

Hepatitis C virus seroprevalence in defined populations in New Zealand: data from a general practice-based screening programme

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ABSTRACT

AIM: To assess the hepatitis C virus (HCV) seroprevalence data for defined regions in New Zealand.

METHODS: Email or mobile phone text invitations were sent out to adults enrolled with three participating general practices in different parts of New Zealand. Patients who provided informed consent were instructed to self-present for HCV blood tests. Patients with positive HCV antibodies had reflex testing of HCV antigen and ribonucleic acid (RNA) viral load.

RESULTS: In total, 26,247 invitations were issued. Of these, 1,368 (5.2%) people gave informed consent and 1,021 patients (3.9%) had HCV blood tests. Ten out of 1,021 (0.98%; 95% confidence interval [CI] 0.51–1.82%) tested positive for HCV antibodies, of whom two (0.2%; 95% CI <0.01–0.76%) had positive antigen and elevated RNA viral load. The proportion of NZ Māori and Pacific people was low, at 3.8% and 0.4%, respectively. Volunteers with a high deprivation index were under-represented (3% from New Zealand Index of Deprivation deciles 9 and 10).

CONCLUSIONS: The HCV viraemia prevalence in this general practice-based screening programme is 0.2%, which is lower than previous estimates. This may have implications for appropriate resource allocations and the determination of the best strategies to find new HCV infections. Participation rates of people with high deprivation indexes or who were NZ Māori and Pacific people were low, suggesting that a tailored screening approach is needed.

Chronic hepatitis C virus (HCV) infection results in significant increases in morbidity and mortality from end-stage liver disease and hepatocellular carcinoma (HCC), as well as extrahepatic manifestations including cryoglobulinaemic vasculitis, chronic lethargy, skin conditions and increased risk of diabetes mellitus and lymphoma. In New Zealand, chronic HCV infection has been a leading indication for liver transplantation.¹

Oral direct-acting antiviral therapies can cure almost all people with chronic HCV infection.² These medicines are significantly more tolerable, have shorter durations and are more efficacious than past therapies, making elimination of HCV infection from New Zealand a possibility, with major benefits for both individual health and the overall health system. New Zealand is a signatory to the World Health Organization's (WHO) goal of eliminating viral hepatitis by 2030.

To achieve HCV elimination, all individuals with HCV infection need to be identified and treated. In an individual with positive HCV antibody, the presence of HCV antigen and HCV (ribonucleic acid) RNA confirms active chronic

HCV infection; absence of HCV antigen and HCV RNA indicates past infection.³ New Zealand currently has no universal screening programme for HCV infection; testing is usually performed based on a risk factor assessment. Important risk factors associated with chronic HCV infection include history of injecting drug use, unsafe therapeutic injections, transfusion of blood products and organ transplantation from infected donors and occupational exposure to blood (primarily contaminated needle sticks).⁴ However, this approach is missing some people with infection, as demonstrated by data from New Zealand's national tertiary HCC service, where 28% of patients with HCC related to chronic HCV received the diagnosis of advanced HCC prior to diagnosis of HCV.⁵ Universal screening has been shown to be cost-effective in other healthcare settings,⁶ but it is unclear if this is the case for New Zealand. There is a lack of robust epidemiological data for New Zealand, so a comprehensive evaluation of the potential economic and public health costs and benefits of universal screening cannot be undertaken. We also have no registry for chronic HCV;

therefore, the retesting of people with known past infection would reduce cost effectiveness of any screening programme.

The global prevalence of individuals with HCV viraemia from a 2020 modelling study was reported at 0.7%.⁷ The same modelling study estimated a New Zealand viraemic prevalence of 0.9% in 2020. This number is similar to modelling undertaken by local experts in 2014, equating to roughly 45,000 individuals with HCV infections in New Zealand.⁸ However, there is evidence these numbers may be an over-estimate. For instance, only 29 cases of acute HCV were detected by laboratories and notified nation-wide in 2020.⁹ Also, unpublished Auckland community laboratory data indicate that approximately two-thirds of patients with positive HCV antibody tests have previous positive tests (personal communication, in an email from Dr A Upton, clinical microbiologist, Southern Community Laboratories, 10 June 2020). This raises the following possibilities: firstly, patients with chronic HCV infection are not accessing healthcare, and the current testing is targeting the wrong population; and/or secondly, the estimate of 45,000 infected New Zealanders is an over-estimate. Both these scenarios will result in inappropriate estimation and misallocation of resources for HCV elimination in New Zealand.

In contrast, a 2015 study in Dunedin, New Zealand, among patients aged 40–59 years presenting for community and hospital blood tests, found an HCV antibody seroprevalence of 4%. The study included a questionnaire about HCV infection that found significant gaps in knowledge among randomly selected individuals in Dunedin.¹⁰ The finding of relatively high antibody seroprevalence among the age groups studied is consistent with the current understanding of HCV epidemiology. In addition, the findings may point to variable prevalence in different regions of New Zealand. However, this study did not measure HCV viraemia to separate active chronic infection from past infections. Also, data from a recent study using point-of-care HCV antibody testing on a group of construction workers in Christchurch, New Zealand showed an HCV antibody prevalence of 1.3% out of the 234 participants, all of whom also had positive HCV RNA.¹¹

The current study has been designed to assess the prevalence of HCV infection based on community screening in defined regions to improve estimates of the HCV burden in New Zealand. The study also evaluates the screening uptake of a primary care-based HCV screening

approach that utilises phlebotomy. These data could help determine appropriate methods to identify HCV-infected people in New Zealand, inform appropriate future resource allocation and contribute to overall strategies for HCV elimination.

Methods

The study design is a cross-sectional observational study where all adults enrolled with participating general practices were invited to have a phlebotomy for HCV antibody testing with reflex HCV RNA and antigen testing for antibody positive cases. Three general practices participated in this study.

In order to minimise introduction of bias due to location, socio-economic factors and ethnicity, we identified three large medical practices located in areas that serve a mixed population, incorporating regional, urban and suburban populations (Christchurch and Motueka in the South Island and New Plymouth in the North Island) and avoiding practices with potentially enriched at-risk populations (e.g., those providing opioid substitution services). Practices were also required to have the appropriate IT support and capacity to manage the additional study-related workload.

Standardised email or mobile phone text invitations were sent to all enrolled adult clients aged 18 and above in the participating practices. They were provided links to an electronic patient information sheet and consent form on an electronic data capture system software (REDCap). Those who provided consent were instructed to self-present to a local laboratory for a phlebotomy after they completed the consent form. Additionally, posters were displayed in practice waiting areas to allow the option of enrolment of casual (non-enrolled) patients who may be attending the practice for healthcare, and paper-based consent forms were available if requested by patients. An email reminder was sent 1 month after the initial invitation to people who had provided consent but had not yet presented for a phlebotomy.

HCV antibody serology was performed on all participant samples in the study, regardless of prior test results. Testing was performed on the Abbott ARCHITECT platform in a two-step immunoassay, using chemiluminescent micro-particle immunoassay technology, for the qualitative detection of anti-HCV in human serum and plasma. Where the HCV antibody was positive (reactive), the samples were reflexed

to HCV antigen testing utilising the ARCHITECT HCV Ag assay, which uses chemiluminescent microparticle immunoassay for the quantitative determination of hepatitis C core antigen in human serum and plasma. HCV RNA viral load testing was also performed on samples with a positive HCV antibody. No further testing was performed on samples with a negative HCV antibody result.

All results were entered into laboratory test repositories, as per usual practice, and were communicated by electronic notification to general practitioners. Additional specific communication was undertaken to general practitioners about positive HCV viral load results to ensure that the general practitioner would arrange appropriate assessment and HCV antiviral treatment for the participant according to standard of care protocols. Results were communicated to study participants via a unique password-protected email, with individual access details provided to participants when they presented for the blood test. There was no further follow-up from the study for participants with negative HCV antibody results, or those with positive HCV antibody but with negative HCV antigen and negative HCV viral load results.

For data analysis, the primary end point was the percentage of positive HCV antibody and/or HCV RNA results in the participating general practice populations. The secondary end point was the percentage of screening uptake in these populations. Basic demographic data were collected from the general practices and the New Zealand Ministry of Health statistics database. Participants were included in the analysis if they were 1) adults aged 18 years or older enrolled in or attending the participating primary care practices, and 2) provided consent for phlebotomy and HCV testing. People were excluded if they were unable or unwilling to provide informed consent.

It was planned to invite a minimum of 10,000 individuals with provision to invite up to 30,000 individuals from three medical practices, with a scheduled data analysis after a minimum enrolment of 1,000 individuals for HCV antibody testing. Enrolment was planned to be allowed to continue for 12 months to a maximum of 5,000 individuals. The minimum sample size of 1,000 enrolments was based on the stated sensitivity of the test as 99.1% and specificity of 99.6%.¹² For an estimated prevalence in the population tested of 1%, at a 95% confidence level (CI), the precision estimate interval width would be 0.013 (giving a

lower limit of 0.005 and upper limit of 0.018 for the prevalence).

This study was approved by the New Zealand Health and Disability Ethics Committee (approval reference: 20/NTB/261).

Results

Between February 2021 and August 2022, a total of 26,247 invitations were issued from the three participating general practices. The duration of recruitment was extended beyond the planned 12 months because of disruption to primary health-care systems caused by the COVID-19 pandemic. A total of 1,368 (5.2%) individuals provided electronic consent, and 1,021 (3.9%) underwent a phlebotomy (Figure 1). No patients participated utilising written paper consent. Of the 1,021 who presented for phlebotomy and make up the population of interest, 10 (0.98%; 95% CI 0.51–1.82%) tested positive for HCV antibody. Two patients (0.2%; 95% CI <0.01–0.76%) tested positive for HCV RNA and HCV antigen and eight (0.8%) tested negative for HCV RNA (Figure 1). Out of the eight who tested negative for HCV RNA, three were previously known to have a positive HCV antibody.

The majority of participants were female (59.4%) in the 50–79-year age group (68.2%) with a median age of 59 years (Figure 2). Participants overwhelmingly self-identified as NZ European or Other European (83.2%), with the proportion identifying as NZ Māori or Pacific low at 3.8% and 0.4%, respectively (Figure 3). New Zealand Index of Deprivation deciles (NZDep) data are shown in Figure 4, demonstrating a low representation of participants with a high deprivation index (3% from deciles 9 and 10).

Discussion

The prevalence of positive HCV antibody in the combined group of participants from all three participating general practices was 0.98% (95% CI 0.51–1.82%) with 0.2% (95% CI <0.01–0.76%) positive HCV antigen and viraemia rate. This is lower than the estimates of HCV viraemia reported by the modelling performed by Polaris Observatory, at 1.1% and 0.9% in 2015 and 2020, respectively.⁷ Similarly, this rate of positive HCV antibody is lower than results from the 2015 study in Dunedin, New Zealand, which tested patients aged 40–59 years presenting for community and hospital blood tests and found an antibody seroprevalence of 4%.¹⁰ However, as noted, the

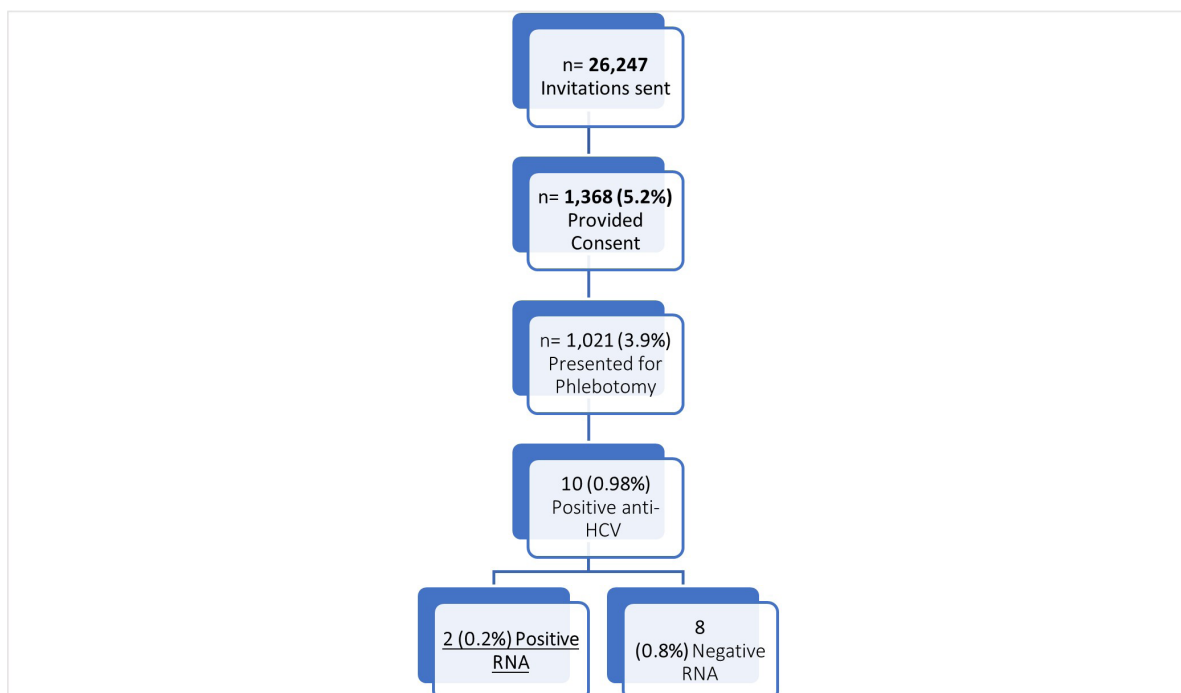
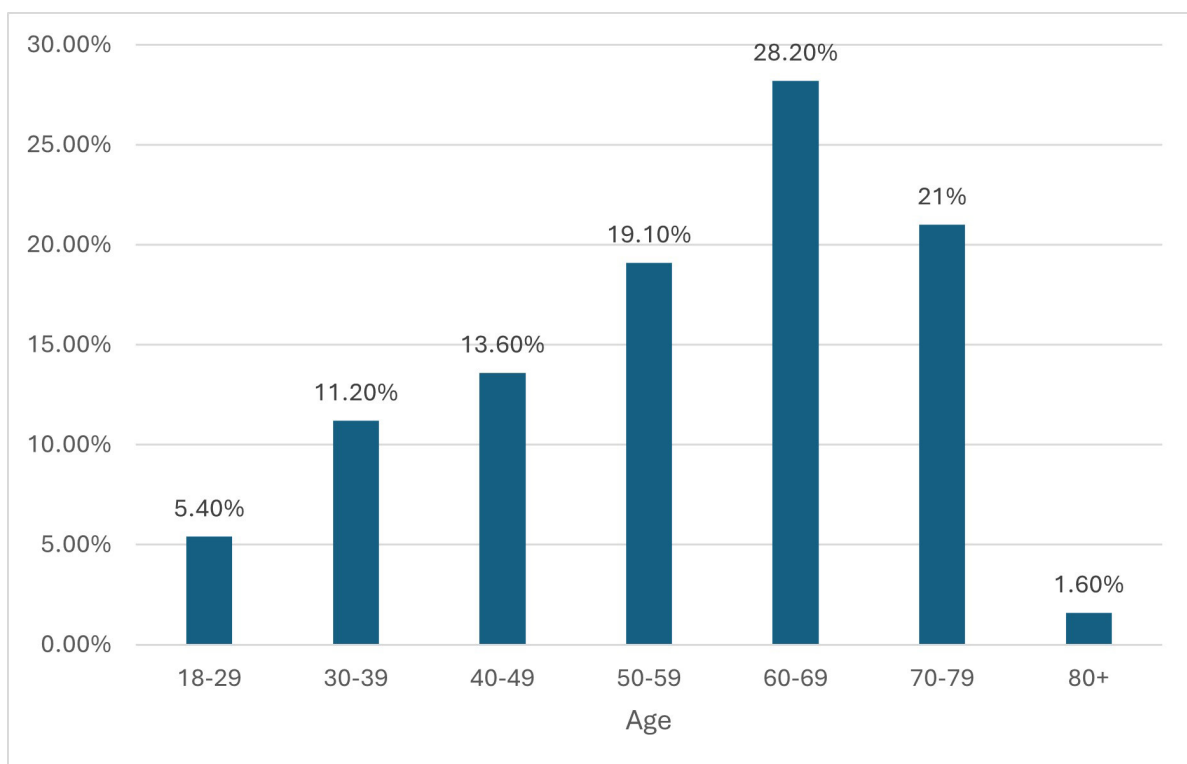
Figure 1: Study flowchart.**Figure 2:** Age of participants (n=1,021).

Figure 3: Ethnicity of participants (n=1,021).

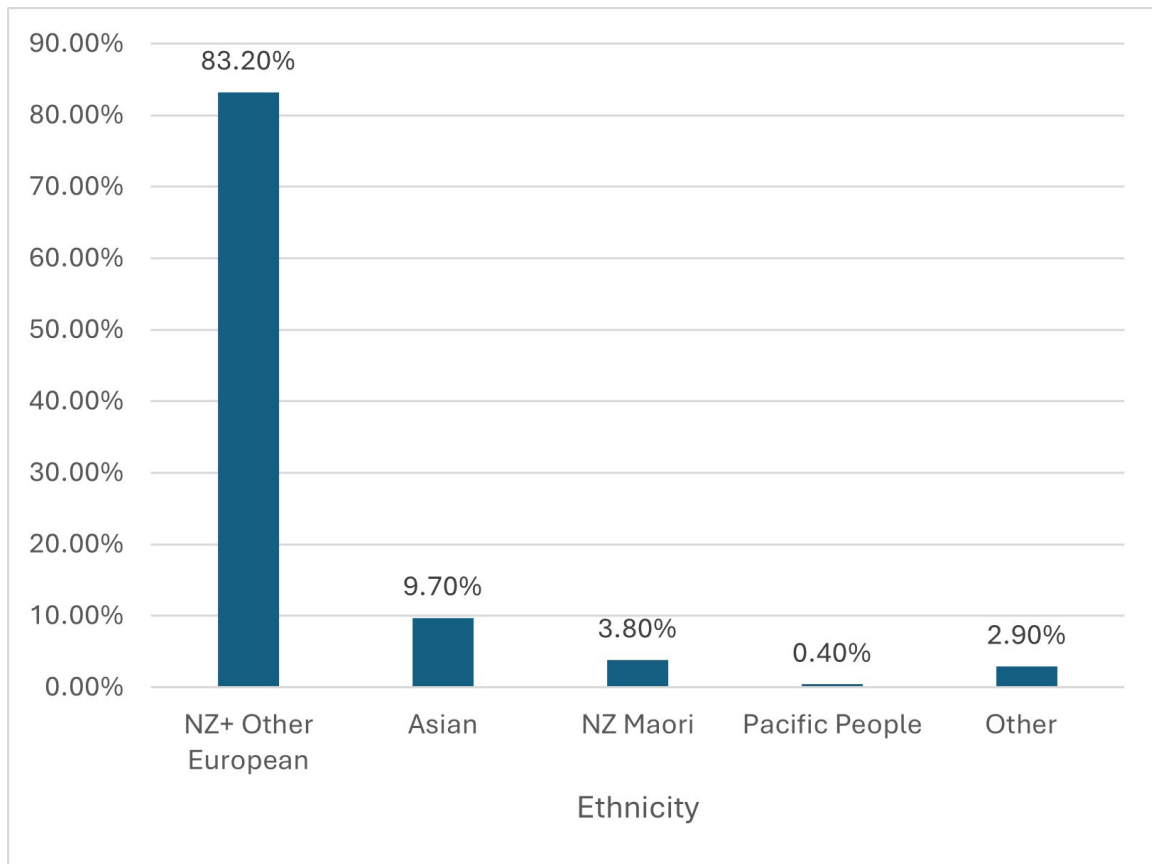
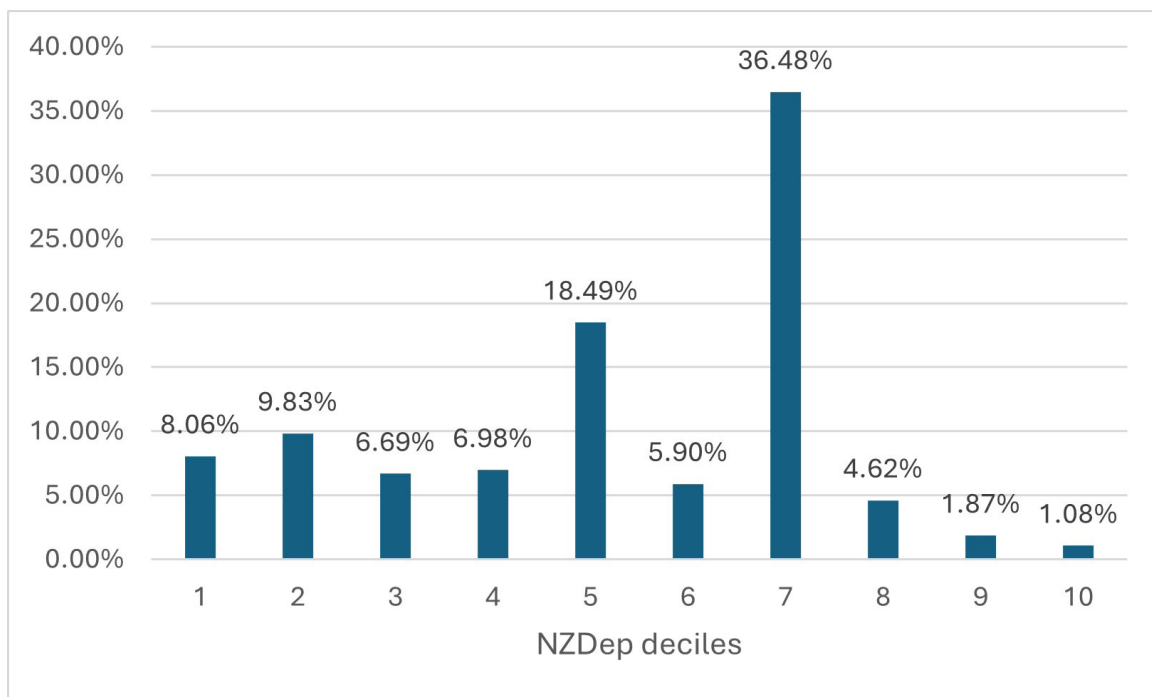


Figure 4: New Zealand Index of Deprivation deciles of participants (n=1,021).



Dunedin study did not test for the HCV antigen or viraemia so would be expected to over-estimate of the prevalence of active infection, and the study population selection differed from our study by focussing on a specific age group of people who were presenting for blood tests for other reasons.

This is the first study in New Zealand to estimate the HCV prevalence from an unselected adult population via primary care. We obtained real-world data from a group of participants, regardless of risk factors, rather than focussing on high-risk groups (e.g., prison populations, age cohort screening). We recruited participants from three general practices across different regions of New Zealand to obtain a broad representation of the general New Zealand population.

However, caution is required to interpret our data as there are limitations. Foremost, the overall participation rate from everyone who received email and text invitations is low at 3.9%. Potential reasons for this include the requirement for phlebotomy, potential for stigma associated with a hepatitis study, and also an individual's perception that they are not at risk for hepatitis C. The low participation rate could affect the representativeness of our volunteer group to the general New Zealand population. There is potential this could be an enriched group including participants who are aware they have risk factors for HCV infection and may therefore be more likely to volunteer for this study. Alternatively, the study could be affected by healthy volunteer bias, where those who volunteered were at a lower risk of having chronic HCV compared to the general population; further, evidence from some studies suggests people who inject drugs have low rates of engagement with primary care;^{13,14} therefore, they would be unlikely to be captured in a study through general practice and would be less represented in our study. Although this study was moderately effective in targeting the age cohort of 50–79 years, which made up more than two-thirds of our volunteer population, and overseas data has suggested that this age cohort (people born between 1945 and 1965) made up the majority of people with chronic HCV infections,¹⁵ the HCV prevalence is still low in our participants. However, more recent United States Centers of Disease Control and Prevention (CDC) data suggest that the infection rate is also high within the age group of 20–39 years.¹⁶ Overall, it is difficult to predict what the net effect on our HCV estimate is from the alternatives and combination of the different factors mentioned above.

Secondly, some demographic groups are under-represented in our volunteer population. With regards to ethnicity, representation of NZ Māori and Pacific people was low at 3.8% and 0.4%, respectively. This is lower than the estimated proportion of these ethnicities in these regions as reported by the 2018 New Zealand Census, which ranged from 8.7% to 27.6% for NZ Māori and 1.5% to 3.8% for Pacific people.^{17,18} With respect to the deprivation index, there is a low representation of participants with high deprivation index, with only 3% of participants from deciles 9 and 10. This is not an unexpected finding as one of the three general practices included provided the deprivation index data for their patients, which showed only 8.15% of their patients were from the two most deprived deciles (no further deprivation index data were available from the other general practices).

This study provides the first real-world New Zealand data of HCV screening uptake in response to electronic (email and text) and poster invitations for phlebotomy using a primary care-based universal invitation to patients from selected general practices. Lower screening uptake among NZ Māori and Pacific people and a low participation rate from people with high deprivation index suggest that a more targeted screening approach is needed to engage these groups of people. This may include utilising community-based point-of-care testing methods and partnership with local iwi (Māori tribes) or community leaders.

Conclusion

The HCV viraemia prevalence in this general practice-based screening programme is 0.2%, which is lower than previous estimates of New Zealand HCV infection prevalence. However, the prevalence estimate needs to be interpreted with caution, due to the risk of bias affecting the estimate.

These data may have implications for appropriate resource allocations and the determination of the best strategies to find undiagnosed HCV infections in New Zealand. A cost-effective analysis needs to be carried out to determine if universal screening is cost-effective in the New Zealand healthcare setting.

Low participation rates of people with high deprivation index, NZ Māori and Pacific people suggest that a tailored screening approach is needed to engage these populations.

COMPETING INTERESTS

HT has no relevant interests to declare. CS has received Speaker bureau fee from AbbVie. AL is an employee of AbbVie and owns AbbVie stock.

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