| **Author year Country**  ***Quality*** | **Type of study** | **Dates of enrollment** | **Treatment duration Followup** | **Inclusion criteria** | **Intervention(s)** | **N** | **Population** | **Outcomes** | **Funding source** |
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| Butt 2019169  U.S.  *Fair* | Retrospective cohort | NR | Treatment duration: NR  Followup ≥5 years  Group A: 3.7%  Group B: 82%  Group C: 43% | Adults with HCV infection included in the ERCHIVES database  Excluded: HBV, HIV coinfection | A. DAA regimen (sofosbuvir + simeprevir, ledipasvir, or daclatasvir +/- ribavirin; paritaprevir + ritonavir + ombitasvir + dasabuvir +/- ribavirin; elbasvir + grazoprevir +/- ribavirin) (n=12,667)  B. Pegylated IFN + ribavirin (n=4,436)  C. Matched, untreated controls (n=17,103) | 34,206 | (A + B) vs. C  Mean age 59 vs. 58 years  4% vs. 4% female  56% vs. 56% white; 24% vs. 24% black; 3% vs. 3% Hispanic; 17% vs. 17% other/unknown  Fibrosis stage: <1.25: 23% vs. 33%; 1.26 to 3.25: 56% vs. 50%; >3.25: 21% vs. 17%  Statin use: 22% vs. 26% | A vs. B vs. C  CVD event (acute MI, unstable, angina, congestive heart failure, peripheral vascular disease, percutaneous transluminalcoronary angioplasty, CABG, stroke): 3.4% (435/12,667) vs. 18.1% (804/4,436) vs. 13.8% (2,361/17,103); A vs. C: aHR 0.57 (95% CI, 0.51 to 0.65); B vs. C: aHR 0.78 (95% CI, 0.71 to 0.85)  Incidence rate/1,000 person-years of followup: 16.3 (95% CI, 14.7 to 18) vs. 23.5 (95% CI, 21.8 to 25.3) vs. 30.4 (95% CI, 29.2 to 31.7); A vs. C: p<0.001; B vs. C: p<0.001 | Gilead |
| Carrat 2019168 France  *Fair* | Prospective cohort | Aug 2012 to Dec 2015 | Treatment duration: NR  Followup: median 33.4 months (IQR 24.0 to 40.7 months) | Patients with chronic HCV infection recruited from 32 hepatology centers in France. Excluded: HBV, HIV coinfection, previous HCC diagnosis, history of decompensated cirrhosis, liver transplant recipient | A. DAA regimen (sofosbuvir + simeprevir +/- ribavirin; sofosbuvir + daclatasvir +/- ribavirin; sofosbuvir + ledipasvir +/- ribavirin; sofosbuvir + ribavirin; sofosbuvir + IFN alpha + ribavirin; sofosbuvir + velpatasvir +/- voxilaprevir; paritaprevir + ritonavir + ombitasvir +/- dasabuvir +/- ribavirin; elbasvir + grazoprevir +/- ribavirin) (n=4,521, *non-cirrhosis only*) B. Untreated patients (n=2,329, *non-cirrhosis only*) | 6,850 | *Total study population, including additional 3,045 patients with cirrhosis* A vs. B Mean age: 57 vs. 54 Female: 44% vs. 54% Race NR Fibrosis stage: F0, F1, or F2: 41% vs. 84% F3: 17% vs. 6% F4: 42% vs. 10% Genotype: GT1: 67% vs. 64%; GT2: 6% vs. 10%; GT3: 13% vs. 9%; GT4: 13% vs. 14%; GT5-7: 2% vs. 3% | A vs. B (noncirrhotics only) All-cause mortality: 0.8% (35/4,521) vs. 2.1% (48/2,329); aHR: 0.74 (95% CI, 0.43 to 1.28) Liver-related mortality: 0.1% (6/4,521) vs. 0.3% (6/2,329); unadjusted HR: 1.33 (95% CI, 0.46 to 3.84) HCC: 0.5% (21/4,521) vs. 0.6% (14/2,329); AHR: 1.02 (95% CI, 0.40 to 2.61) Decompensated cirrhosis: 0.2% (7/4,521) vs. 0.2% (4/2,329); unadjusted HR: 3.59 (95% CI, 0.66 to 19.5) | French National Agency for Aids and Viral Hepatitis Research; French National Agency of Research; French Ministry of Social Affairs and Health; Merck Sharp & Dohme; Janssen; AbbVie; Bristol-Myers Squibb; Roche |
| Li 2018170  U.S.  *Fair* | Retrospective cohort | 2002 to 2016 | Treatment duration: ≥28 days  Followup: 7.4 years (group A); 1.1 year (group B) | Adults with HCV infection included in the ERCHIVES database  Excluded: HBV, HIV coinfection; HCC diagnosis | A. Pegylated IFN + ribavirin (n=3,534)  B. DAA regimen (sofosbuvir + simeprevir +/- ribavirin; sofosbuvir + ledipasvir +/- ribavirin; sofosbuvir + daclatasvir +/- ribavirin; ombitasvir + paritaprevir + ritonavir + dasabuvir +/- ribavirin) (n=5,834)  C. No antiviral treatment (n=8,468) | 17,836 | A vs. B vs. C  Mean age 54 vs. 62 vs. 58 years  4% vs. 3% vs. 3% female  67% vs. 51% vs. 50% white; 17% vs. 31% vs. 35% black; 6% vs. 3% vs. 6% Hispanic; 11% vs. 15% vs. 9% other  Fibrosis stage: <1.45: 46% vs. 37% vs. 49%; 1.45 to 3.50: 41% vs. 43% vs. 37%; >3.5: 13% vs. 20% vs. 15% | A vs. B vs. C  HCC: 5.6% (196/3,534) vs. 0.9% (50/5,834) vs. 5.0% (436/8,468)  Incidence rate/1,000 person-years/followup: -Total cohort: 7.48 (95% CI, 6.50 to 8.61) vs. 7.92 (95% CI, 6.00 to 10.45) vs. 10.90 (95% CI, 9.92 to 11.97); A vs. B: p=0.72; A vs. C: p<0.001 | NR |
| Younossi 2015135  ION 1-3  Multinational (U.S., Europe)  *Fair* | Retrospective cohort | October 2012 to June 2013 | Treatment duration: 8 to 24 weeks  Followup: 12 weeks post-treatment | Treatment-naïve or experienced with chronic HCV infection enrolled in ION-1, 2 or 3 trials | A. Sofosbuvir + ledipasvir (n=420)  B. Sofosbuvir + ledipasvir + ribavirin (n=286) | 706 | *Population with no/mild fibrosis, NR by intervention group*  Mean age 54 years  33% female  77% white  97% U.S.-based population  Treatment-naïve: 71%  Treatment-experienced: 29% | A vs. B  Quality of life score, mean change from baseline SF-36 physical component score (scale 0 to 100): 1.70 (SD 5.85; p<0.05\*) vs. 1.92 (SD 6.17; p<0.05\*)  SF-36 mental component score (scale 0 to 100): 2.51 (SD 7.95; p<0.05\*) vs. 2.18 (SD 8.09; p<0.05)  FACIT-F fatigue score (scale 0 to 52): 4.18 (SD 8.90; p<0.05) vs. 4.34 (SD 9.21; p<0.05)  FACIT-F total score (scale 0 to 160): 10.27 (SD 19.57; p<0.05) vs. 10.75 (SD 20.02; p<0.05)  CLDQ-HCV total score (scale 1 to 7): 0.61 (SD 0.88; p<0.05) vs. 0.50 (SD 0.85; p<0.05)  WPAI:SHP work productivity impairment score (scale 0-1): -0.032 (SD 0.210; p<0.05) vs. -0.076 (SD 0.238; p<0.05)  WPAI:SHP activity impairment score (scale 0-1): -0.082 (SD 0.240; p<0.05) vs. -0.093 (SD 0.230; p<0.05)  SF-6D health utility score (0.2-1): 0.052 (SD 0.130; p<0.05) vs. 0.042 (SD 0.124; p<0.05) | Gilead |
| Younossi 2017136  ASTRAL 1-4  Multinational (U.S., Canada, Europe, Hong Kong)  *Fair* | Retrospective cohort | July 2014 to December 2014 | Treatment duration: 12 to 24 weeks  Followup: 12 weeks post-treatment | Chronic HCV infection with no cirrhosis or compensated cirrhosis enrolled in ASTRAL-1, 2 or 3 trials (ASTRAL-4 enrolled only patients with decompensated cirrhosis) | A. Sofosbuvir + velpatasvir (n=813)  B. Sofosbuvir +/- velpatasvir + ribavirin (n=299) | 1,112 | *Population with no cirrhosis, NR by intervention group*  Mean age 52 years  41% female  84% white; 6% black; 8% Asian  42% U.S.-based population  Treatment-naïve: 80%  Treatment-experienced: 20% | A vs. B  Mean improvement in patient-reported outcomes (composite SF-36, FACIT-F, CLDQ-HCV, WPAI:SHP; scale 0-100): 5.5 (SD NR; p>0.05\*) vs. 6.1 (SD NR; p>0.05\*) | Gilead |

**\*** Within group difference from baseline

**Abbreviations:** aHR = adjusted hazard ratio; CABG = coronary artery bypass graft;CI = confidence interval; CLDQ-HCV = Chronic Liver Disease Questionnaire-Hepatitis C Version; CVD = cardiovascular disease; DAA = direct acting antiviral; ERCHIVES = Electronically Retrieved Cohort of HCV-Infected Veterans; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; HBV = hepatitis B virus; HCC = hepatocellular carcinoma; HCV = hepatitis C virus; HR = hazard ratio; IFN = interferon; IQR = interquartile range; MI = myocardial infarction; NR = not reported; SD = standard deviation; SF-36 = Short Form 36; SF-6D = Short Form 6D; U.S. = United States; WPAI:SHP = Work Productivity and Activity Impairment Questionnaire: Specific Health Problem.Study names are not acronyms.