%) | | 40,709 (22.2%) | 12,618 (23.7%) | |
| Body mass index (kg/m$^2$) | 23.50±2.36 | 23.85±2.20 | 0.153 | 29.66±4.43 | 30.60±4.80 | 0.203 |
| Waist circumference (cm) | 77.39±7.06 | 79.98±7.17 | 0.363 | 96.48±10.51 | 100.51±11.71 | 0.363 |
| Type 2 diabetes | 2,843 (1.9%) | 1,987 (14.2%) | 0.466 | 17,824 (9.7%) | 19,111 (35.9%) | 0.658 |
| Dyslipidemia | 12,533 (8.3%) | 13,201 (94.3%) | 3.387 | 33,123 (18.1%) | 51,171 (96.2%) | 2.578 |
| Hypertension | 32,440 (21.4%) | 8,620 (61.6%) | 0.895 | 77,261 (42.1%) | 42,237 (79.4%) | 0.828 |
| ALT (U/L) | 17.20±7.55 | 20.22±8.74 | 0.369 | 26.13±15.16 | 27.73±14.72 | 0.107 |
| GGT (U/L) | 21.41±13.05 | 23.75±13.42 | 0.177 | 41.40±41.31 | 46.59±44.62 | 0.121 |
| Platelet (10$^9$/L) | 254.81±57.83 | 247.04±59.75 | 0.132 | 256.53±60.14 | 246.88±60.32 | 0.160 |
| Albumin (g/L) | 4.53±0.25 | 4.53±0.26 | 0.021 | 4.51±0.25 | 4.52±0.26 | 0.059 |

Data are described as mean ± standard deviation or n (%). IPTW, inverse probability of treatment weighting; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; SMD, standardized mean difference.

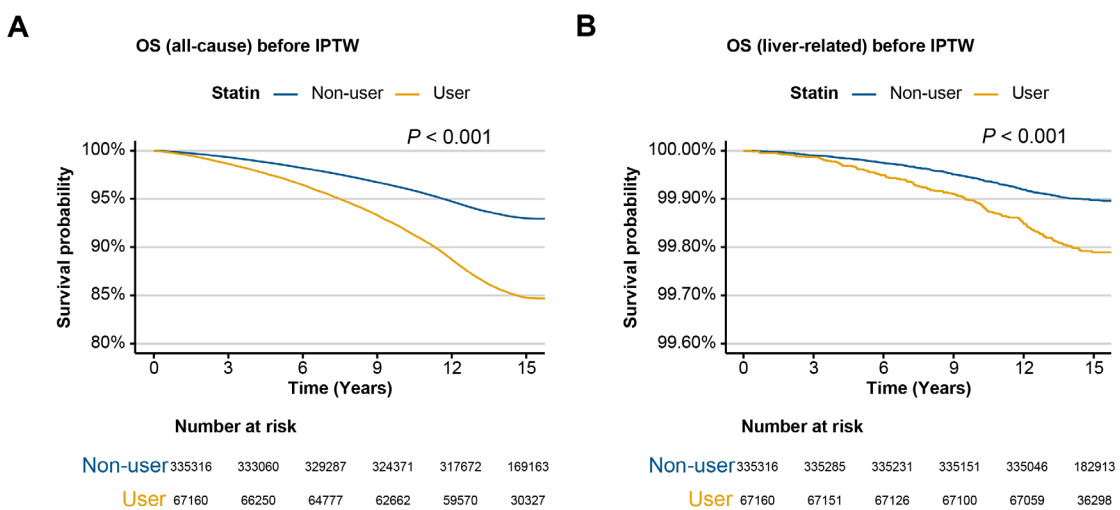


**Figure S3** Kaplan-Meier survival curves of statin users and non-users for all-cause and liver-related mortality in the entire cohort before IPTW. (A) All-cause mortality. (B) Liver-related mortality. OS, overall survival; IPTW, inverse probability of treatment weighting.


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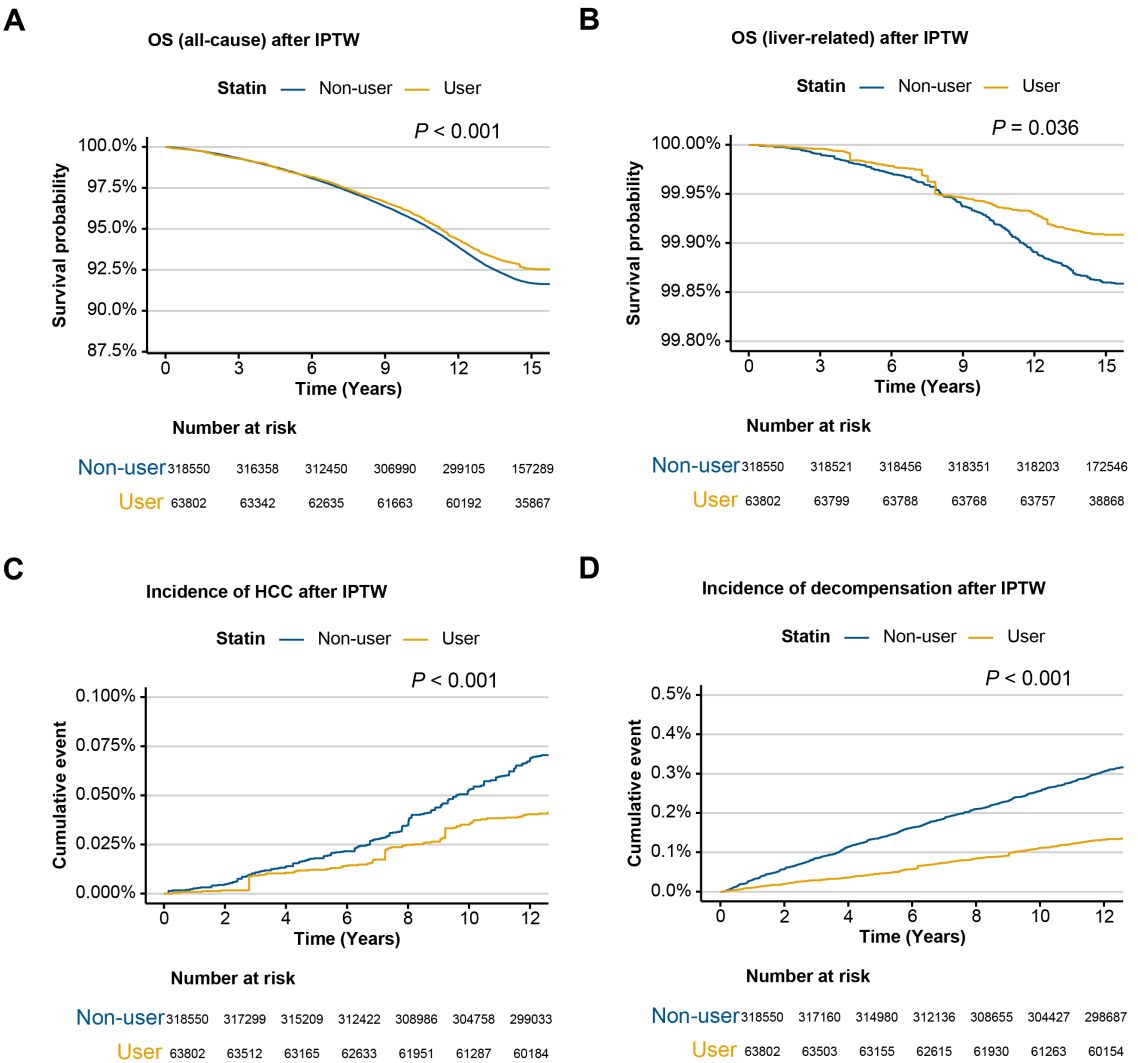


**Figure S4** Analysis of statin users and non-users for all-cause mortality, liver-related mortality, incidence of HCC, and decompensation in the entire cohort after IPTW. (A) All-cause mortality (B) Liver-related mortality (C) Incidence of HCC after IPTW. (D) Incidence of hepatic decompensation. OS, overall survival; IPTW, inverse probability of treatment weighting; HCC, hepatocellular carcinoma.


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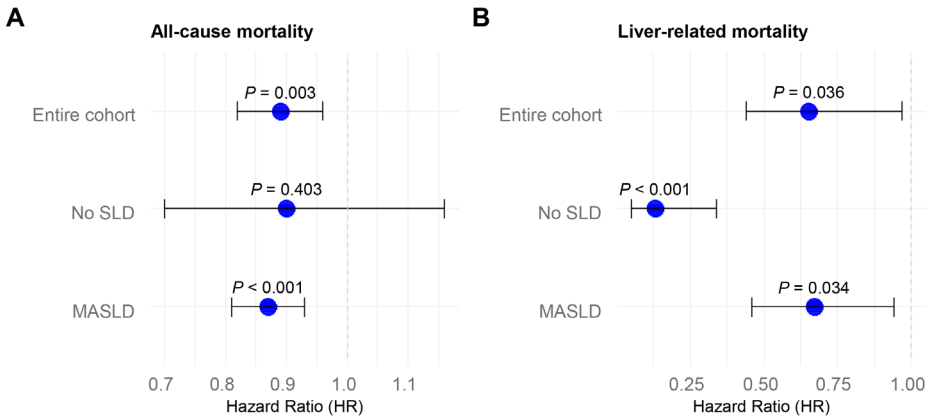


**Figure S5** Forest plots for HRs and 95% CIs for all-cause mortality and liver-related mortality of statin users in each cohort. (A) All-cause mortality. (B) Liver-related mortality. SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; HR, hazard ratio; CI, confidence interval.

**Table S4** Risk of hepatocellular carcinoma according to statin use

| Statin | Entire cohort | | | | |
|---|---|---|---|---|---|
| | Number of patients | Number of events | Number of events/100 patient-years | HR (95% CI) | P value |
| Non-user | 335,316 | 174 | 0.004 | Reference | |
| User | 67,160 | 81 | 0.009 | 0.60 (0.37, 0.96) | 0.033 |
| Statin | No SLD | | | | |
| | Number of patients | Number of events | Number of events/100 patient-years | HR (95% CI) | P value |
| Non-user | 151,824 | 30 | 0.001 | Reference | |
| User | 13,994 | 3 | 0.001 | 0.25 (0.07, 0.81) | 0.021 |
| Statin | MASLD | | | | |
| | Number of patients | Number of events | Number of events / 100 patient-years | HR (95% CI) | P value |
| Non-user | 183,492 | 144 | 0.005 | Reference | |
| User | 53,166 | 78 | 0.010 | 0.57 (0.35, 0.93) | 0.026 |

HR, hazard ratio; CI, confidence interval; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease.


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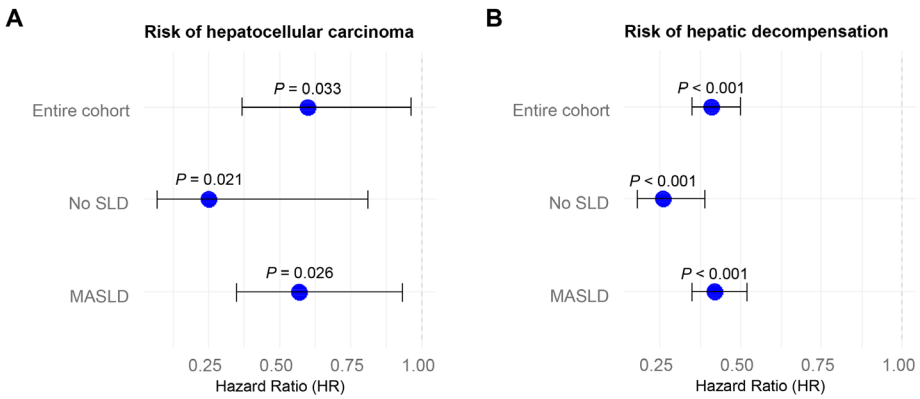


**Figure S6** HRs and 95% CIs for the incidence of hepatocellular carcinoma and hepatic decompensation, of statin users in each cohort. (A) Incidence of hepatocellular carcinoma. (B) Incidence of hepatic decompensation. SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; HR, hazard ratio; CI, confidence interval.

**Table S5** Effect of statin on incidence of liver cirrhosis after IPTW

| Cohort | Incidence of liver cirrhosis | | | |
|---|---|---|---|---|
| | Univariate | | Multivariate | |
| | HR (CI 95%) | P value | HR (CI 95%) | P value |
| Entire cohort | 0.96 (0.64, 1.45) | 0.789 | - | - |
| No SLD | 0.22 (0.15, 0.33) | <0.001 | 0.18 (0.12, 0.28) | <0.001 |
| MASLD | 0.94 (0.65, 1.36) | 0.802 | - | - |

IPTW, inverse probability of treatment weighting; HR, hazard ratio; CI, confidence interval; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease.


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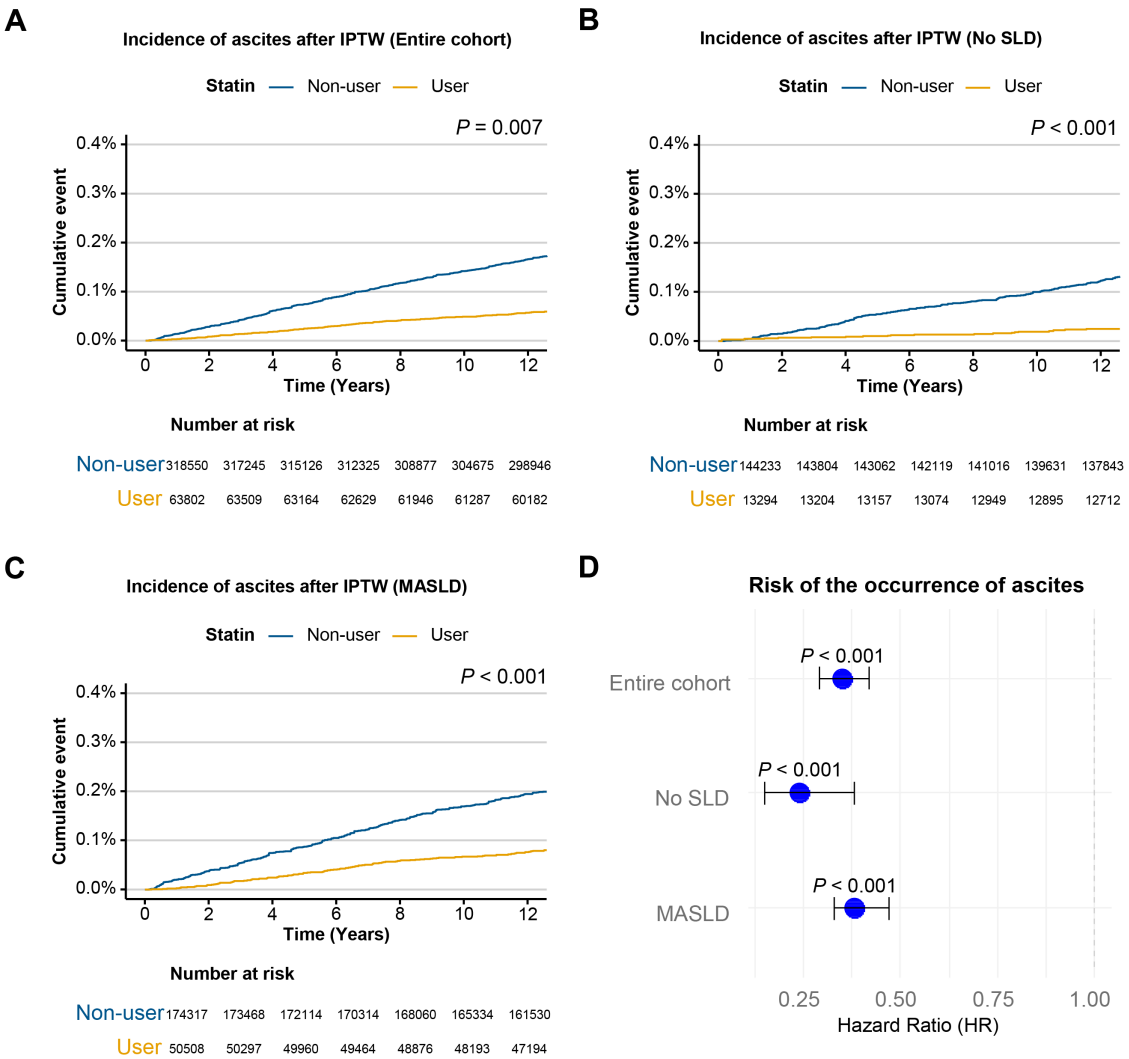


**Figure S7** Analysis of statin users and non-users for the incidence of ascites in each cohort after IPTW. (A) Entire cohort. (B) No SLD cohort. (C) MASLD cohort (D) HRs and 95% CIs for the occurrence of ascites, of statin users. IPTW, inverse probability of treatment weighting; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; HR, hazard ratio; CI, confidence interval.


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**Table S6** Risk of hepatic decompensation according to statin use

| Statin | Entire cohort | | | | |
|---|---|---|---|---|---|
| | Number of patients | Number of events | Number of events/ 100 patient-years | HR (95% CI) | P value |
| Non-user | 335,316 | 958 | 0.020 | Reference | |
| User | 67,160 | 304 | 0.032 | 0.41 (0.35, 0.5) | <0.001 |
| Statin | | | No SLD | | |
| | Number of patients | Number of events | Number of events / 100 patient-years | HR (95% CI) | P value |
| Non-user | 151,824 | 283 | 0.013 | Reference | |
| User | 13,994 | 33 | 0.016 | 0.26 (0.18, 0.39) | <0.001 |
| Statin | | | MASLD | | |
| | Number of patients | Number of events | Number of events / 100 patient-years | HR (95% CI) | P value |
| Non-user | 183,492 | 675 | 0.025 | Reference | |
| User | 53,166 | 271 | 0.036 | 0.42 (0.35, 0.52) | <0.001 |

HR, hazard ratio; CI, confidence interval; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease.

**Table S7** Risk of the occurrence of ascites according to statin use

| Statin | Entire cohort | | | | |
|---|---|---|---|---|---|
| | Number of patients | Number of events | Number of events/ 100 patient-years | HR (95% CI) | P value |
| Non-user | 335,316 | 561 | 0.011 | Reference | |
| User | 67,160 | 141 | 0.015 | 0.35 (0.29, 0.42) | <0.001 |
| Statin | | | No SLD | | |
| | Number of patients | Number of events | Number of events / 100 patient-years | HR (95% CI) | P value |
| Non-user | 151,824 | 210 | 0.009 | Reference | |
| User | 13,994 | 21 | 0.010 | 0.24 (0.15, 0.38) | <0.001 |
| Statin | | | MASLD | | |
| | Number of patients | Number of events | Number of events / 100 patient-years | HR (95% CI) | P value |
| Non-user | 183,492 | 351 | 0.013 | Reference | |
| User | 53,166 | 120 | 0.016 | 0.38 (0.3, 0.47) | <0.001 |

HR, hazard ratio; CI, confidence interval; SLD, steatotic liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease.


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**Table S8** Subgroup analysis according to statin components in MASLD

| Group | All-cause mortality | | Liver-related mortality | |
|---|---|---|---|---|
| | HR (CI 95%) | P value | HR (CI 95%) | P value |
| No statin | Reference | | Reference | |
| Pravastatin | 1.37 (0.90, 2.07) | 0.139 | 0.59 (0.26, 1.36) | 0.202 |
| Simvastatin | 1.22 (1.12, 1.32) | <0.001 | 1.03 (0.65, 1.64) | 0.854 |
| Rosuvastatin | 0.78 (0.62, 0.97) | 0.025 | 0.61 (0.24, 1.58) | 0.285 |
| Atorvastatin | 0.43 (0.37, 0.49) | <0.001 | 0.26 (0.12, 0.54) | <0.001 |
| Group | Hepatocellular carcinoma | | Hepatic decompensation | |
| | HR (CI 95%) | P value | HR (CI 95%) | P value |
| No statin | Reference | | Reference | |
| Pravastatin | 0.86 (0.34, 2.17) | 0.785 | 0.96 (0.58, 1.59) | 0.875 |
| Simvastatin | 0.78 (0.43, 1.40) | 0.354 | 0.66 (0.52, 0.84) | <0.001 |
| Rosuvastatin | 0.18 (0.03, 1.33) | 0.093 | 0.27 (0.11, 0.67) | 0.005 |
| Atorvastatin | 0.48 (0.19, 0.91) | 0.028 | 0.20 (0.15, 0.26) | <0.001 |

HR, hazard ratio; CI, confidence interval; MASLD, metabolic dysfunction-associated steatotic liver disease.


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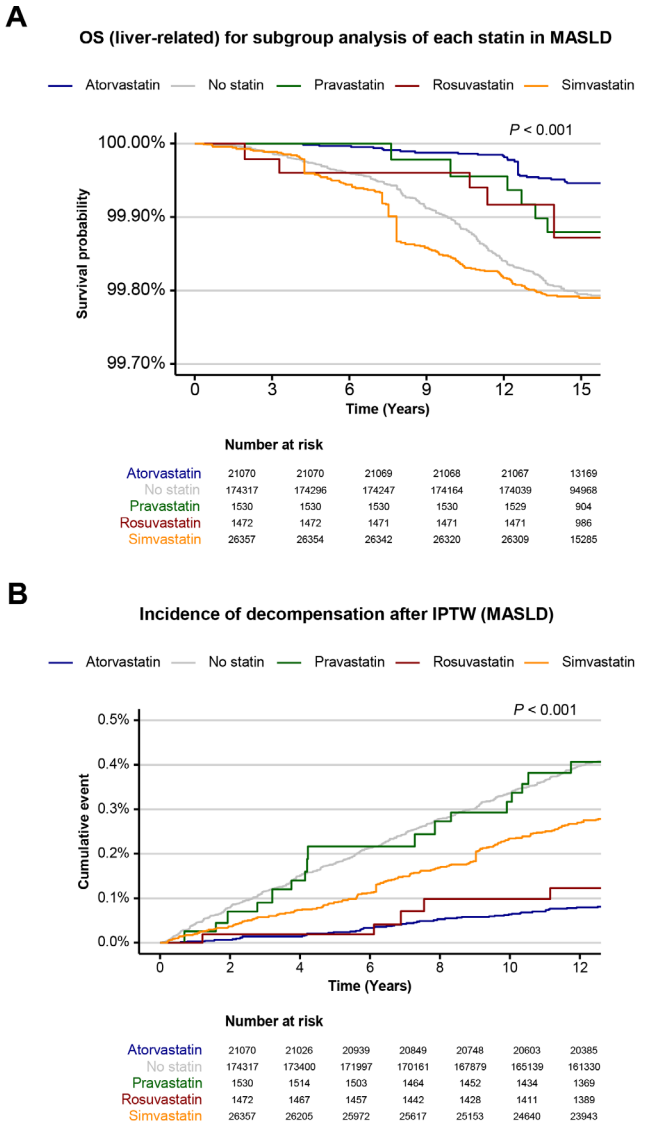


**Figure S8** Investigation of users with each statin for the liver-related mortality and the incidence of hepatic decompensation in the MASLD cohort after IPTW. (A) MASLD cohort. (B) Incidence of hepatic decompensation. OS, overall survival; IPTW, inverse probability of treatment weighting; MASLD, metabolic dysfunction-associated steatotic liver disease.

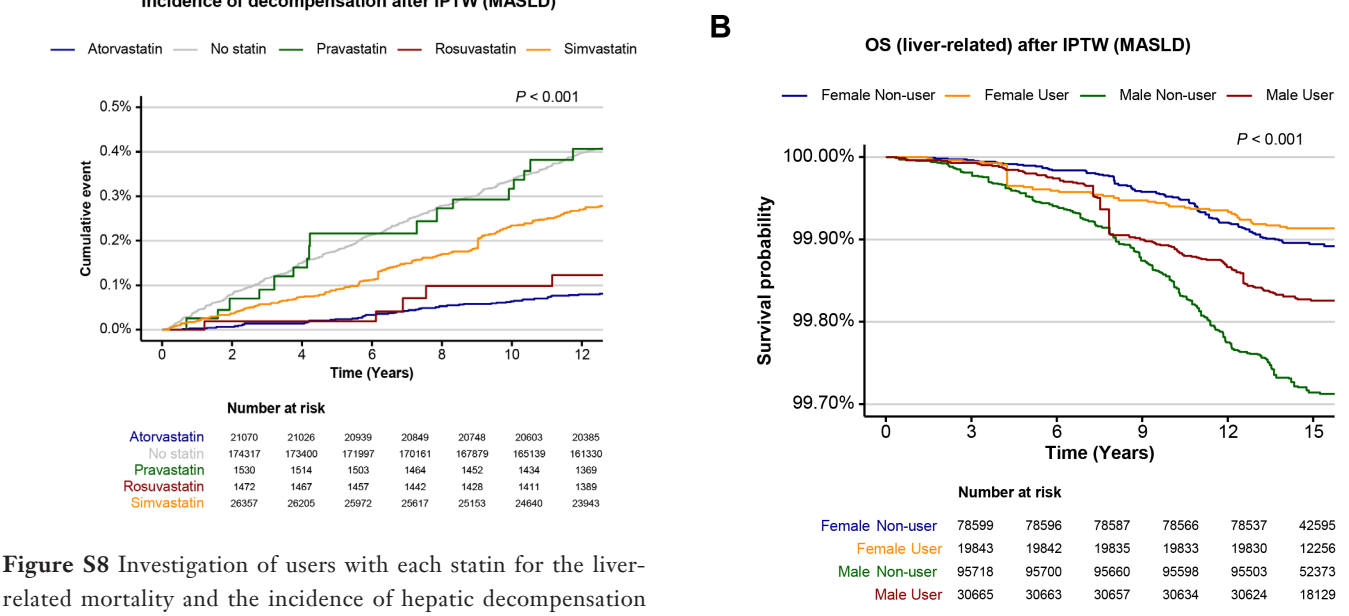


**Figure S9** Kaplan-Meier curves for gender-specific analysis of all-cause and liver-related mortality in the MASLD cohort. (A) Kaplan-Meier curve for all-cause mortality in MASLD, stratified by gender and statin use. (B) Kaplan-Meier curve for liver-related mortality in MASLD, stratified by gender and statin use. OS, overall survival; IPTW, inverse probability of treatment weighting; MASLD, metabolic dysfunction-associated steatotic liver disease.


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**Table S9** Subgroup analysis according to gender and statin use in MASLD

| Group | All-cause mortality | | Liver-related mortality | |
|---|---|---|---|---|
| | HR (CI 95%) | P value | HR (CI 95%) | P value |
| Male / Non-user | Reference | | Reference | |
| Male / User | 0.88 (0.81, 0.96) | 0.003 | 0.61 (0.38, 0.98) | 0.041 |
| Female / Non-user | 0.71 (0.69, 0.74) | <0.001 | 0.38 (0.27, 0.52) | <0.001 |
| Female / User | 0.57 (0.50, 0.65) | <0.001 | 0.31 (0.16, 0.59) | <0.001 |
| Group | Hepatocellular carcinoma | | Hepatic decompensation | |
| | HR (CI 95%) | P value | HR (CI 95%) | P value |
| Male / Non-user | Reference | | Reference | |
| Male / User | 0.50 (0.30, 0.81) | 0.005 | 0.50 (0.38, 0.65) | <0.001 |
| Female / Non-user | 0.26 (0.16, 0.40) | <0.001 | 1.01 (0.84, 1.21) | 0.865 |
| Female / User | 0.26 (0.08, 0.81) | 0.020 | 0.41 (0.32, 0.52) | <0.001 |

HR, hazard ratio; CI, confidence interval; MASLD, metabolic dysfunction-associated steatotic liver disease.


https://dx.doi.org/10.21037/tgh-25-54

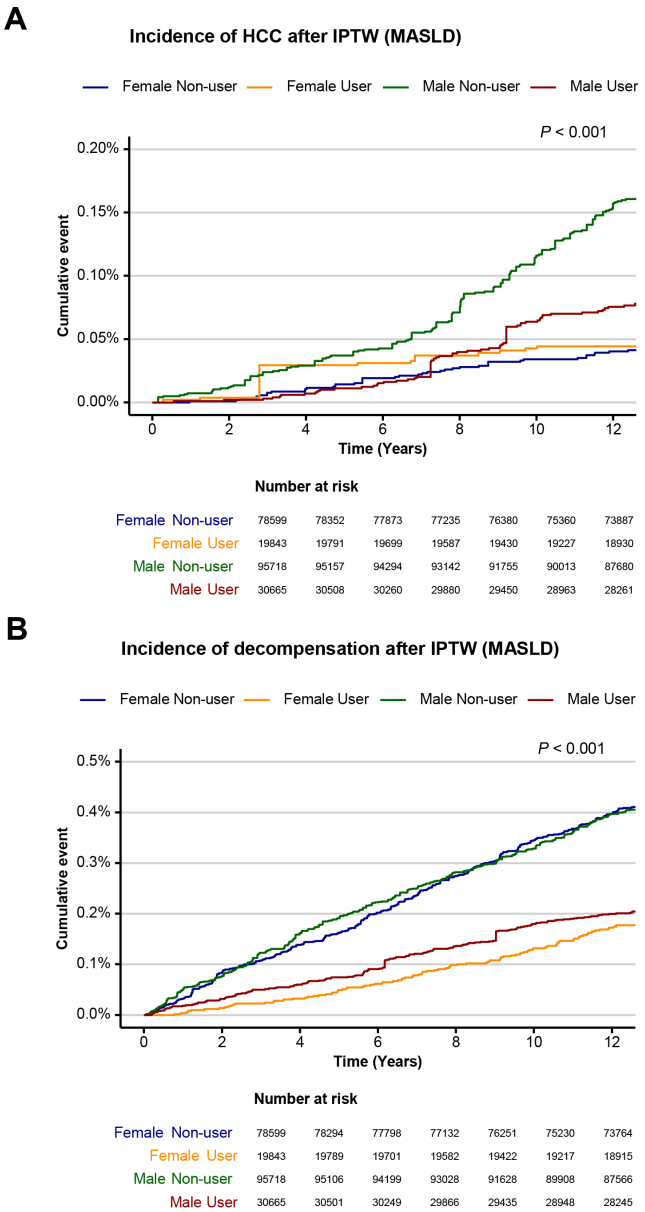


**Figure S10** Gender-specific analysis of HCC and hepatic decompensation incidence in the MASLD cohort. (A) Incidence of HCC (B) Incidence of hepatic decompensation. HCC; hepatocellular carcinoma; IPTW, inverse probability of treatment weighting; MASLD, metabolic dysfunction-associated steatotic liver disease.


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