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Prevalence of Spontaneous Clearance of Hepatitis C Virus Infection Doubled From 1998 to 2017

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INTRODUCTION

Strategic planning for hepatitis C virus (HCV) screening and treatment requires up-to-date information on prevalence of HCV spontaneous clearance. Published estimates of HCV spontaneous clearance range from 15% to 60%.[1–3] We conducted an observational study over 20 years to evaluate trends in prevalence of HCV spontaneous clearance. Our goals were to estimate the proportion of HCV antibody-positive patients who were viremic, and to identify factors associated with viremia, thus facilitating prediction of the number of patients needing treatment.

METHODS

We conducted a cross-sectional study of adult members of Kaiser Permanente Northern California (KPNC) who had a positive HCV-antibody test and subsequent HCV PCR test during 1998–2017, with continuous membership and drug coverage between tests and no evidence of HCV treatment at KPNC. We defined spontaneous clearance as a positive HCV-

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antibody test followed by a negative PCR test. We excluded members with a negative HCV-antibody test following their positive HCV-antibody test. Systemic lupus erythematosus and rheumatoid arthritis are associated with false-positive HCV-antibody tests; thus, members with either diagnosis were also excluded.[4, 5] The institutional review board at KPNC approved this study with a waiver of written informed consent.

We computed the proportion with clearance by year of PCR test during 1998–2017. In a sensitivity analysis, we applied more conservative criteria to rule out the possibility of HCV treatment, including restricting to members with ≥5 years of health plan membership without evidence of treatment, and restricting to those with ≤14 days between HCV-antibody and PCR tests. We assessed factors potentially associated with spontaneous clearance, including age, sex, race/ethnicity, hepatitis B virus (HBV) and HIV coinfection, HCV-antibody testing in the emergency department (ED), and year of PCR test, evaluated by adjusted prevalence ratios (PRs) from Poisson regression models with robust variance.

RESULTS

Of 25,248 eligible individuals, 67.7% were born during 1945–1965, 58.4% were male, and 41.2% were of minority racial/ethnic backgrounds. Overall, 11,481 (45.5%) met the definition of spontaneous clearance of HCV; prevalence increased from 32.6% in 1998 to 68.7% in 2017 (Figure 1). Estimates of spontaneous clearance were similar in sensitivity analyses, with a prevalence of 72.3% in 2017 for those with ≥5 years of health plan membership without evidence of treatment, and 70.2% in 2017 for those with ≤14 days between HCV-antibody and PCR tests.

In multivariable analysis, there was a lower prevalence of spontaneous clearance in older birth cohorts, with PRs of 0.73 (95% confidence interval [CI]: 0.69–0.77) for patients born before 1945 and 0.79 (95% CI: 0.77–0.81) for patients born during 1945–1965 compared with those born after 1965. Males had a 21% lower prevalence of clearance than females (PR 0.79, 95% CI: 0.77–0.81). Black (PR 0.63, 95% CI: 0.59–0.66) and Hispanic patients (PR 0.94, 95% CI: 0.0.90–0.97) had a lower prevalence of clearance compared with White patients, while Asian patients had a higher prevalence (RR 1.21, 95% CI: 1.17–1.25). Finally, HCV-antibody testing in the ED was associated with a reduced prevalence of clearance (PR 0.82, 95% CI: 0.74–0.91).

DISCUSSION

In this large healthcare system, the prevalence of HCV spontaneous clearance doubled over the past decade and reached 68.7% in 2017, which is substantially higher than reported in prior natural history studies[1–3] but approaches more recent estimates from HCV screening efforts in the 1945–1965 birth cohort.[6, 7] One possible explanation for the observed trend is that patients tested earlier were more likely to be tested for diagnostic purposes or because of known risk factors rather than as true screening. Consistent with this hypothesis, we found that patients tested in the ED had a lower prevalence of clearance. We identified subgroups with a lower prevalence of clearance, highlighting populations that may benefit from targeted HCV screening. Our finding that younger patients had a higher prevalence of

clearance is consistent with prior studies and may suggest a more robust response to acute HCV infection.

Our study had several limitations. First, patients treated outside of KPNC may have been misclassified as having clearance. However, most KPNC patients have comprehensive insurance coverage and do not receive treatment outside of the health plan. Our sensitivity analyses further confirmed that this potential misclassification had minimal impact. Second, our data did not allow us to identify the timing of HCV infection or clearance. Third, although HIV and HBV coinfection were not associated with clearance, we did not assess other comorbid conditions. Strengths included the size of the KPNC population, and that it mirrors the age, sex, and race/ethnicity distributions of the surrounding population, increasing generalizability.[8]

In conclusion, our results suggest that fewer patients than previously expected will be identified as viremic through expanded HCV screening, but that some subgroups are less likely to spontaneously clear HCV. These findings can be useful in strategic planning for HCV screening and treatment on a large scale.

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Abbreviations:

HCV	hepatitis C virus
PR	prevalence ratio
HBV	hepatitis B virus
KPNC	Kaiser Permanente Northern California
ED	emergency department

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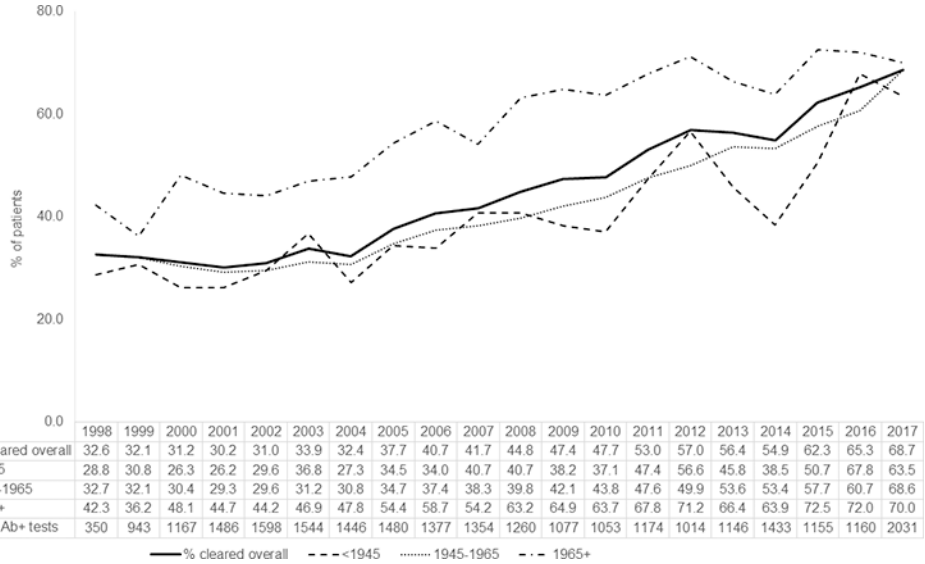

	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
% cleared overall	32.6	32.1	31.2	30.2	31.0	33.9	32.4	37.7	40.7	41.7	44.8	47.4	47.7	53.0	57.0	56.4	54.9	62.3	65.3	68.7
<1945	28.8	30.8	26.3	26.2	29.6	36.8	27.3	34.5	34.0	40.7	40.7	38.2	37.1	47.4	56.6	45.8	38.5	50.7	67.8	63.5
1945-1965	32.7	32.1	30.4	29.3	29.6	31.2	30.8	34.7	37.4	38.3	39.8	42.1	43.8	47.6	49.9	53.6	53.4	57.7	60.7	68.6
1965+	42.3	36.2	48.1	44.7	44.2	46.9	47.8	54.4	58.7	54.2	63.2	64.9	63.7	67.8	71.2	66.4	63.9	72.5	72.0	70.0
Total Ab+ tests	350	943	1167	1486	1598	1544	1446	1480	1377	1354	1260	1077	1053	1174	1014	1146	1433	1155	1160	2031

Figure 1. Prevalence of spontaneous clearance of HCV by year of PCR test during 1998–2017.

HCV, hepatitis C virus; Ab, antibody. Solid line displays percent with spontaneous clearance for all patients testing HCV-antibody positive. Dotted and dashed lines display percentage with spontaneous clearance for birth years ≥1965, 1945–1965, and <1945.