**Supplementary Material**

**Supplementary Table 1. International Classification of Diseases, versions 9 and 10 (ICD-9-CM, ICD-10-CM) codes used to identify diabetes and long-term outcomes**

|  |  |
| --- | --- |
| **Condition** | **Related diagnosis codes** |
| Diabetes mellitus II | ICD-9-CM 250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, 250.92  ICD-10-CM E11 |
| Hypertension | ICD-9-CM 401 ~ 405;  ICD-10-CM I10, I11.0, I11.9, I12.0, I12.9, I13.10, I13.11, I13.2 |
| Hyperlipidemia | ICD-9-CM 272.0 ~ 272.3;  ICD-10-CM E78 |
| Retinopathy | ICD-9-CM 362.01~ 362.06;  ICD-10-CM E11.3 |
| End Stage Renal Disease | ICD-9-CM: 585.6  ICD-10-CM: N18.6 |
| Acute Coronary Syndrome | ICD-9-CM: 410.XX, 411.XX  ICD-10-CM: I20.0 I21 I22 |
| Ischemic stroke | ICD-9-CM: 433.X1, 434.X1, 436.XX  ICD-10-CM: I63 |

**Supplementary Table 2. Full analysis results: Estimated estimated subdistribution hazard ratios (sHR) and cause specific hazard ratios (csHR) for acute coronary syndrome (ACS), end-stage renal disease (ESRD), ischemic stroke, and retinopathy by antiviral treatment status and outcome for the full sample and subgroup analyses.**

| **subdistribution hazard ratios** | **ACS** | | **ESRD** | | **Ischemic Stroke** | | **Retinopathya** | | **Retinopathyb** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** |
| **Full sample (n=1242)** | |  |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.36 (0.25, 0.54) | <.001 | 0.46 (0.31, 0.67) | <.001 | 0.34 (0.21, 0.56) | <.001 | 0.24(0.17,0.36) | <.001 | 0.61(0.48,0.79) | <.001 |
| TF vs Untreated | 0.59 (0.40, 0.87) | 0.007 | 1.11 (0.80, 1.54) | 0.521 | 0.64 (0.39, 1.03) | 0.068 | 0.37(0.25,0.55) | <.001 | 0.62(0.45,0.84) | 0.002 |
| SVR vs TF | 0.62 (0.38, 1.02) | 0.057 | 0.41 (0.27, 0.63) | <.001 | 0.53 (0.29, 0.98) | 0.044 | 0.66(0.40,1.10) | 0.110 | 1.00(0.71,1.40) | 0.983 |
| **DAA treated sub-cohort vs untreated (n=988)** | | | |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.30 (0.19, 0.48) | <.001 | 0.36 (0.22, 0.58) | <.001 | 0.20 (0.10, 0.38) | <.001 | 0.16(0.08,0.30) | <.001 | 0.47(0.35,0.64) | <.001 |
| TF vs Untreated | 1.08 (0.49, 2.38) | 0.842 | 0.38 (0.09, 1.57) | 0.181 | 0.44 (0.11, 1.77) | 0.248 | 0.12(0.01,1.12) | 0.063 | 0.20(0.06,0.74) | 0.015 |
| SVR vs TF | 0.28 (0.12, 0.66) | 0.004 | 0.94 (0.22, 4.10) | 0.935 | 0.45 (0.10, 2.02) | 0.297 | 1.29(0.13,12.76) | 0.826 | 2.32(0.63,8.54) | 0.206 |
| **IFN-treated subcohort vs untreated (n=733)** | | | |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.32(0.17,0.60) | <.001 | 0.36(0.19,0.66) | <.001 | 0.44(0.21,0.92) | 0.029 | 0.58(0.34,0.97) | 0.037 | 0.84(0.58,1.19) | 0.324 |
| TF vs Untreated | 0.54(0.35,0.82) | 0.005 | 0.97(0.69,1.36) | 0.841 | 0.68(0.41,1.13) | 0.138 | 0.63(0.42,0.94) | 0.025 | 0.68(0.49,0.93) | 0.018 |
| SVR vs TF | 0.60(0.29,1.23) | 0.162 | 0.37(0.19,0.71) | 0.003 | 0.65(0.29,1.49) | 0.313 | 0.92(0.50,1.67) | 0.777 | 1.24(0.80,1.91) | 0.336 |
| **Cirrhotic (n=441)** | |  |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.10 (0.04, 0.27) | <.001 | 0.31 (0.14, 0.67) | 0.003 | 0.26 (0.09, 0.70) | 0.008 | 0.39(0.20,0.76) | 0.006 | 0.54(0.34,0.84) | 0.007 |
| TF vs Untreated | 0.18 (0.05, 0.59) | 0.005 | 0.72 (0.34, 1.53) | 0.392 | 0.54 (0.17, 1.69) | 0.286 | 0.38(0.14,1.01) | 0.052 | 0.39(0.19,0.83) | 0.014 |
| SVR vs TF | 0.56 (0.12, 2.57) | 0.455 | 0.43 (0.17, 1.13) | 0.088 | 0.48 (0.12, 1.87) | 0.288 | 1.02(0.36,2.89) | 0.963 | 1.37(0.63,2.95) | 0.424 |
| **Non-cirrhotic (n=801)** | | |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.54 (0.35, 0.83) | 0.005 | 0.52 (0.34, 0.81) | 0.004 | 0.37 (0.21, 0.67) | <.001 | 0.30(0.18,0.52) | <.001 | 0.63(0.46,0.85) | 0.003 |
| TF vs Untreated | 0.78 (0.51, 1.20) | 0.251 | 1.24 (0.86, 1.79) | 0.243 | 0.65 (0.38, 1.10) | 0.109 | 0.54(0.34,0.85) | 0.007 | 0.68(0.48,0.96) | 0.027 |
| SVR vs TF | 0.70 (0.41, 1.17) | 0.172 | 0.42 (0.26, 0.68) | <.001 | 0.58 (0.29, 1.15) | 0.120 | 0.56(0.30,1.06) | 0.075 | 0.93(0.63,1.38) | 0.711 |
| **Cause specific hazard model** | **csHR (95%CI)** | **p** | **csHR (95%CI)** | **p** | **csHR (95%CI)** | **p** | **csHR (95%CI)** | **p** | **csHR (95%CI)** | **p** |
| **Full sample (n=1242)** | |  |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.30 (0.20,0.45) | <.001 | 0.39 (0.27,0.57) | <.001 | 0.29 (0.18,0.49) | <.001 | 0.20(0.14,0.30) | <.001 | 0.53(0.41,0.69) | <.001 |
| TF vs Untreated | 0.49 (0.33,0.73) | <.001 | 1.02 (0.73,1.42) | 0.917 | 0.57 (0.35,0.94) | 0.03 | 0.31(0.20,0.47) | <.001 | 0.54(0.40,0.75) | <.001 |
| SVR vs TF | 0.61 (0.37,1.01) | 0.05 | 0.38 (0.25,0.59) | <.001 | 0.52 (0.27,0.97) | 0.04 | 0.66(0.39,1.11) | 0.118 | 0.98(0.69,1.39) | 0.916 |
| **DAA treated sub-cohort vs untreated (n=988)** | | | |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.29 (0.18,0.47) | <.001 | 0.35 (0.21,0.57) | <.001 | 0.19 (0.10,0.36) | <.001 | 0.15(0.08,0.29) | <.001 | 0.45(0.33,0.62) | <.001 |
| TF vs Untreated | 1.17 (0.53,2.57) | 0.7 | 0.41 (0.10,1.69) | 0.218 | 0.46 (0.11,1.90) | 0.29 | 0.13(0.01,1.17) | 0.069 | 0.21(0.06,0.74) | 0.016 |
| SVR vs TF | 0.25 (0.11,0.59) | 0 | 0.84 (0.20,3.56) | 0.809 | 0.40 (0.09,1.83) | 0.24 | 1.19(0.12,11.85) | 0.884 | 2.19(0.60,7.97) | 0.235 |
| **IFN-treated subcohort vs untreated (n=733)** | | | |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.24(0.13,0.46) | <.001 | 0.27(0.15,0.50) | <.001 | 0.35(0.17,0.72) | 0.004 | 0.41(0.24,0.70) | <.001 | 0.67(0.47,0.95) | 0.025 |
| TF vs Untreated | 0.44(0.28,0.70) | <.001 | 0.85(0.60,1.22) | 0.390 | 0.59(0.34,1.01) | 0.053 | 0.49(0.31,0.75) | 0.001 | 0.57(0.41,0.80) | 0.001 |
| SVR vs TF | 0.54(0.26,1.14) | 0.105 | 0.32(0.17,0.61) | <.001 | 0.59(0.26,1.36) | 0.217 | 0.85(0.46,1.57) | 0.597 | 1.17(0.76,1.81) | 0.472 |
| **Cirrhotic (n=441)** | |  |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.09 (0.03,0.24) | <.001 | 0.27 (0.13,0.57) | <.001 | 0.21 (0.08,0.59) | 0.003 | 0.31(0.16,0.60) | <.001 | 0.46(0.29,0.72) | <.001 |
| TF vs Untreated | 0.16 (0.05,0.55) | 0.003 | 0.69 (0.32,1.48) | 0.345 | 0.49 (0.15,1.57) | 0.231 | 0.33(0.12,0.90) | 0.030 | 0.35(0.16,0.75) | 0.007 |
| SVR vs TF | 0.53 (0.11,2.47) | 0.417 | 0.39 (0.15,1.01) | 0.052 | 0.44 (0.11,1.78) | 0.248 | 0.95(0.32,2.80) | 0.919 | 1.31(0.60,2.89) | 0.501 |
| **Non-cirrhotic (n=801)** | | | |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.45 (0.29,0.70) | <.001 | 0.43 (0.28,0.67) | <.001 | 0.33 (0.18,0.58) | <.001 | 0.24(0.14,0.41) | <.001 | 0.55(0.40,0.75) | <.001 |
| TF vs Untreated | 0.66 (0.43,1.02) | 0.064 | 1.14 (0.78,1.66) | 0.495 | 0.59 (0.34,1.02) | 0.060 | 0.44(0.27,0.71) | <.001 | 0.60(0.42,0.86) | 0.005 |
| SVR vs TF | 0.68 (0.40,1.16) | 0.157 | 0.38 (0.23,0.62) | <.001 | 0.56 (0.27,1.13) | 0.105 | 0.54(0.28,1.03) | 0.062 | 0.91(0.61,1.35) | 0.633 |

*SVR: sustained virological response; TF: treatment failure;*

a*: retinopathy cases within 1 year post index were excluded* b*: retinopathy cases within 1 year post index were included.*

**Supplementary Table 3: Estimated cause specific hazard ratios (csHR) and subdistribution hazard ratios (sHR) for acute coronary syndrome (ACS), end-stage renal disease (ESRD), ischemic stroke, and retinopathy among the full sample and the sub group analyses, when SVR and TF/OF treatment status was treated as time-varying. Analyses included adjustment for inverse probability of treatment weighting and death as a competing risk.**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ACS** | | **ESRD** | | **Ischemic Stroke** | | **Retinopathya** | | **Retinopathyb** |  |
| **subdistribution hazard ratios** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** |
| **Full sample(n=1242)** |  |  |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.47 (0.30,0.74) | 0.001 | 0.57 (0.38,0.85) | 0.005 | 0.36 (0.27,0.49) | 0.001 | 0.49(0.32,0.74) | <.001 | 0.48 (0.33,0.68) | <.001 |
| TF/OT vs Untreated | 0.43 (0.29,0.62) | <.001 | 0.80 (0.57,1.12) | 0.195 | 0.39 (0.27,0.56) | 0.002 | 0.36(0.23,0.56) | <.001 | 0.67 (0.53,0.86) | 0.002 |
| SVR vs TF/OT | 1.11 (0.64,1.93) | 0.701 | 0.71 (0.45,1.12) | 0.141 | 0.93 (0.61,1.42) | 0.698 | 1.37(0.77,2.42) | 0.285 | 0.71 (0.48,1.05) | 0.086 |
| **DAA treated sub-cohort vs untreated (n=988)** | | |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.42 (0.23,0.75) | 0.003 | 0.54 (0.32,0.91) | 0.02 | 0.28 (0.19,0.40) | <.001 | 0.32(0.17,0.63) | <.001 | 0.38 (0.24,0.61) | <.001 |
| TF/OT vs Untreated | 0.31 (0.17,0.57) | <.001 | 0.17 (0.07,0.41) | <.001 | 0.07 (0.01,0.61) | 0.002 | 0.02(0.00,0.18) | <.001 | 0.49 (0.34,0.71) | <.001 |
| SVR vs TF/OT | 1.35 (0.58,3.18) | 0.487 | 3.12 (1.17,8.27) | 0.022 | 4.16 (0.44,38.87) | 0.857 | 17.60(1.59,194) | 0.019 | 0.77 (0.43,1.37) | 0.376 |
| **IFN-treated subcohort vs untreated (n=733)** | | |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.40(0.21,0.78) | 0.007 | 0.36(0.18,0.73) | 0.005 | 0.53(0.23,1.21) | 0.131 | 0.74(0.43,1.30) | 0.295 | 0.72(0.42,1.22) | 0.220 |
| TF vs Untreated | 0.46(0.30,0.70) | <.001 | 0.85(0.60,1.19) | 0.341 | 0.59(0.36,0.97) | 0.038 | 0.54(0.36,0.82) | 0.003 | 0.74(0.56,0.98) | 0.037 |
| SVR vs TF | 0.89(0.41,1.91) | 0.762 | 0.43(0.20,0.91) | 0.026 | 0.90(0.37,2.21) | 0.821 | 1.37(0.71,2.64) | 0.344 | 0.97(0.55,1.70) | 0.913 |
| **Cause specific hazard model** | **csHR (95%CI)** | **p** | **csHR (95%CI)** | **p** | **CsHR (95%CI)** | **p** | **csHR (95%CI)** | **p** | **csHR (95%CI)** | **p** |
| **Full sample (n=1242)** |  |  |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.37 (0.23,0.58) | <.001 | 0.46 (0.31,0.69) | <.001 | 0.31 (0.23,0.42) | <.001 | 0.38(0.24,0.58) | <.001 | 0.39 (0.27,0.57) | <.001 |
| TF/OT vs Untreated | 0.37 (0.26,0.54) | <.001 | 0.75 (0.54,1.04) | 0.08 | 0.34 (0.23,0.49) | <.001 | 0.31(0.20,0.47) | <.001 | 0.62 (0.48,0.79) | <.001 |
| SVR vs TF/OT | 0.98 (0.57,1.67) | 0.939 | 0.62 (0.39,0.98) | 0.042 | 0.92 (0.59,1.43) | 0.513 | 1.23(0.71,2.12) | 0.463 | 0.64 (0.43,0.95) | 0.028 |
| **DAA treated sub-cohort vs untreated (n=988)** | | |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.41 (0.23,0.72) | 0.002 | 0.53 (0.30,0.93) | 0.028 | 0.26 (0.18,0.39) | <.001 | 0.36(0.22,0.58) | <.001 | 0.36 (0.22,0.58) | <.001 |
| TF/OT vs Untreated | 0.31 (0.17,0.56) | <.001 | 0.17 (0.07,0.42) | <.001 | 0.07 (0.01,0.63) | 0.001 | 0.49(0.33,0.71) | <.001 | 0.49 (0.33,0.71) | <.001 |
| SVR vs TF/OT | 1.31 (0.58,2.97) | 0.521 | 3.04 (1.08,8.55) | 0.035 | 3.89 (0.41,36.68) | 0.787 | 0.74(0.40,1.34) | 0.317 | 0.74 (0.40,1.34) | 0.317 |
| **IFN-treated subcohort vs untreated (n=733)** | | |  |  |  |  |  |  |  |  |
| SVR vs Untreated | 0.40(0.21,0.78) | 0.007 | 0.36(0.18,0.73) | 0.005 | 0.53(0.23,1.21) | 0.131 | 0.50(0.28,0.87) | 0.014 | 0.51(0.30,0.85) | 0.010 |
| TF vs Untreated | 0.46(0.30,0.70) | <.001 | 0.85(0.60,1.19) | 0.341 | 0.59(0.36,0.97) | 0.038 | 0.43(0.28,0.67) | <.001 | 0.64(0.48,0.86) | 0.003 |
| SVR vs TF | 0.89(0.41,1.91) | 0.762 | 0.43(0.20,0.91) | 0.026 | 0.90(0.37,2.21) | 0.821 | 1.14(0.61,2.16) | 0.677 | 0.79(0.46,1.36) | 0.399 |

*SVR: sustained virological response; TF/OT: treatment failure, ongoing treatment;*

a*:retinopathy cases within 1 year post index were excluded.*

b*: retinopathy cases within 1 year post index were included.*

**Supplementary Table 4: Estimated cause specific hazard ratios (csHR) and subdistribution hazard ratios (sHR) for acute coronary syndrome (ACS), end-stage renal disease (ESRD), ischemic stroke, and retinopathy within subgroups of FIB4≤1.45 and FIB4≥3.25.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ACS** | | **ESRD** | | **Ischemic Stroke** | | **Retinopathya** | |
|  | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** |
| **FIB4≤1.45 subgroup (n=359)** | |  |  |  |  |  |  |  |
| *SVR vs Untreated* | 0.09(0.02,0.34) | <.001 | 0.99(0.60,1.64) | 0.969 | 0.29(0.11,0.80) | 0.017 | 0.17(0.07,0.46) | <.001 |
| *TF vs Untreated* | 0.34(0.15,0.79) | 0.013 | 0.73(0.40,1.34) | 0.306 | 0.76(0.33,1.73) | 0.507 | 0.74(0.40,1.38) | 0.344 |
| *SVR vs TF* | 0.26(0.06,1.17) | 0.078 | 1.36(0.69,2.68) | 0.373 | 0.39(0.12,1.22) | 0.106 | 0.24(0.08,0.69) | 0.008 |
| **FIB4≥3.25 subgroup (n=405)** | |  |  |  |  |  |  |  |
| *SVR vs Untreated* | 0.29(0.14,0.63) | 0.002 | 0.40(0.18,0.86) | 0.019 | 0.23(0.08,0.65) | 0.006 | 0.83(0.40,1.75) | 0.630 |
| *TF vs Untreated* | 0.74(0.37,1.48) | 0.393 | 1.09(0.57,2.08) | 0.797 | 0.57(0.21,1.56) | 0.272 | 0.43(0.14,1.34) | 0.146 |
| *SVR vs TF* | 0.40(0.16,1.02) | 0.055 | 0.36(0.15,0.86) | 0.021 | 0.40(0.10,1.53) | 0.180 | 1.93(0.59,6.28) | 0.275 |

*ACS: acute coronary syndrome; ESRD: end-stage renal disease; SVR: sustained virological response; TF: treatment failure;*

a*: retinopathy cases within 1 year post index were excluded.*

**Supplementary Table 5: Comparison in estimated cause subdistribution hazard ratios (sHR) for acute coronary syndrome (ACS), end-stage renal disease (ESRD), ischemic stroke, and retinopathy between results from the main analysis and an analysis using propensity scores recalculated after excluding cirrhosis status and weighted Charlson-Deyo comorbidity index.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **ACS** | | **ESRD** | | **Ischemic Stroke** | | **Retinopathya** | |
|  | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** | **sHR (95%CI)** | **p** |
| ***Main analysis*** |  |  |  |  |  |  |  |  |
| *SVR vs Untreated* | 0.36 (0.25, 0.54) | <.001 | 0.46 (0.31, 0.67) | <.001 | 0.34 (0.21, 0.56) | <.001 | 0.24(0.17,0.36) | <.001 |
| *TF vs Untreated* | 0.59 (0.40, 0.87) | 0.007 | 1.11 (0.80, 1.54) | 0.521 | 0.64 (0.39, 1.03) | 0.068 | 0.37(0.25,0.55) | <.001 |
| *SVR vs TF* | 0.62 (0.38, 1.02) | 0.057 | 0.41 (0.27, 0.63) | <.001 | 0.53 (0.29, 0.98) | 0.044 | 0.66(0.40,1.10) | 0.110 |
| ***Sensitivity analysis\**** |  |  |  |  |  |  |  |  |
| *SVR vs Untreated* | 0.36 (0.24,0.54) | <.001 | 0.49 (0.33,0.71) | <.001 | 0.32 (0.19,0.53) | <.001 | 0.39(0.26,0.58) | <.001 |
| *TF vs Untreated* | 0.59 (0.39,0.89) | 0.013 | 1.06 (0.75,1.50) | 0.726 | 0.60 (0.36,1.00) | 0.050 | 0.54(0.36,0.83) | 0.004 |
| *SVR vs TF* | 0.61 (0.36,1.03) | 0.064 | 0.46 (0.30,0.71) | <.001 | 0.53 (0.28,1.01) | 0.052 | 0.71(0.43,1.19) | 0.198 |

*ACS: acute coronary syndrome; ESRD: end-stage renal disease; SVR: sustained virological response; TF: treatment failure;*

a*: retinopathy cases within 1 year post index were excluded.*