Cost-effectiveness of chronic hepatitis C screening and treatment

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Abstract

Hepatitis C virus (HCV) infection is the second most common cause of chronic liver disease in South Korea. The prevalence of HCV infection in South Korea ranges from 0.6% to 1.5%, and HCV incidence increases with age. The anti-HCV antibody test is widely used to screen for HCV infections and is cheaper than the HCV RNA assay. Underdiagnosis is a major barrier to the elimination of HCV infection.

Although there are several risk factors for HCV infection, such as intravenous drug use, blood transfusion, and hemodialysis, most HCV patients have no identifiable risk factors. Thus, universal screening for HCV in adults has been suggested to detect HCV infection. Here, we review the cost-effectiveness of HCV screening, as well as methodologies used for evaluation. Recent studies have shown that HCV screening and treatment using direct-acting antivirals are cost-effective approaches. However, the optimal timing and frequency of HCV screening are still unclear. Further studies are required to enhance awareness for elimination of HCV infection.
Natural history of hepatitis C virus infection

Hepatitis C virus (HCV) infections constitute a substantial medical and economic burden worldwide. Approximately 58 million people worldwide had chronic HCV infection in 2021. Although HCV transmission has decreased since HCV screening for blood donors was introduced in 1992, it remains the second most common cause of chronic liver diseases in South Korea. The epidemiological transition of HCV infection has varied in the past few decades. The prevalence of HCV infection in South Korea is 0.6–0.78%, and its incidence increases with age. The Korea National Health and Nutrition Examination Survey reported that the prevalence of anti-HCV antibodies among Koreans aged ≥ 10 and ≥ 20 years was 0.66% and 0.71% between 2012 and 2016, respectively. In a nationwide epidemiological study, 0.78% of participants tested positive for anti-HCV antibodies after adjustment for age, sex, and area of residence. Additionally, 30.5–46.5% of the anti-HCV antibody-positive population had detectable HCV RNA. Risk factors for HCV infections reportedly include older age, needle-stick injuries, dental procedures, multiple sexual partners, blood transfusions before 1991, and surgeries. A prospective multicenter cohort study found that drug abuse, needle-stick injury, blood transfusion before 1995, tattoos, and age were independent risk factors for HCV infections.

HCV disease burden

HCV infections are often asymptomatic, but disease progression over time leads to complications such as ascites, variceal bleeding, and liver cancer. Symptoms appear only in advanced stages of hepatitis C, when the disease is difficult to reverse and incurs considerable medical expenses. Chronic hepatitis C (CHC) may progress to cirrhosis over 20–30 years; the annual incidences of hepatocellular carcinoma (HCC) and hepatic decompensation are 1-7% and 3-6%, respectively. A study of Korean national health insurance data showed that the total cost (direct and indirect) of hepatitis C increased from 501.4 million United States dollars (USD, $) in 2008 to 607.8 million USD in 2011. Furthermore, the mean cost per month increased with disease progression from CHC to compensated cirrhosis (CC),
decompensated cirrhosis (DC), or HCC (CHC: 77 ± 80 USD; compensated cirrhosis: 98 ± 94 USD; decompensated cirrhosis: 512 ± 1,115 USD; HCC: 504 ± 717 USD).\textsuperscript{14}

In the United States (US), the economic burden of CHC exceeds 10 billion USD annually.\textsuperscript{15} A study of 34,597 CHC patients aged ≥18 years, performed between 2002 and 2013, demonstrated an all-cause healthcare cost of 19,665 USD per patient per year.\textsuperscript{16} Another study in the US found that the mean lifetime cost of CHC was approximately 64,490 USD.\textsuperscript{17} Data from the Korean National Health Insurance database showed that all-cause healthcare cost of 181,768 CHC patients was 997 USD per patient per year in 2013.\textsuperscript{18} Differences in healthcare systems and national economies contribute to this disparity. Furthermore, healthcare costs increased markedly with increasing liver disease severity. In 2013, the annual per-patient costs for CHC, liver cirrhosis, HCC, and the first year post-liver transplant were 895, 1,873, 6,945, and 67,359 USD, respectively.\textsuperscript{18}

**HCV elimination**

Before the introduction of direct-acting antivirals (DAAs) in the mid-2010s, treatment of HCV infections using pegylated interferon and ribavirin was difficult because of adverse events, low response rates, and long treatment durations. DAAs enabled physicians to treat HCV infections in various patients. Because of higher sustained virologic response (SVR), fewer adverse events, and short treatment durations, international guidelines recommend the use of DAA therapy for patients with HCV viremia. The World Health Organization (WHO) previously proposed that by reducing the number of new infections and mortality by 90% and 65%, respectively, hepatitis B and C viral infections could be eliminated by 2030. Accordingly, many countries, including the US, Japan, Australia, and Taiwan, have attempted to devise strategies for HCV elimination through political and administrative efforts. However, there remain barriers to HCV elimination. Because HCV-infected patients are generally asymptomatic until the disease has progressed to advanced cirrhosis or HCC, many of these patients are unaware of their disease. According to a telephone survey, only 9.1% (91/1003) of participants
reported receiving an HCV test.\textsuperscript{19} The most common reasons for HCV testing were routine check-ups, physician’s recommendations, and elevated liver enzymes. In this survey, 75.1\% of the respondents agreed that an anti-HCV antibody test should be included in the National Health Examination. Lack of awareness regarding hepatitis C among healthcare workers also contributes to delayed diagnosis and treatment. Active screening of asymptomatic individuals is necessary because untreated patients have the potential to spread HCV.

**Chronic hepatitis C screening**

The anti-HCV antibody test has limited application in diagnosis of HCV infections, but it is a useful screening test because of its high sensitivity and specificity ($\geq 99\%$).\textsuperscript{20} HCV screening has not been included in the Korean national health program because of the low prevalence of HCV infections in Korea, as well as the lack of validation regarding cost-effectiveness in Korea. However, global attitudes toward HCV screening are changing. The WHO and United States Centers for Disease Control and Prevention (CDC) recommend that HCV screening should be performed regardless of prevalence. The CDC recommends HCV screening at least once per lifetime for all adults, except where the prevalence of HCV infection is $< 0.1\%$.\textsuperscript{21}

Methodology and modeling studies regarding the cost-effectiveness of HCV screening in Korea are described below.

**Interpretation of cost-effectiveness studies**

Cost-effectiveness analysis (CEA) compares the economic feasibility of an intervention to a comparator (or an alternative); it is typically used interchangeably with economic evaluation (EE). Unlike cost of illness or outcomes research, CEA assesses input costs and outcomes simultaneously (Figure 1); the results are reported as the incremental cost-effectiveness ratio (ICER).\textsuperscript{22}
Types of economic evaluation

CEA can be regarded as a type of EE. There are four types of EE, distinguished based on outcome measurement methods: cost-minimization analysis (CMA), cost-benefit analysis (CBA), CEA, and cost-utility analysis (CUA). CMA can be performed when the outcome is equivalent between two alternatives. In this analysis, the alternative with lower input cost is regarded as being more economical. If outcomes are expressed in monetary units (e.g., USD), CBA can be used. CBA has been criticized because of ethical and methodological issues in converting health outcomes into monetary values; however, it is useful for performance assessment in large-scale healthcare programs. In CEA, outcomes are estimated using natural units. For example, in CEA of CHC treatments, the following natural units can be used for assessing outcomes: number of HCC cases averted, or life-years gained (LYG). Thus, CEA is preferred by clinicians because its outcomes are readily comprehensible. Numerous government healthcare agencies recommend performing CUA. In CUA, outcomes are measured in quality-adjusted life-years (QALYs), which is a combination of quantity of life (i.e., LYG) and quality of life (QoL; death and perfect health are represented by values of 0 and 1, respectively). For example, if one patient lives for 1 year with perfect health (quantity of life × QoL = 1 × 1), while another patient lives for 2 years with a value of 0.5 for QoL (2 × 0.5), the result is 1 QALY in both instances. Because outcomes are represented by a single measure (i.e., QALY), CUA can be used to compared different types of interventions (i.e., treatments for CHC vs. anticancer agents), so numerous government healthcare agencies recommend performing CUA.

Principles of CEA and study perspectives
To perform CEA, values for comparative effectiveness, costs, and utility weights are required. A meta-
analysis and systematic review provides the highest level of evidence for the comparative effectiveness of two alternatives. Costs are usually estimated from real-world data, such as electronic medical records or insurance claims. Cost estimates vary between different perspectives (i.e., payers, the healthcare system, and society). From the payer’s perspective, costs related to productivity loss need not be estimated, but from the societal perspective, these indirect costs should be included. Utility values are measured directly from the patients or public using validated tools (e.g., Eq-5D or SF-36) for assessing the QoL, or extracted from previous studies.

**Decision-analytic modeling**

Most CEA studies use decision-analytic models. These models are constructed to reflect relevant evidence, link intermediate and final endpoints, extrapolate long-term outcomes, and aid decision-making in real-world settings. There are two common model types: decision-tree and Markov models. The decision tree model is typically employed to evaluate a discrete event within a short period, while the Markov model is used for evaluating long-term or chronic illnesses that persist until death. The models consist of several health states; they should be simple while reflecting the natural history of the disease. Assume that the Markov model shown in **Supplementary Figure 1** was constructed for CEA of two CHC alternatives (a new medicine I vs. an existing medicine C). This model includes seven health states, which are represented as “bubbles”: CHC, SVR, CC, DC, HCC, liver transplantation, and death. The CEA was performed by constructing a hypothetical cohort of 1,000 patients that entered the CHC state. If the cycle length is set to 1 year, 70% (transition probability: 0.7) of the starting cohort will move to SVR, 7% will transition to CC, and 3% will transition to HCC in the new medicine group after 1 year. With repeated analyses, the distribution of the cohort changes according to the transition probability. As shown in **Supplementary Figure 1**, after cycle 1, 200 patients remain in the CHC state (200 × 0.2), while after cycle 2, 40 patients (200 × 0.2) are left. This process is repeated for all health
states via transition probabilities until the end of the time horizon (analysis period). Then, the costs and outcomes are calculated based on the distribution of the cohort in each health state.

**Incremental cost-effectiveness ratio (ICER)**

ICER is calculated from CEA or CUA; it is defined as the difference of costs divided by the difference of outcomes between two alternatives. ICER indicates the cost required to gain an additional outcome (number of cases averted or QALY), when using the intervention instead of the comparator. Although the acceptability of the additional cost depends on the individual standards, 1 GDP is generally considered to be the threshold of willingness to pay (WTP) for 1 QALY.

**Is HCV screening cost-effective in Korea?**

Table 1 summarizes the cost-effectiveness study of screening and treating CHC in Korea. According to Korean studies, one-time HCV screening and treatment is highly cost-effective, because it significantly reduces the morbidity and mortality rates of hepatitis C. Kim et al. investigated the cost-effectiveness of a one-time HCV screening and treatment program in people aged 40-70 years, using a Markov model in conjunction with a screening and treatment decision tree model. Patients were divided into cohorts based on age: 40-49, 50-59, and 60-69 years. The prevalence of infection was estimated to be 0.6%, 0.8%, and 1.53% in individuals aged 40–49, 50–59, and 60–69 years, respectively. An estimated 71.7% of the individuals were screened and 39.4% of patients were treated with DAA over 5 years. Screening resulted in the detection of 43,635 new cases across all cohorts. The model predicted that 17,193 patients would require DAA treatments after screening (40-49 years: 31.0%, 50-59 years: 30.5%, and 60-69 years: 38.4%). The costs for the HCV antibody test, HCV RNA quantitative test and ultrasound were $3.49, $147.33 and $61.43, respectively. The medical costs for CHC, CC, DC and HCC were $972.73, $1,238.02, $6,468.01, and $6,366.94,
respectively. Predicted ICER ranged from $5,714 to $8,889 per QALY gained for all patients. Screening and treatment were expected to be highly cost-effective across patients aged 40-69 years, based upon a WTP threshold of $27,512. Incremental costs associated with screening and treatment ranged from 156.47 to 181.85 million USD. An important finding in this study was that anti-HCV antibody testing was most cost-effective for individuals aged 40-49 years. This is because diagnosis and treatment initiation in younger individuals could prevent disease progression, ultimately reducing overall costs.

Kim et al.28 also investigated the cost-effectiveness of screening and DAA treatment among individuals aged 40-65 years. The prevalence of HCV infection was estimated to be 0.38–0.53%, 0.63–0.91%, and 0.8–1.32% in individuals aged 40–49, 50–59, and 60–69 years, respectively. The costs for the HCV antibody test and HCV RNA quantitative test were $3.4 and $81.5, respectively. The annual healthcare costs for CHC, CC, DC and HCC were $744.4, $947.8, $6,113.4, and $6,017.6, respectively. Screening an estimated 14,103,806 Koreans identified 82,394 individuals with anti-HCV positivity, 38,313 with HCV RNA positivity, and 31,608 with chronic HCV infection. Finally, 20,134 individuals were treated with DAA over 3 years. Screening and treatment increased QALY by 0.0015 at a cost of 11.27 USD (ICER 7,435 USD per QALY gained). The probability of the screening strategy being cost-effective was 98.8% at WTP of 27,205 USD. This screening and treatment strategy was predicted to prevent 32 HCV-related deaths, 19 cases of HCC, and 15 cases of decompensated cirrhosis per 100,000 screened individuals. The presence of low ICERs, despite the low prevalence of HCV in Korea, indicates that the cost of HCV screening and treatment is very low. Therefore, the authors conclude that a one-time HCV screening and DAA treatment program is highly cost-effective for reducing HCV-related morbidity and mortality. However, the authors did not investigate indirect, non-medical costs (e.g., lost working days) that may further increase the cost-effectiveness of screening.

Two studies have previously investigated whether a ‘screen all’ strategy would be cost-effective, compared with no screening; however, these studies did not include new DAA regimens, such as ledipasvir/sofosbuvir (LDV/SOF) in genotype 2 patients (reimbursed in Korea from June 2019). To
reflect the changes in treatment, Kim et al. investigated the cost-effectiveness of increased screening, with subsequent DAA treatment for all CHC patients aged \( \geq 40 \) years (screening and DAA treatment offered again at the age of 65 years if a participant initially refused them), compared with the current practice of screening high-risk patients only. The prevalence of HCV infection was estimated at 0.38%, 0.63%, 1.08%, and 1.64% in individuals aged 40–49, 50–59, 60–69 years and \( \geq 70 \) years, respectively. The costs for the HCV antibody test, HCV RNA quantitative test and ultrasound were $3.14, $31.70, and $125.13, respectively. The annual costs for DC and HCC were $6,161.7 and $6,065.4, respectively. A high-risk screening strategy led to the screening of 2,546,832 patients, identification of 6,539 HCV RNA-positive patients, and DAA treatment of 4,165 patients. A “screen all once” scenario led to the screening of 15,818,833 patients, identification of 40,614 HCV RNA-positive patients, and DAA treatment of 25,871 patients. A “screen all twice” scenario led to the screening of 4,429,273 additional patients once they reached 65 years of age. Using a Markov disease progression model, the “screen all twice” scenario led to the lowest rates of advanced liver disease, compared with “screen all once” and “high-risk only” screening. A “screen all once” strategy led to 49,612 more QALYs, compared with a risk-based screening strategy; a “screen all twice” strategy led to a further increase of 5,075 QALYs. Using the same LDV/SOF treatment for GT1 and 2, the ICERs of the “screen once” and “screen twice” strategies were $4,535.96 and $4,636.33, respectively, compared to the high-risk screening. When two-time screening was compared to one-time screening (reference), the ICER of the “screen all twice” strategy was $3,558.18. Thus, the authors concluded that screening twice, followed by treatment if required, would be more cost-effective than the current risk-based screening approach. Another study demonstrated that increasing hepatitis C screening and DAA coverage by national health insurance are necessary. The estimated prevalence rate of hepatitis C antibody in Korea is 0.7%. The costs for the HCV antibody test and HCV RNA quantitative test were $20 and $150, respectively. The treatment costs for CHC, CC, DC and HCC were $10,000, $2,064, $6,146, and $8,000, respectively. This study estimated that, in 2016, approximately 46% of Koreans with chronic HCV infection and 16% with HCV antibodies received DAA treatment. This study used a compartmental age-sex structured
model of hepatitis C progression to analyze the cost-effectiveness of scaled up hepatitis C screening and treatment with DAAs. Policy scenarios included: status quo, population screening from age 60, population screening from age 40, and screening from age 20 were cost-effective compared with no treatment in terms of averted infections. Increased screening for people aged ≥ 60 and ≥ 40 was estimated to avoid 15,231 and 17,374 HCV infections, respectively, as well as 5,310 and 5,798 deaths, respectively, for the period from 2017 to 2050.

Hepatitis C screening: experience in other countries

Approximately 2.7 million people in the US have chronic HCV infection. Of HCV-infected persons, 81% were born between 1945 and 1965. In the US, high-risk groups (i.e., intravenous drug abusers, patients who received a blood transfusion before 1992, hemodialysis patients, inmates, babies of HCV-infected mothers, and individuals with tattoos) and birth cohorts (cohorts with a high prevalence of HCV infection) are screened and treated for HCV. When screening a birth cohort for treatment with interferon/ribavirin, the ICER was $15,700/QALY, compared with the high-risk group. With respect to pegylated-interferon/ribavirin/DAA therapy, the ICER was $35,700/QALY; treatment following birth cohort screening was reportedly cost-effective. Therefore, screening all individuals born between 1945 and 1965 is recommended by the CDC. Because treatment outcomes have significantly improved with the use of DAAs, in 2020 the CDC recommended that all individuals aged ≥ 18 years should undergo at least one screening test. Recently, Eckman et al. analyzed the cost effectiveness of universal one-time screening for HCV infection in the US in the era of pangenotypic DAA therapy, compared with the current standard of birth cohort screening. Using the Markov state transition model, universal one-time screening of the general US population with a with a prevalence of HCV antibody greater than 0.07% cost less than $50,000/QALY compared with a strategy of no screening. The model also showed that, compared with 1-time birth cohort screening, universal 1-time screening and treatment with pangenotypic DAA cost $11,378/QALY gained. This study highlighted the importance of HCV
screening in young persons in the US.

HCV infection is the leading cause of cirrhosis and liver cancer in Japan, where approximately 2 million individuals were estimated to be infected with HCV in the year 2000.\textsuperscript{35} According to a cost-effectiveness study based on the national HCV screening program, the rates of HCV infection in the general population and high-risk groups were 0.36\% and 0.81\%, respectively.\textsuperscript{36} Screening for HCV is reportedly cost-effective in both high-risk groups and the general population ($749–2,297 and $848–4,825, respectively). Due to the high prevalence of HCV infection, nationwide screening for HCV was initiated in Japan in 2002. A recent study compared the cost-effectiveness of screening plus IFN-free therapy, no screening and screening plus IFN-based therapy.\textsuperscript{37} The base-case model involved screening all Japanese individuals aged 40–89 years. Screening plus IFN-free therapy was more cost-effective than no screening and screening plus IFN-based therapy under a WTP of $45,163 per QALY gained in the base-case model, with ICERs of $10,157/QALY and $9802/QALY, respectively. Importantly, in the age subgroup analysis, the ICERs were lower for the younger population (Table 2). Except in the population aged 85 years, screening plus IFN-free therapy was cost-effective under the WTP setting. Based on this result, it would be reasonable to screen all adults aged below 85 years for HCV infection in Japan.

According to a systematic review from Europe, the cost of prolonging survival by 1 year through hepatitis C screening ranged between $17,520 and $2,856,\textsuperscript{38} suggesting that screening is cost-effective only in areas with a high prevalence of HCV infection. Unlike the US and Japan, the prevalence of HCV infection is not very high in England; an estimated 143,000 people had HCV infection in that country in 2015.\textsuperscript{39} Another study evaluated the cost-effectiveness of a one-time HCV screening intervention for individuals born between 1950 and 1979, as part of a National Health Service (NHS) health check.\textsuperscript{40} The base-case ICERs ranged from $10,408 to $33,411, with the lowest ICER seen for people born in 1970-1974, and the highest for people born in 1950-1954. Thus, birth cohort screening in England is likely to be cost-effective for younger birth cohorts. However, it is uncertain whether
HCV screening will be cost-effective for other birth cohorts.

France has one of the most extensive HCV screening programs. A health economic study from France aimed to evaluate the cost-effectiveness of different HCV screening strategies. There were five screening scenarios: S1, current strategy targeting at-risk population; S2, S1 plus all men aged 18–59 years; S3, S1 plus all individuals aged 40–59 years; S4, S1 plus all individuals aged 40–80 years; S5, all individuals aged 18–80 years (universal screening). Universal screening was more effective and cost-effective ($36,446/QALY) than targeting people aged 40–80 years. However, this strategy is cost-effective only if treatment is started at an early stage of infection, and not if treatment is started in advanced stages of fibrosis.

The prevalence of HCV seroprevalence in Canada is estimated to be 0.3–0.9%. Despite being neighboring countries, the epidemiology of HCV and health care system in Canada is different from those in the US. A Canadian study analyzed the cost-effectiveness of one-time HCV screening for individuals aged 25–64 and 45–64 years. The ICERs ranged from $34,359 to $44,034 per QALY gained, compared with no screening, depending on the age group screened and antiviral therapy administered. The authors concluded that one-time program to screen for and treat HCV infection in Canada, aimed at birth cohort populations (25–64 or 45–64 years of age), is likely to be cost-effective. They also stated that an increase in treatment uptake rates would further enhance the cost-effectiveness of the HCV screening program.

**Future perspectives**

The Global Health Sector Strategy on Viral Hepatitis (2016–21), published by the WHO, calls on all countries to establish firm targets for elimination of viral hepatitis. For a nation to have successful HCV elimination, all the steps of care-of-cascade from awareness of disease to treatment have to be kept. Among the steps, national screening might be the most important. This is why national health
policy should have a HCV screening program to reduce the HCV-related disease burden.

Hepatitis C testing should be performed as part of routine screening in individuals with progressive liver disease after the age of 40 years. In a 2019 survey of the general public, more than 75% of respondents believed that screening for hepatitis C is necessary.\textsuperscript{19} Because of its low prevalence, hepatitis C testing has not been included in national screening programs. However, the findings of various studies highlighting the importance of HCV screening suggest that it must be included in national health policy.
References


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<td>1) $4,535.96  2) $4,636.33  3) REF</td>
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<td>Kim JY, et al. (2019)</td>
<td>1) No treatment 2) Status quo 3) Screening population aged over 60 years 4) Screening population aged over 40 years 5) Screening population aged over 20 years</td>
<td>Compartmental age-sex structured model</td>
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<td>The expansion of DAAs coverage by national health insurance and scale-up of hepatitis C screening and treatment with DAAs are cost-effective</td>
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<td>Kim KA, et al. (2018)</td>
<td>1) No screening 2) Screening once (aged 40-65 years) and DAA treatment</td>
<td>Markov model</td>
<td>Costs and QALY</td>
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<td>Kim DY, et al. (2017)</td>
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<td>1) REF  2) $5,385.36  3) $6,451.44  4) $8,380.46</td>
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Abbreviations: HCV, hepatitis C virus; Anti-HCV Ab, anti-hepatitis C virus antibody; DCC, decompensated cirrhosis; HCC, hepatocellular carcinoma; QALYs, quality-adjusted life-years; WTP, willingness to pay; GDP, gross domestic product; GLE/PIB, glecaprevir/pibrentasvir; LDV/SOF, ledipasvir/sofosbuvir; REF, reference;
### Table 2. Cost-effective studies of screening and treatment for hepatitis C in other countries

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<tr>
<td>Eckman MH, et al. 34</td>
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<td>Universal screening was cost effective compared with birth cohort screening when antibody positivity was greater than 0.07%</td>
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<td>(2019)/US</td>
<td>Birth-cohort screening (born from 1945 through 1965)</td>
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<td>Nagai K, et al. 37</td>
<td>Population aged 45</td>
<td>Markov model</td>
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<td>Population aged 75</td>
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<td>Population aged 85</td>
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<td>Williams J, et al. 40</td>
<td>Born from 1950 through 1954</td>
<td>Markov model</td>
<td>Birth cohort screening is likely to be cost-effective for younger birth cohorts</td>
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<td>Born from 1975 through 1979</td>
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<td>$11,207</td>
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<tr>
<td>Wong WW, et al. 42</td>
<td>No screening</td>
<td>Markov model</td>
<td>A selective one-time HCV screening program for people 25-64 or 45-64 years of age in Canada would likely be cost-effective</td>
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<td>One-time screening (age 45-64)</td>
<td></td>
<td></td>
<td>$44,034</td>
</tr>
<tr>
<td>Sylvie DB, et al. 41</td>
<td>Screening risk population</td>
<td>Markov model</td>
<td>Universal screening is the most effective screening strategy for HCV</td>
<td>REF</td>
</tr>
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<td>(2018)/France</td>
<td>One-time screening (age 18-59)</td>
<td></td>
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<td>One-time screening (age 40-59)</td>
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<td>One-time screening (age 40-80)</td>
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<td>Universal screening (age 18-80)</td>
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**Abbreviations:** ICER, incremental cost-effectiveness ratio; US, united states; QALY, quality-adjusted life years; IFN, interferon; DAA, direct-acting antivirals; UK, united kingdom; HCV, hepatitis C virus; REF, reference
Figure legends

**Figure 1.** The concept of cost-effectiveness analysis (Source: Drummond et al., 2015. Fig. 1.1. Re-quotation)

Cost-effectiveness analysis is characterized to assess both costs and outcomes of the intervention and the comparator simultaneously.
Supplementary figure 1. The example of Markov model for cost-effectiveness analysis of a treatment in patients with chronic hepatitis C

This model is composed of seven health states (represented as bubbles), which reflect the natural history of chronic hepatitis C. The numbers accompanying the arrow are the transition probabilities per cycle from one health state to another. For example, if the cycle length is set as 1-year, 0.7 (in bold) means that 70 out of 100 patients with chronic hepatitis C will move to a sustained virological response for 1 year.