ASSESSING THE IMPACT OF DIRECT-ACTING ANTIVIRALS ON HEPATITIS C COMPLICATIONS:
A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction

Globally, 1.5 million new patients get infected with Hepatitis C Virus (HCV) per year.[1] Yet, the breakthrough of Direct-acting Antivirals (DAAs) has allowed WHO's target to eliminate HCV by 2030 become realistic.[1] While there are obvious improvements in clinical and biochemical liver function following DAA therapy, especially in decompensated cirrhosis, **there is currently insufficient evidence to assess the treatment's overall benefits, particularly in terms of preventing the need for liver transplantation or reducing mortality.** There is also insufficient understanding of which particular patient cohorts will benefit most from DAA therapy.

Objectives

1. To synthesise existing evidence on the impact of DAAs on 5 outcomes – **Hepatocarcinoma (HCC) occurrence and recurrence, all-cause mortality, liver decompensation and liver transplant (LT).**
2. To outline the patient cohorts that would benefit most from DAA therapy, using subgroup analyses.

Materials and Methods

MEDLINE, EMBASE and Cochrane were sourced for papers from March 1993 to March 2022. Subsequently, data was extracted and processed by 2 reviewers, before analysis using the the random-effects model. Inclusion criteria were:

- Randomised controlled trials (RCTs), cohort and case-control studies
- English language publications only
- Studies must have 2 arms involving a no-treatment control

Search terms: Direct-acting antiviral, Hepatitis C, liver cirrhosis, liver fibrosis or end stage liver disease, carcinoma, hepatocellular, mortality, liver failure, and decompensation
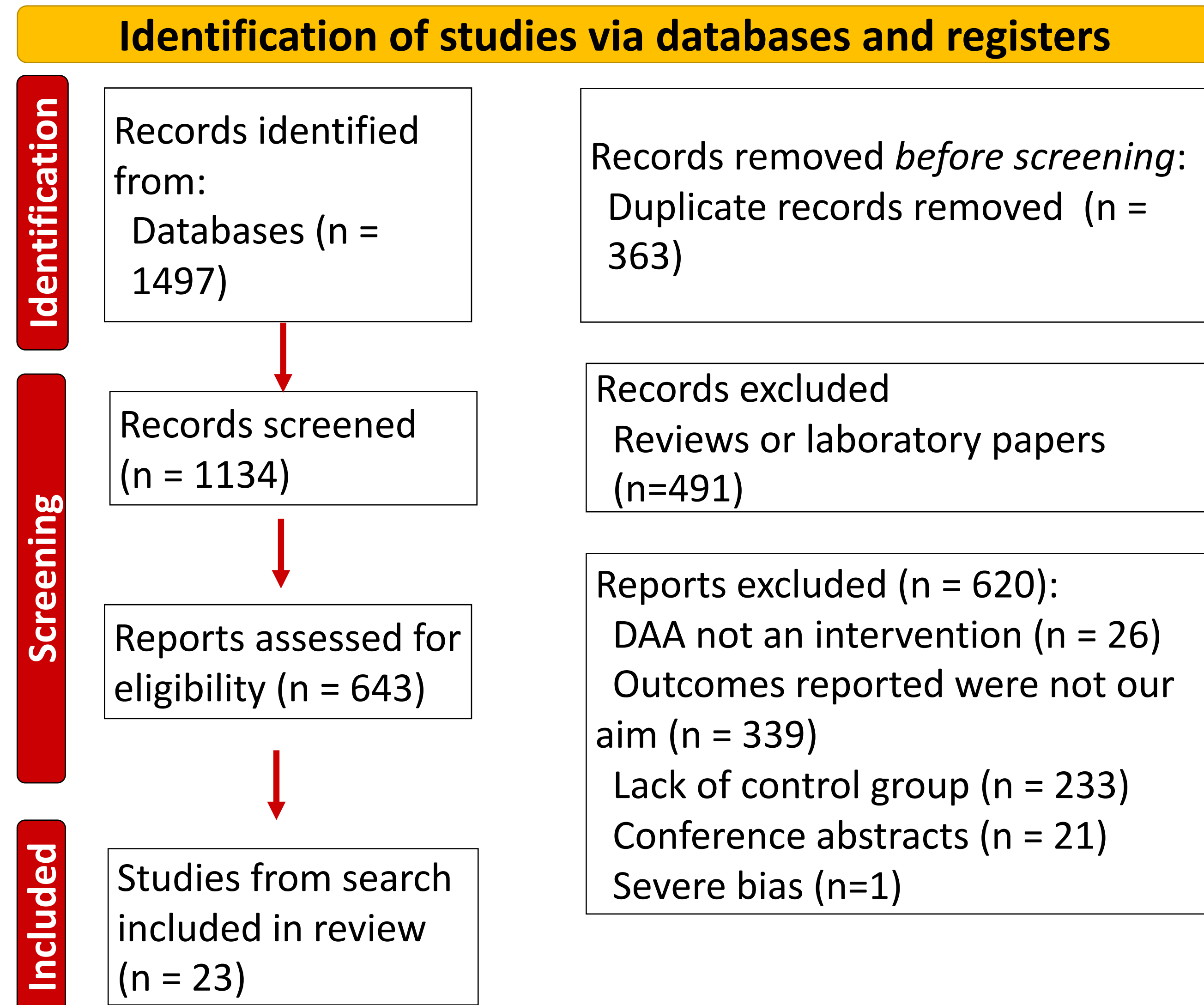
Identification of studies via databases and registers

Identification

Records identified from:
Databases (n = 1497)

Records removed *before screening*:
Duplicate records removed (n = 363)

Screening

Records screened (n = 1134)

Records excluded
Reviews or laboratory papers (n=491)

Reports assessed for eligibility (n = 643)

Reports excluded (n = 620):
DAA not an intervention (n = 26)
Outcomes reported were not our aim (n = 339)
Lack of control group (n = 233)
Conference abstracts (n = 21)
Severe bias (n=1)

Included

Studies from search included in review (n = 23)

Fig 1: Data extraction of 23 final papers were done using PRISMA method

Results

- Overall, DAA treatment lowered HCC recurrence (RR 0.71, 95%CI 0.55 – 0.92), all-cause mortality (RR 0.43, 95%CI 0.23-0.78) and liver decompensation (RR 0.52, 95%CI 0.33-0.83) significantly
- DAAs reduced HCC occurrence significantly in non-cirrhosis (RR 0.80, 95%CI 0.69-0.92) and cirrhosis (RR 0.39, 95%CI 0.24-0.64) but not in decompensated cirrhosis
- Meta-regression analysis showed that male gender (r = -0.036; 95% CI -0.0455, -0.0266; $p<0.0001$) in DAA treatment groups and and patients with genotype 1 in untreated group (r = 0.0263; 95% CI 0.0206, 0.0320; $p<0.001$) showed significant contribution to all-cause mortality.
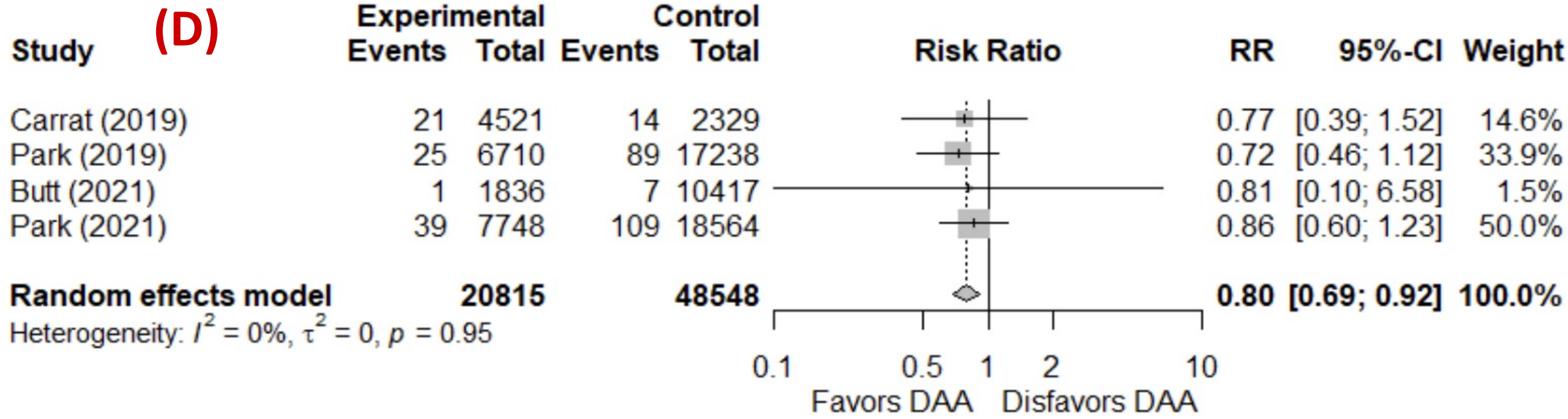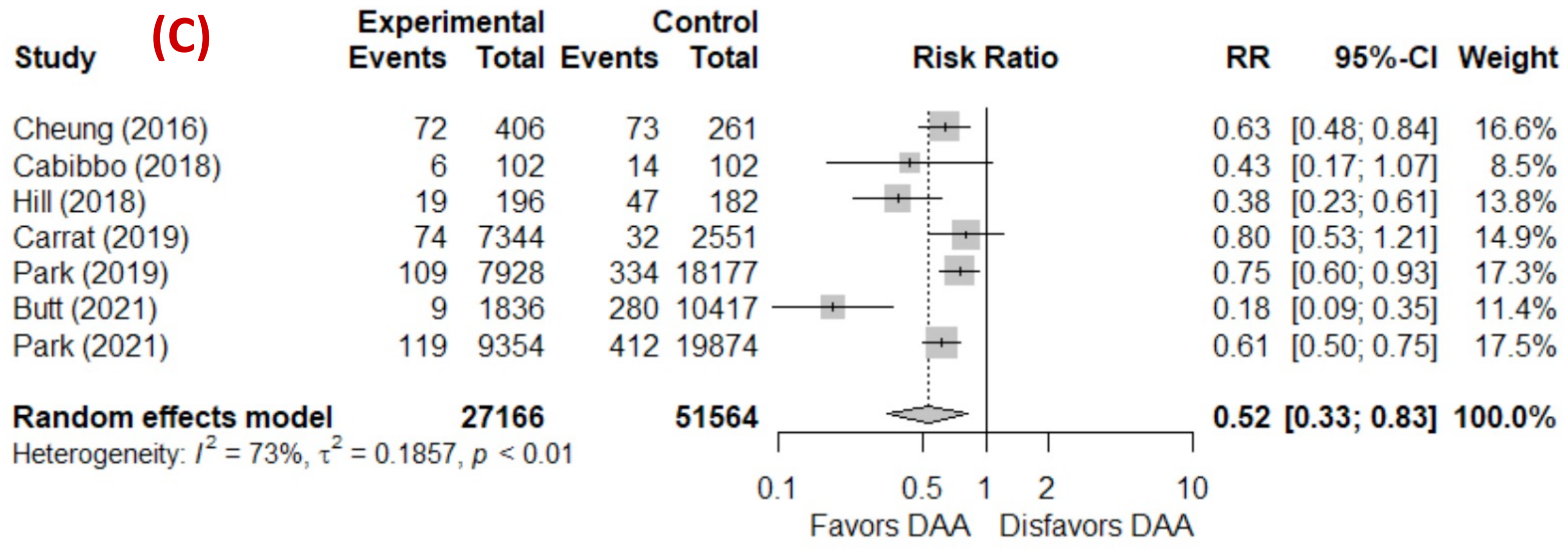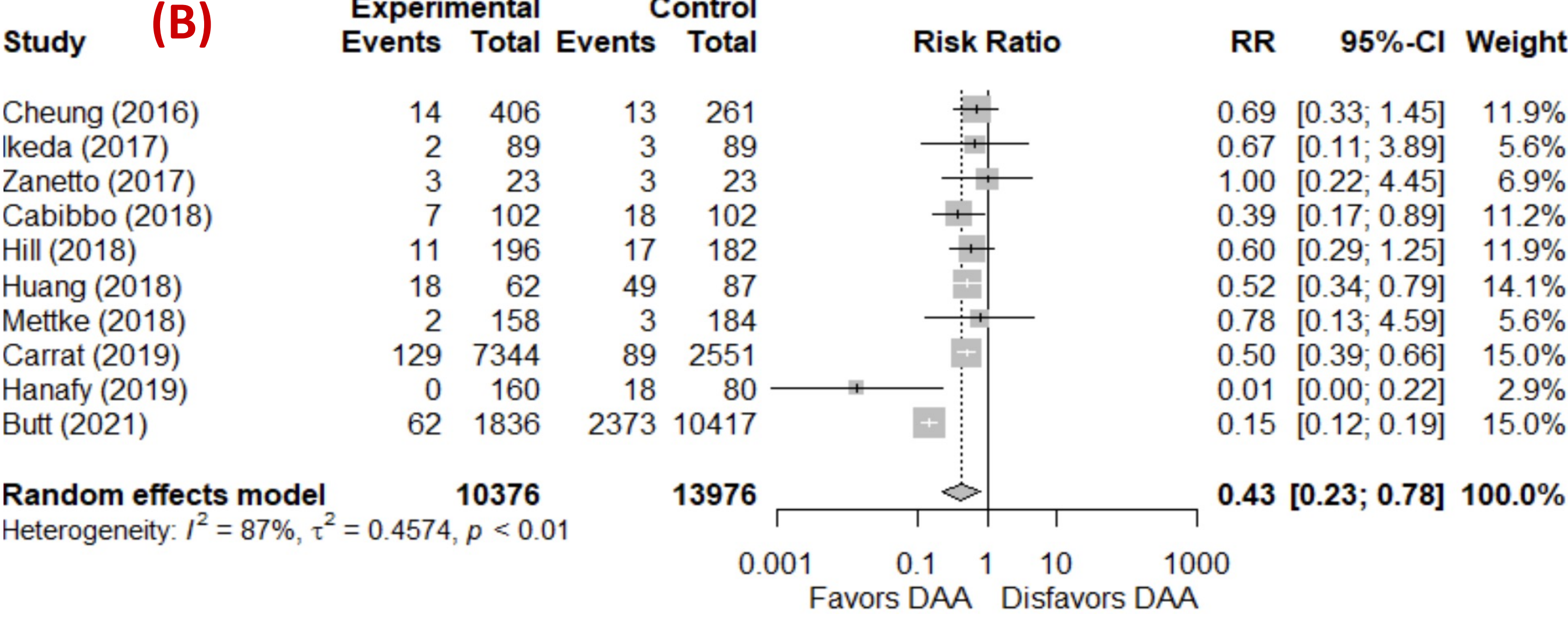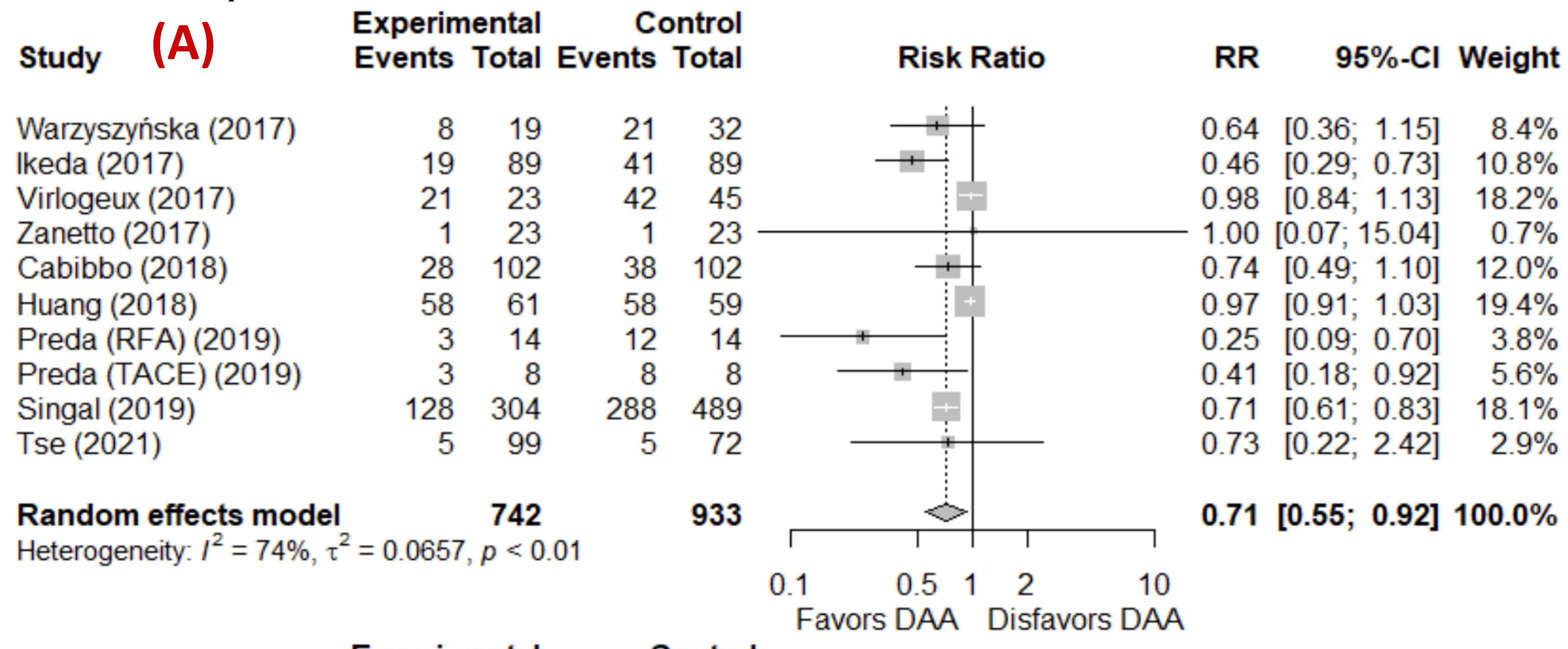

Fig 2: Forest Plots showing significant effect of DAAs on A) overall HCC recurrence B) Overall all-cause mortality HCC C) Overall liver decompensation D) HCC occurrence in non-cirrhosis patients

Conclusion

- DAA therapy is beneficial in reducing HCC recurrence, all-cause mortality and liver decompensation.
- The study findings indicate that initiating DAA treatment early could be advantageous even for non-cirrhotic patients, challenging the prevailing rationale of some countries using justification for prescribing or reimbursing DAAs based on fibrosis severity.[2,3]
- Active screening and early treatment of HCV shall be considered for better outcomes.

References

1. Hepatitis C. World Health Organisation. Accessed 11 June, 2022. https://www.who.int/news-room/fact-sheets/detail/hepatitis-c
2. Recommendations for testing, managing, and treating hepatitis C. Accessed 27 Feb 2023, 2023. http://www.hcvguidelines.org
3. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (2022) . https://www.hepcguidelines.org.au/