Research Article

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Is antenatal screening for hepatitis C virus cost-effective? A decade's experience at a London centre

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Background & Aims: This study aims to assess the cost-effectiveness of a routine universal antenatal hepatitis C virus (HCV) screening programme at a London centre.

Methods: Ten years' retrospective antenatal screening and outcome data informed a cost-effectiveness analysis using the previously validated MONARCH model. The cost and quality of life outcomes associated with the screening and treatment of newly identified hepatitis C cases were used to generate cost-effectiveness estimates for the screening programme.

Results: A total of 35,355 women were screened between 1st November 2003 and 1st March 2013; 136 women (0.38%) were found to be HCV antibody positive. Of 78 (0.22%) viraemic cases, 44 (0.12%) were newly diagnosed. In addition, the screening programme identified three (6.8%) vertical transmissions in children of newly diagnosed mothers. Of 16 newly diagnosed mothers biopsied, all were in the F0-F2 METAVIR disease stages, and 50% had HCV genotype 1. Postnatal treatment with pegylated interferon and ribavirin was initiated in 19 women, with 14 (74%) achieving sustained virologic response. The total cost of screening and confirmation of diagnoses was estimated to be £240,641. This translates to £5469 per newly diagnosed individual. The incremental cost-effectiveness ratio of this screening and treatment strategy was £2400 per QALY gained. Treatment with newer direct-acting antiviral regimens would have a projected cost of £9139 per QALY gained, well below the £20,000-30,000/QALY gained willingness-to-pay threshold applied by policy advisory bodies.

Conclusions: This study demonstrates that an antenatal screening and treatment programme is feasible and effective, at a cost considered acceptable.

Keywords: Antenatal; Pregnancy; Screening; Hepatitis C; Cost-effectiveness; MONARCH.

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Abbreviations: HCV, hepatitis C virus; ESLD, end stage liver disease; HCC, hepatocellular carcinoma; DAA, direct acting antiviral; HBV, hepatitis B virus; REDCAP, research electronic data capture; MONARCH, modelling the natural history and cost-effectiveness of hepatitis C; QALY, quality adjusted life year; SVR, sustained virologic response; eRVR, extended rapid virologic response; SA, sensitivity analysis; BC, base case; ICER, incremental cost-effectiveness ratio.

Introduction

Hepatitis C virus (HCV) is a blood borne virus with a chronic course in most infected individuals. It is usually asymptomatic in the early years, but persistent infection can lead to end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC) [1]. In the UK, both hospital admissions and deaths from HCV-related ESLD and HCC are continuing to rise, and the number of transplants indicated due to HCV-related cirrhosis has more than quadrupled between 1996 and 2013 [2]. Previously published European antenatal data suggest an HCV prevalence of up to 0.6% in this population [3,4].

It is estimated that at least 40% of cases remain undiagnosed in the UK [2]. In 2012, birth cohort screening for HCV was recommended by the Centers for Disease Control and Prevention (CDC) [5]; however, outside the US, screening for HCV is generally only undertaken in high risk populations. Risk based screening may not be effective for three main reasons: firstly, in the primary care setting, HCV risk factors are often not fully explored [6,7]; secondly, patients do not always report transient behaviours (e.g. injecting drug use) that occurred years or decades ago; thirdly, many acquire infection iatrogenically in their country of origin and are unaware of exposure risk. Other strategies for HCV case finding are therefore becoming increasingly pertinent, especially given the recent advances in treatments with the introduction of new generation direct-acting antivirals (DAAs). Antenatal screening for several infectious diseases, including HIV and hepatitis B virus (HBV), is performed routinely in many countries including the UK [8]. This is commonly motivated by the risk of perinatal transmission; this is estimated at 6% amongst HCV patients [9,10]. However, in the absence of interventions available to prevent HCV transmission, routine screening for HCV in pregnancy has not been recommended in most countries [11]. Successful

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identification and treatment of HCV-infected individuals is associated with improved long-term health, through the avoidance of ESLD, and increased life expectancy [12,13].

Previous studies have shown a benefit in the adoption of a routine antenatal screening programme for HCV over risk based testing strategies [3,14]. These studies demonstrate that up to 75% of newly diagnosed mothers have no reported "high risk" behaviour. Whilst many of these women were born in countries with a higher prevalence and risk of infection, screening of migrants would potentially be stigmatising. Women screened and diagnosed with HCV during the antenatal period are generally healthy and motivated, with high rates of attendance to follow-up observed [3]. Given that testing for HCV antibodies can be carried out using the same laboratory samples taken for routine antenatal virology screening for HIV and HBV, minimal additional resource use is required. The costs of diagnostic confirmation and the treatment of newly identified patients pose potentially significant costs, but these may be offset against the potential future costs of late diagnosis and the treatment of complications, should these women be diagnosed only when the disease has progressed.

This study aims to evaluate the cost-effectiveness of routine screening for HCV antibodies in the antenatal population of a London hospital, based on data from a ten-year screening programme, using a previously published and validated simulation model of HCV.

Methods

Screening and treatment

Between 1st November 2003 and 1st March 2013, all pregnant women attending the antenatal clinics at St Mary's Hospital, Imperial College Healthcare NHS Trust, London for their "booking in" visit were offered HCV antibody testing as part of their screening. All positive results were directly reported from the virology lab to a specialist midwifery team trained in the management of patients with viral hepatitis. All mothers in which HCV antibodies were identified were referred to a named consultant hepatologist working closely with the antenatal team. Mothers with initial undetectable viral load results had a further viral load assessment after the pregnancy to confirm spontaneous resolver status, before being discharged from follow-up. Mothers with identified viraemia were counselled in the antenatal hepatology clinic and reviewed in a family clinic following delivery, with their child, by the same hepatologist and a paediatric consultant with specialist interest in infectious diseases. All children of infected mothers were tested serologically for HCV at 15 months. These mothers were then offered regular hepatology follow-up and worked up for treatment per standard practice.

Antenatal and medical records were reviewed to evaluate the service provided to these women over the last ten years and their outcomes. Individual patient data were anonymised. Data were managed using REDCap electronic data capture tools [15]. Information recorded included patient demographics, antenatal data, maternal HCV status and their risk factors, dates of hepatology appointments, outcomes of work up and, if relevant, treatment records and outcomes.

Cost-effectiveness model

The MONARCH (MOdelling the NAtural histoRy and Cost-effectiveness of Hepatitis C) model is a previously published and validated HCV disease progression and cost-effectiveness model designed to progress a cohort of subjects in annual cycles through METAVIR fibrosis stages and potentially to ESLD complications and death [16,17]. Patients in METAVIR fibrosis stages F0–F4 incur an annual probability of all-cause mortality [18], whilst patients suffering from ESLD complications incur disease-specific mortality rates. Fig. 1 shows the model flow diagram and Supplementary Table 1 reports the transition rates applied in the model. Disease progression is modelled over a lifetime assuming a maximum age of 100 years. Total costs, quality-adjusted life-years (QALYs), and numbers of predicted ESLD complications and deaths are estimated over the simulated period.

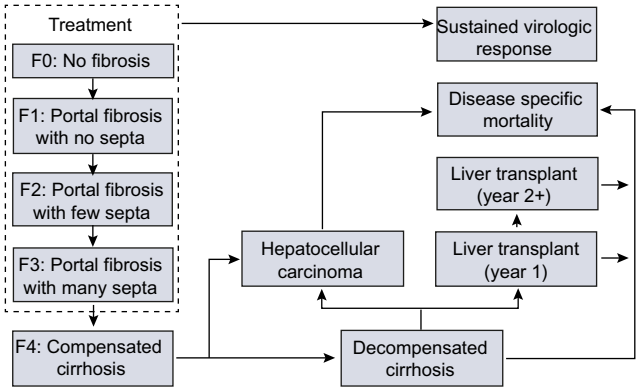

Fig. 1. Flow diagram of the MONARCH model. Annual transition probabilities control progression through disease states.

Fibrosis stage transition probabilities were informed by characteristics of the screened population with respect to age, sex, HCV genotype and source of infection (Supplementary Table 1). Initially, patients' disease stage was reported as either mild, moderate or severe. To inform the initial distribution of patients across fibrosis stages, it was assumed that mild and moderate disease corresponded to fibrosis stages F0–F1 and F2–F3, respectively.

The outcomes of the screening programme were used as the basis of a cost-effectiveness analysis using the MONARCH model. The additional costs of screening were compared to the benefits of identifying new cases and the opportunity for treating them, in terms of future quality of life, survival and cost implications of long-term HCV complications. The results of modelling were used to determine an upper threshold for the cost of screening. The UK advisory body, the National Institute of Health and Care Excellence (NICE), considers an intervention cost-effective at a threshold of £20,000 to £30,000 per QALY gained [19]; in the US, the threshold is $50,000 per QALY gained [20], and a previous European evaluation of an antenatal HCV screening programme applied a threshold of €20,000 to €50,000 [21].

A healthcare payer perspective was taken and only direct medical costs considered. Patient and societal costs, such as increased productivity among working adults, were not included. HCV-specific treatment and monitoring costs were derived from weekly estimated costs, accommodating duration of treatment by HCV genotype. Testing costs were based on cost tariffs at Imperial College Healthcare NHS Trust, as demonstrated in Supplementary Table 2. Costs associated with the screening programme included the costs of identifying patients through the use of both HCV antibody and confirmatory testing amongst all patients; those subsequently identified as having HCV antibodies underwent RNA, genotype and baseline liver screening. Costs associated with liver biopsy were applied to the patients that underwent the procedure, whilst patients that were treated incurred antiviral therapy-related costs. All costs and health utility estimates (measured as QALYs), presented in Table 1, are independent of age and were discounted annually at a rate of 3.5%, to reflect their present value. All costs were inflated to 2013 values using the Health and Social Care index [22].

In the base case, the identification and treatment of patients was modelled as observed in the women in our study centre treated with pegylated interferon alpha and ribavirin (IFN/RBV) only. It was assumed that patients infected with HCV genotypes 1 and 4 received 48 weeks of treatment, and those with HCV genotypes 2 and 3 received 24 weeks of therapy. Conservative assumptions around drug cost were made; it was assumed no patients ended treatment early due to discontinuation or extended rapid virologic response (eRVR). Any bias introduced by this assumption would be against the screening strategy. Amongst all treated patients, there was no evidence of significant anaemia or dose reduction and no blood or platelet transfusions; as such, the costs of treating any adverse events were not modelled. Therapy-specific disutility was applied to patients whilst receiving treatment, upon completion of treatment no further disutility was incurred.

Two additional scenarios were modelled relating to the introduction of new generation DAAs: as either the initial treatment option or as subsequent treatment for patients failing to achieve SVR with IFN/RBV; to illustrate this, a treatment success rate (SVR) of 95% for 12 weeks of sofosbuvir triple therapy (SOF + IFN/RBV) was applied across all genotypes and fibrosis stages, estimated