To Screen or Not to Screen, before DAA Therapy? A Decision Curve Analysis of Age-Based Fibrosis Screening Strategies

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Background: Australia has committed to hepatitis C virus (HCV) elimination, yet treatment uptake has plateaued despite universal access to direct-acting antivirals (DAAs). Pre-treatment fibrosis staging can delay DAA commencement. We propose a "Treat First" model that initiates pan-genotypic DAA therapy without fibrosis assessment when the probability of cirrhosis is low, reserving assessment for those at higher risk. We evaluated the clinical utility of simple age cut-offs to selectively trigger fibrosis assessment, compared with the current "screen all" strategy.

Methods: We performed a two-stage meta-analysis of 10 HCV studies (observational cohorts and clinical trials). Our outcomes were cirrhosis and clinically significant portal hypertension (CSPH), defined as median liver stiffness ≥12.5kPa and >20 kPa, respectively by transient elastography. We compared strategies that assessed fibrosis only in people aged ≥35, ≥40, or ≥45 years with "screen all" and "screen none" approaches. Decision curve analysis quantified net benefit (balancing true-positive detection against unnecessary assessment) across threshold probabilities from 0-30%. Threshold probability reflects the minimum cirrhosis risk at which clinicians would choose to assess fibrosis before treatment.

Results: The pooled sample included 6,581 individuals (median age 48 years; 72% male); cirrhosis prevalence was 16% (n=1,074). For identifying cirrhosis, age-based strategies yielded higher net benefit than screening all at threshold probabilities of ≥1%, ≥3%, and ≥5% for people aged ≥35 years, ≥40 years, and ≥45 years, respectively. For identifying CSPH, age-based strategies were superior at threshold probabilities of ≥1%, ≥1%, and ≥5% for people aged ≥35 years, ≥40 years, and ≥45 years, respectively.

Conclusion: Across clinically plausible threshold probabilities, universal fibrosis screening outperformed selective age-based approaches only at an extremely low cirrhosis threshold probability (<1%). Incorporating an age-based selective assessment within a "Treat First" pathway could reduce unnecessary pre-treatment fibrosis testing, enhance DAA uptake, shorten time to DAA initiation, and support progress toward HCV elimination.

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