# The cost-effectiveness of integrating simplified HCV testing into HIV pre-exposure prophylaxis (PrEP) and treatment services among men who have sex with men in Taiwan

Huei-Jiuan Wu,[a,*] Tanya L. Applegate,[a] Jisoo A. Kwon,[a] Evan B. Cunningham,[a] Jason Grebely,[a] Richard T. Gray,[a,b] and Sophy T. F. Shih[a,b]

[a]The Kirby Institute, University of New South Wales Sydney, Sydney, NSW 2052, Australia

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## Summary

**Background** Simplified hepatitis C virus (HCV) testing integrated into existing HIV services has the potential to improve HCV diagnoses and treatment. We evaluated the cost-effectiveness of integrating different simplified HCV testing strategies into existing HIV pre-exposure prophylaxis (PrEP) and treatment services among men who have sex with men (MSM) in Taiwan.

**Methods** Mathematical modeling was used to assess the cost-effectiveness of integrating simplified HCV tests (point-of-care antibody, reflex RNA, or immediate point-of-care RNA) with HCV treatment into existing HIV prevention and care for MSM from a healthcare perspective. The impact of increasing PrEP and HIV treatment coverage among MSM in combination with these HCV testing strategies was also considered. We reported lifetime costs (2022 US dollars) and quality-adjusted life years (QALYs) and calculated incremental cost-effectiveness ratios (ICERs) with a 3% annual discounting rate.

**Findings** Point-of-care HCV antibody and reflex RNA testing are cost-effective compared to current HCV testing in all PrEP and HIV treatment coverage scenarios (ICERs <$32,811/QALY gained). Immediate point-of-care RNA testing would be only cost-effective compared to the current HCV testing if coverage of HIV services remained unchanged. Point-of-care antibody testing in an unchanged HIV services coverage scenario and all simplified HCV testing strategies in scenarios that increased both HIV PrEP and treatment coverage form an efficient frontier, indicating best value for money strategies.

**Interpretation** Our findings support the integration of simplified HCV testing and people-centered services for MSM and highlight the economic benefits of integrating simplified HCV testing into existing services for MSM alongside HIV PrEP and treatment.

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**Keywords:** Point-of-care testing; Integrated services; Hepatitis C; HIV oral-pre-exposure prophylaxis; Men who have sex with men

## Introduction

The complexity of the conventional HCV diagnostic algorithm requiring multiple clinic visits to receive a diagnosis, impedes HCV treatment access.[1] There is a need for simplified HCV diagnostic approaches that shorten the time from diagnosis to treatment and reduce loss to follow-up. One such approach is point-of-care testing, which offers on-site testing with rapid results to increase access to diagnosis, care, and treatment. Specifically, point-of-care RNA testing has demonstrated its potential to expedite HCV diagnosis and treatment within one clinic visit.[2–5] Other simplified testing approaches, such as reflex HCV RNA testing, which requires blood samples collected at a single visit for both

*Corresponding author.
*E-mail address:* jjwu@kirby.unsw.edu.au (H.-J. Wu).
[b]Contributed equally.

## Research in context

### Evidence before this study

We searched PubMed and Embase databases for studies published from their inception to 14 September 2023 using the terms (HCV OR Hepatitis C OR Hepatitis C virus) AND (cost-effectiveness) AND ((testing) OR (test) OR (diagnose)) AND ((men who have sex with men) OR (MSM) OR (gay men) OR (bisexual men) OR (HIV pre-exposure prophylaxis [MeSH Terms])) to identify existing cost-effectiveness studies for HCV testing strategies among men who have sex with men. Our search identified 18 articles. Most studies evaluated the cost-effectiveness of HCV testing and treatment among MSM living with HIV only and did not consider HIV-negative MSM or those taking HIV pre-exposure prophylaxis (PrEP). Only one study evaluated the case-finding strategies among MSM regardless of status of HIV infection and found that scaling-up HCV screening in HIV-negative MSM on PrEP could be cost-effective in the UK but did not consider which screening technology and approach would be most cost-effective to achieve HCV elimination.

### Added value of this study

We used an epidemiological HCV transmission model to estimate the cost-effectiveness of integrating simplified HCV testing strategies into HIV PrEP and treatment services among Taiwanese MSM. To the best of our knowledge, no cost-effectiveness analysis of such intervention has been evaluated. Our findings identify which simplified HCV testing strategy within the framework of HIV PrEP and treatment services is more cost-effective to implement among MSM. This research provides valuable economic evidence to guide integration of point-of-care HCV testing and people-centered HCV simplified services delivery for MSM. This study offers critical insights for policymakers to optimize resource allocation and addressing the potential evolving HCV epidemic among MSM.

### Implications of all the available evidence

Our findings lend support to the integration of simplified HCV testing and people-centered services for MSM. We identified five strategies (point-of-care antibody testing in HIV PrEP and treatment coverage remained unchanged scenario and all testing strategies under the scenario that both HIV PrEP and treatment coverage expanded) representing the most economically advantageous options for MSM. These results highlight the economic benefits of integrating simplified HCV testing into existing services for MSM alongside the added benefits of scaling up HIV PrEP and treatment in the context of the HCV epidemic. These findings offer nuanced insights that extend beyond cost-effectiveness, guiding decision-makers for shaping HCV prevention policies and planning for MSM to facilitate progress toward HCV elimination targets.

antibody and RNA testing if needed, is also efficacious at enhancing HCV diagnosis.[6,7]

Alongside simplified testing, adopting a people-centered approach is crucial in mitigating the gaps between HCV testing and treatment. Populations vulnerable to HCV often face limited access to healthcare services due to social stigma and discrimination, creating substantial obstacles that impede access to HCV treatment.[8,9] Therefore, integrating HCV testing into the existing services for populations at risk of HCV infection is pivotal to expand the reach and uptake of HCV testing and treatment.

Recent evidence showed the HCV epidemic has evolved among men who have sex with men (MSM) with increasing HCV burden among those HIV negative.[10] This increase has been associated with the biomedical advances in HIV prevention, including treatment as prevention (TasP)[11] and HIV pre-exposure prophylaxis (PrEP).[12] As such, it is critical to integrate HCV testing and treatment into existing HIV services for MSM to control the evolving HCV epidemic in MSM.

Taiwan has one of the Western Pacific region's highest HCV prevalence rates among the general population as well as in MSM, with 5.5% and 0.4% of HCV seroprevalence among MSM living with HIV and HIV-negative MSM, respectively before PrEP became available in 2016.[13] Additionally, there has been an observed increase in HCV incidence among MSM living with HIV in Taiwan, from 16.4 to 28.1 per 1000 person-years of follow-up between 2011 and 2018.[14] Although access to HCV treatment has been universally available in Taiwan since 2019, testing and treatment coverage has been low among MSM on PrEP, despite its recommendation in the national HIV PrEP guidelines.[15,16] This low testing and treatment coverage is a missed opportunity to control the HCV epidemics among MSM.

The impact and cost-effectiveness of HCV testing integrated into HIV services among MSM has been done predominately in MSM living with HIV in western Europe.[17–19] Given the evolving HCV epidemic among MSM, there is a significant knowledge gap in cost-effectiveness of integrating HCV and HIV services for MSM, irrespective of their HIV and PrEP status. Only one previous study conducted in the United Kingdom assessed the cost-effectiveness of HCV screening among MSM regardless of HIV status.[20] However, that study focused on the impact of HCV screening frequency and population prioritization rather than on interventions that simplify HCV testing and treatment services.

In this study, we aim to evaluate the cost-effectiveness of integrating simplified HCV testing

into HIV services among MSM engaged in HIV services, including MSM living with HIV and MSM on PrEP in Taiwan. The results of this study could serve as a foundation for formulating HCV prevention policy recommendations, as well as support strategic planning and resource allocations to key population programmes in Taiwan and the Western Pacific region.

## Methods

A previously developed dynamic compartmental model was used to evaluate the cost-effectiveness of integrating different simplified HCV diagnostic strategies (based on the point-of-care testing technologies) into HIV PrEP and treatment services for the entire Taiwanese MSM population.[21] The epidemiological impact of HCV diagnostic strategies was modelled for nine years (2022–2030), with healthcare costs and quality-adjusted life years (QALYs) further tracked for those living with HCV to the end of 2090 to capture long-term costs and health gains. The analysis was conducted from the perspective of Taiwanes government as the payer for both HCV and HIV healthcare and services, and reported in 2022 US Dollars ($) with adjustment for inflation and purchasing power parity (PPP).[22–24] All costs and QALYs were discounted at 3% per annum (following Taiwan's Guidelines of Methodological Standards for Pharmacoeconomic Evaluation).[25] We applied one gross domestic product (GDP) per capita as the threshold for value judgement ($32,811).[26] The study design diagram is in the Supplementary Material Figure S2.

### Epidemiological model

In this modelled economic evaluation, the effect of HCV testing on the HCV epidemic among MSM was estimated using a deterministic compartmental HCV model, which includes the cascade of care and detailed HCV disease progression, shown in Supplementary Material Figure S1. In the model, the MSM population was stratified by the status of HIV infection, PrEP use, and HIV treatment to reflect the differences in the HCV epidemic and the level of health services engagement among MSM. We estimated input parameter values using data from Taiwan. If no local data were available, we sourced parameter estimates from published literature with data preference sharing similar context with Taiwan. We used available demographic and epidemiological data to calibrate the model to reflect HCV prevalence and incidence among Taiwanese MSM over 2004–2022 and future trends up to 2030. Treatment initiation probability for MSM living with diagnosed HIV was extracted from ATHENA cohort study[27] due to limited generalizability of Taiwan-specific data from a single-center study.[28] Lower health service engagement for other sub-populations was assumed, referencing the relative increase reported in the ATHENA study (shown in Table 1).[27] We applied simplified HCV testing strategies based on HCV antibody and RNA testing followed by treatment among MSM engaged with HIV prevention services and care (MSM on PrEP and HIV treatment). More details on the epidemiological model are provided in the Supplementary Material (Figures S3–S8). No ethical approval or consent was required since this study used publicly available data only.

### Scenarios and assumptions

Using the model, we simulated the epidemiological impact of each HCV simplified testing scenario on the HCV epidemic between 2022 and 2030. We assumed each testing strategy would replace the current HCV testing approach in the targeted population (MSM on HIV PrEP and/or treatment) within a 2-year scale-up period (2022–2024).

The effect of simplified HCV testing strategies was captured in the model by changing the HCV antibody testing, HCV RNA testing, and HCV treatment initiation rates (Table 1). We parameterized each HCV testing strategy by estimating the relative change in HCV testing and treatment initiation rates compared to the current practice of HCV testing using the data from a meta-analysis.[6] The testing probability of each testing strategy reflects the likelihood of being tested at least once during a year. We assumed the annual testing probability within each population would saturate at 98% allowing the possibility of some loss to follow-up. Fig. 1 illustrates the current HCV testing paradigm and the algorithms for the simplified HCV testing strategies based on the point-of-care testing technologies. These strategies are as follows.

(0) Current HCV testing:

Current practice for HCV testing in Taiwan requires three clinic visits for HCV treatment initiation. Venipuncture blood sample collection for laboratory-based HCV antibody testing is followed by a second venipuncture sample for confirmation of current HCV infection through laboratory-based HCV RNA testing, followed by a prescription of HCV treatment if HCV is detected. This current HCV testing served as a reference strategy for determining integrating simplified HCV testing approaches into existing services for populations at risk of HCV infection, which could result in a higher uptake of testing and treatment relative to current levels.

(1) Point-of-care HCV antibody testing:

The point-of-care HCV antibody testing strategy requires three visits including one non-clinical visit and two clinic visits for HCV treatment. It replaces laboratory-based HCV antibody testing with onsite (nonclinical setting) point-of-care HCV antibody testing

| | HCV testing strategies | | | |
|---|---|---|---|---|
| | Current HCV testing | Point-of-care antibody testing | Reflex RNA testing | Point-of-care RNA testing |
| **Anti-HCV testing rate (%/year)** | | | | |
| HIV-negative not on PrEP | 25.0% (18.8%–31.3%) | –[a] | –[a] | –[a] |
| HIV-negative on PrEP | 25.0% (18.8%–31.3%) | 74.8% (34.8%–98.0%) | 75.3% (74.3%–98.0%) | NA |
| HIV-positive and undiagnosed | 25.0% (18.8%–31.3%) | –[a] | –[a] | –[a] |
| HIV diagnosed and on treatment | 80.0% (60.0%–98.0%) | 98.0% (98.0%–98.0%) | 98.0% (98.0%–98.0%) | NA |
| **HCV RNA testing rate (%/year)** | | | | |
| HIV-negative not on PrEP | 50.0% (37.5%–62.5%) | –[a] | –[a] | –[a] |
| HIV-negative on PrEP | 50.0% (37.5%–62.5%) | 50.0% (37.5%–62.5%) | 89.0% (75.0%–98.0%) | 36.8% (26.5%–56.0%) |
| HIV-positive and undiagnosed | 50.0% (37.5%–62.5%) | –[a] | –[a] | –[a] |
| HIV diagnosed and on treatment | 80.0% (60.0%–98.0%) | 80.0% (60.0%–98.0%) | 89.0% (75.0%–98.0%) | 98.0% (98.0%–98.0%) |
| **DAA initiation rate (%/year)** | | | | |
| HIV-negative not on PrEP | 27.0% (20.2%–33.7%) | –[a] | –[a] | –[a] |
| HIV-negative on PrEP | 27.0% (20.2%–33.7%) | 27.0% (20.2%–33.7%) | 27.0% (20.2%–33.7%) | 36.2% (15.4%–67.4%) |
| HIV-positive and undiagnosed | 27.0% (20.2%–33.7%) | –[a] | –[a] | –[a] |
| HIV diagnosed and on treatment | 67.8% (50.9%–84.8%) | 67.8% (50.9%–84.8%) | 67.8% (50.9%–84.8%) | 90.9% (39.2%–98.0%) |
| **Cost of HCV diagnosis** | **$215.0** | **$195.1** | **$195.1** | **$208.1** |
| HCV antibody test | $17.8 | $18.3 | $18.3 | – |
| Outpatient visit | $40.7 | $20.3 | $20.3 | $20.3 |
| HCV RNA test | $156.5 | $156.5 | $156.5 | $187.8 |
| **Cost of HCV treatment** | **$18,157.4** | | | |
| Pre-treatment assessment | $327.0 | | | |
| During HCV treatment | $17,405.0 | | | |
| End of treatment monitoring | $190.3 | | | |
| SVR monitoring | $235.1 | | | |
| **Cost of HCV management** | **$208.8–$39,593.3** | | | |
| Regularly checkups per year for people diagnosed with HCV | $208.8–$39,593.3[b] | | | |
| Regularly checkups/year for people cured from chronic HCV | $208.8 | | | |

The HCV antibody testing rate is defined as the annual percentage of HCV infected people receiving at least one antibody test; the RNA testing rate defined as the annual percentage of people already diagnosed antibody positive who receive HCV RNA testing; and the DAA initiation rate is defined as the annual percentage of people diagnosed RNA positive who initiate HCV DAA treatment. The annual percentage who receives HCV antibody testing, HCV RNA testing and initiate HCV DAA treatment are converted to a proportion per timestep in the model. [a]The HCV testing strategies only targeted at MSM engaged in HIV PrEP and treatment services and HCV testing strategies will replace the current practice of HCV testing among these populations with the rate of HCV testing and treatment remaining as in current practice for HIV-negative MSM not on PrEP and MSM living with undiagnosed HIV. HCV antibody testing was not required in the point-of-care RNA testing scenario where we assumed the annual percentage of receiving point-of-care HCV RNA testing replaced current antibody testing. [b]Costs varied based on the liver fibrosis stage. All cost values are in 2022 USD.

***Table 1:*** **Key HCV testing and treatment parameters and associated costs for HCV testing strategies.**

using fingerstick blood samples. This is followed by confirmation of current HCV infection as per the current practice scenario. This strategy could expand HCV screening into nonclinical settings and reflect outreach services providing HIV prevention and care.

(2) Reflex RNA testing:

Reflex RNA testing requires two clinic visits to access HCV treatment. An initial antibody point-of-care test at clinics is followed by a venipuncture sample collected for a laboratory-based HCV RNA test if the antibody test is positive during the same clinic visit, with HCV treatment provided on the second visit if the RNA test confirms HCV infection.

(3) Immediate point-of-care RNA testing:

The immediate point-of-care RNA testing strategy incorporates a point-of-care HCV RNA test onsite only with treatment provided immediately onsite following a positive result. This is a single visit test and treat strategy.

Taiwan is committed to eliminating HIV by 2030 with the focus on scaling-up PrEP and meeting the UNAIDS 95-95-95 HIV care cascade targets.[29] To reflect the potential increase in HIV PrEP and treatment coverage, in line with Taiwan CDC's policy for HIV elimination by 2030, we applied each of these HCV testing strategies to four different PrEP and HIV treatment scale-up scenarios. For each PrEP and HIV

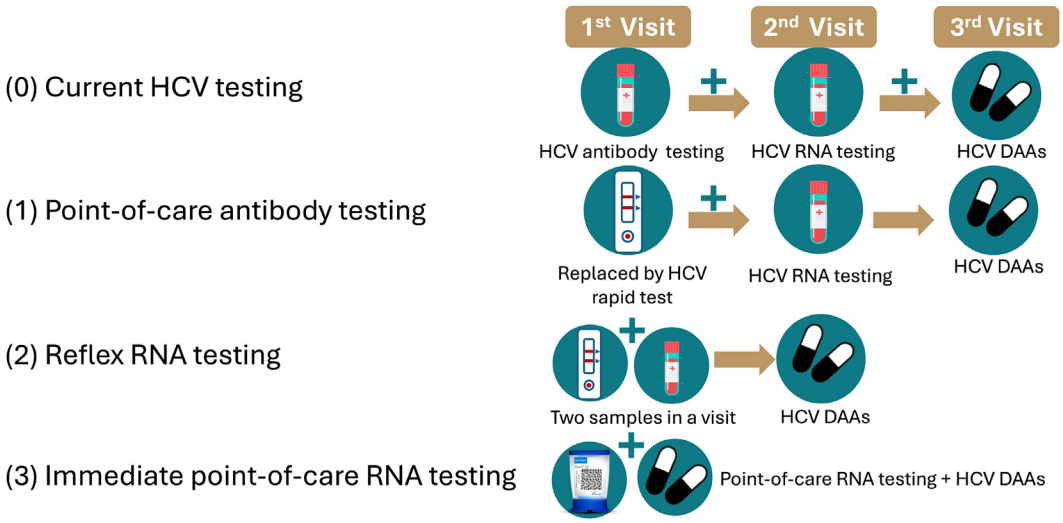


***Fig. 1:*** Current HCV testing paradigm and the algorithms of simplified HCV testing strategies.

treatment scale-up scenario, we assumed the coverage of HIV PrEP and treatment would increase linearly between 2022 and 2030.

(S1) Current coverage of HIV PrEP and treatment:

Coverage of PrEP at 1.6% of all HIV negative MSM and coverage of HIV treatment at 84% of all HIV-positive MSM until 2030.

(S2) Only PrEP coverage increases:

Coverage of PrEP reaching 20% by 2030 and HIV treatment coverage remaining at 84%.

(S3) Only HIV treatment coverage increases:

Coverage of PrEP remaining at 1.6%, and coverage of HIV treatment reaching 95% by 2030.

(S4) Both PrEP and HIV treatment coverage increases:

Coverage of PrEP reaching 20% and coverage of HIV treatment reaching 95% by 2030.

### Costing

Only the costs related to HCV care were considered in the analysis since we focused on the cost impact of HCV testing in addition to existing HIV PrEP and treatment. Those costs associated with the health care items are reimbursed by the National Health Insurance (Taiwan NHI), which is a single-payer and universal coverage national healthcare system.[30] It covers over 99% of the 23 million residents of Taiwan and this system also deals with the financing of healthcare and reimbursement of all medical claims.[31] We separated HCV costs into three categories related to diagnosis, treatment, and management. Firstly, an ingredients approach of costing was used to identify all resources required to perform testing and clinical examination for HCV diagnosis. The cost for HCV diagnosis in each HCV testing strategy is shown in Table 1. Under current practice, the cost for HCV diagnosis was extracted from a single fee-for-service schedule (NHI-FFS), a point-based fee schedule.[32] The cost of performing point-of-care antibody testing was obtained through personal communication with an HIV case manager, who provides HIV/HCV screening services by point-of-care antibody testing in correctional settings in northern Taiwan. The cost for an HCV diagnosis through a reflex RNA test was assumed to be equal to the cost of performing a point-of-care antibody test plus the cost of an RNA test. The cost of an RNA test was obtained from the Taiwan NHI-FFS, which includes staff labor costs and other resource costs. Point-of-care RNA testing, though not widely used in Taiwan, would be reimbursed under the same item code as HCV RNA nucleic acid testing (NAT), with additional costs for reporting immediate results, obtained from a pathology lab scientist in Taiwan (see Supplementary Material 3 for cost estimations).

Secondly, the cost of HCV treatment included the costs of pre-treatment assessment, HCV treatment, and clinic visits and examinations during the treatment period. Pre-HCV treatment assessment cost was sourced from the NHI-FFS,[32] and the items included were based on the HCV policy guidelines in Taiwan.[33] The cost of medications for HCV treatment was based

on the Taiwan National Health Insurance Pharmaceutical Benefits and Reimbursement Schedule (NHI-PBRS).[34] The cost of clinic visits and examination during the period of direct-acting antiviral (DAA) treatment was obtained from published studies, in which cost analysis was conducted using the Taiwan National Health Insurance research database.[35] The cost of achieving SVR after treatment completion was extracted from NHI-FFS.[32]

Thirdly, cost of HCV management included the cost of people diagnosed with HCV but who have not received HCV treatment and those who achieved SVR but required post-SVR monitoring for their liver fibrosis. The cost for HCV management was based on the NHI-FFS and published literature, in which cost analysis was conducted using the Taiwan NHI research database.[36] We assumed people who were diagnosed with HCV and liver fibrosis at Metavir F0–F4 stages but have not received HCV treatment only required follow-up checkups, and no other cost related to liver fibrosis and HCV was involved. We also assumed people who were cured from acute HCV or chronic HCV at Metavir F0–F2 stages did not require regular checkups. Key costs for diagnosis, treatment, and management are shown in Table 1.

For those cost extracted from published literature (reported in New Taiwanese Dollars, NTD), inflation adjustment to the reference year (2022) was applied by using Taiwan consumer price index rates then converted to US dollars by using the PPP conversion rate (NT$14.06 = US$1).[24] See Supplementary Section 3 for details of cost measurement for HCV diagnosis, treatment, and management.

### Health utilities

The health-related quality of life (HRQoL) for each state in the model was extracted from published literature and measured by EuroQol 5-Dimensional 5-Level version (EQ-5D-5L), EuroQol 5-Dimensional 3-Level version (EQ-5D-3L) and SF-6D metric derived from the SF-36 instrument.[37–40] The values ranged from 0 (death) to 1 (perfectly healthy without disability) for different health states and subgroups. Detailed health utility estimates and extractions from the literatures are shown in Supplementary Section 4.

### Model analyses

In the model, health utilities and costs were multiplied by the number of people in the corresponding compartments and transitions between compartments at each time step and summed to give quality-adjusted life years (QALYs) and annual costs, respectively. Lifetime total costs and health outcomes (QALYs) were calculated by adding up all costs and QALYs and discounted at 3% per annum over a 68-year time horizon (to 2090) to capture long-term effects of HCV infection as well as population prevention benefits associated with HCV treatment. The incremental cost-effectiveness ratio (ICER) was calculated by comparing the difference in discounted costs (incremental cost) with the difference in discounted QALYs (incremental outcomes) between each of the simplified HCV testing strategies and the current HCV testing strategy in each HIV PrEP and treatment coverage scenario among the MSM population. We also estimated the cost-effectiveness of each strategy pairwise to identify the cost-effectiveness efficiency frontier, which joins the incrementally most cost-effective interventions as resources increase.

There is no explicit willingness-to-pay threshold for value judgement in healthcare and technology assessment in Taiwan and there is no consensus in the use of appropriate thresholds.[41] Accordingly, we reported our results in alignment with the WHO recommendation of an ICER less than or equal to the Gross Domestic Product (GDP) per capita as cost-effective.[26] The GDP per capita in Taiwan was US$32,811 in 2022,[42] implying that ICERs below $32,811/QALY would be considered cost-effective in Taiwan.

### Sensitivity and uncertainty analyses

We varied all input parameters simultaneously with 1000 model runs to conduct a probabilistic sensitivity analysis to assess the impact of uncertainty on ICERs and report the median with the 2.5th and 97.5th percentiles representing the uncertainty range. Secondly, we computed partial rank correlation coefficients (PRCC) to quantify the relative contribution of each parameter to the uncertainty in the following outputs: 1) HCV incidence between 2022 and 2030; 2) lifetime cost for HCV; and 3) lifetime QALYs for the current practice scenario with the current HIV PrEP and treatment coverage (see Supplementary Material 6 for sensitivity analysis).

All simulations were performed using R (version 4.2.1).[43,44] The codes for the final model are publicly available under an open access license.[21] The results showed as the median of 1000 estimated parameter sets, along with a 95% uncertainty interval (95% UI), which percentiles of 2.5 and 97.5 of the parameter distribution were selected as 95% uncertainty limits derived from the 1000 simulations.

### Role of the funding source

None of the funding parties had any role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

## Results

### Epidemiological impact of the HCV testing strategy

Under the current HCV testing strategy and unchanged PrEP and HIV treatment coverage scenario (S1), HCV

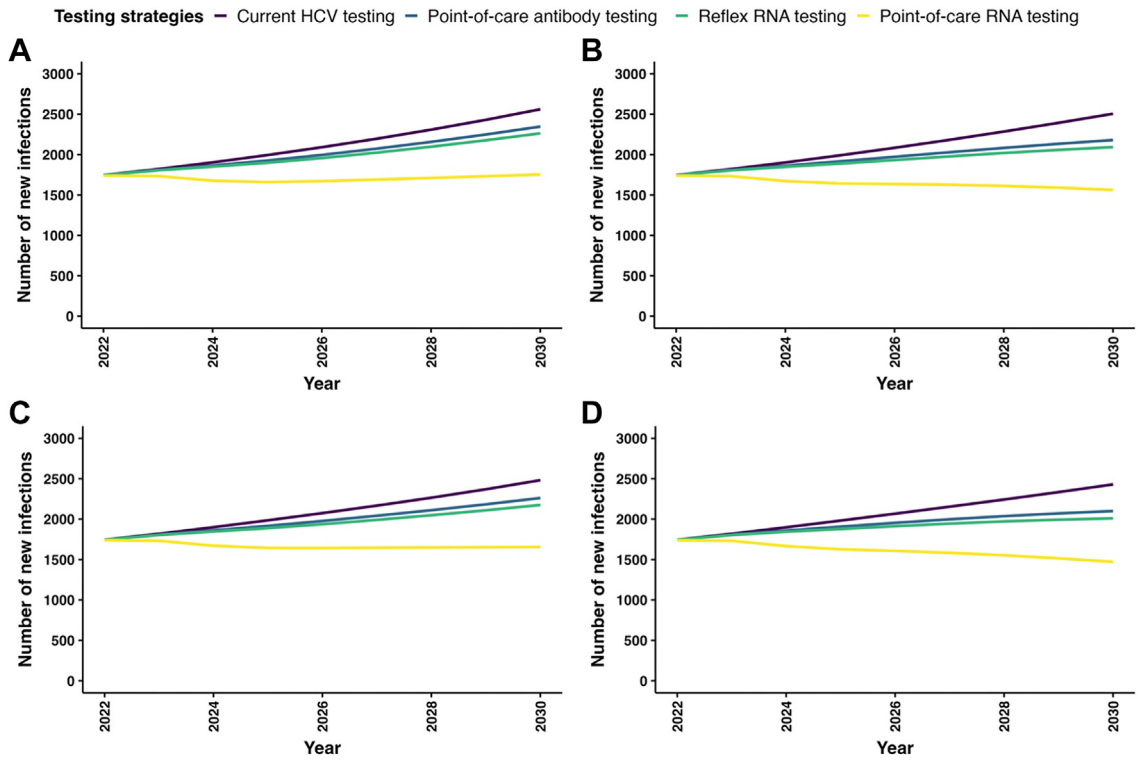


*Fig. 2:* Annual change in number of new HCV infections for each HCV testing strategy and HIV PrEP and treatment coverage scenarios (A) Current PrEP and HIV treatment coverage, (B) PrEP coverage increases to 20% by 2030, (C) HIV treatment coverages increase to 95% by 2030 and (D) PrEP coverage increases to 20% and HIV treatment increased to 95% by 2030.

RNA prevalence would continue to increase from 4.4% (95% UI: 3.1%–5.5%) to 5.2% (95% UI: 3.7%–6.2%) with cumulative 15,340 (95% UI: 5,680–31,480) new HCV infections between 2022 and 2030 (Fig. 2).

The simplified HCV testing strategies could avert between 3.8% and 22.1% of cumulative new HCV infections between 2022 and 2030. Point-of-care RNA testing had a considerable impact on the reduction of new HCV infections (between 18.9% and 22.1%) across HIV PrEP and treatment coverage scenarios. Conversely, reflex RNA testing would only achieve a minor reduction in new HCV infections (between 4.2% and 5.6% during the 2022–2030 period) and point-of-care antibody testing (between 3.8% and 5.8%) compared to current HCV testing strategy in HIV PrEP and treatment coverage scenarios (Fig. 2 and Supplementary Table S4).

### Lifetime costs and QALYs of HCV testing strategies

The lifetime costs and QALYs gained from each HCV testing strategy across all HIV PrEP and treatment coverage scenarios are shown in Table 2. If the current situation continues (current HCV testing and S1 scenario), the median lifetime cost for HCV care would be approximately $43 million, mainly due to cost of HCV diagnosis ($35 million, 81.4% of the total cost). It also results in a median total lifetime QALYs of 5,265,727 years in the entire MSM population in Taiwan.

Compared to the current HCV testing strategy in the S1 scenario, the point-of-care antibody testing strategy and reflex RNA testing would result in cost saving $8.5 million and $4.3 million, respectively. Nevertheless, point-of-care RNA testing would lead to incremental costs of $72.1 million. Incremental QALYs gained are 1,138, 1,359, and 2,776 in point-of-care antibody testing, reflex RNA testing, and point-of-care RNA testing scenarios, respectively.

Under the PrEP coverage increased scenario (S2), the point-of-care antibody testing would result in cost saving $2.7 million and reflex RNA testing and point-of-care RNA testing would incur additional lifetime costs of $2.3 million, and $120.4 million, respectively. Incremental QALYs gained are 1,816, 2,030, and 3,471 in point-of-care antibody testing, reflex RNA testing, and point-of-care RNA testing scenarios, respectively.

Under the scenario where only HIV treatment coverage is increased (S3), the point-of-care antibody testing strategy would save $1.2 million; however, reflex RNA testing and point-of-care RNA testing would result in additional costs of $2.3 million and $83.0 million,

respectively. Incremental QALYs gained would be 725, 942, and 2,291 in the point-of-care antibody testing, reflex RNA testing and point-of-care RNA testing scenarios, respectively.

Our projections suggest high lifetime costs and QALYs gained in each of the simplified HCV testing strategies in the scenario where both PrEP and HIV treatment coverage increase (S4). Compared to current HCV testing in the S4 scenario, there would be $3.9 million, $8.1 million, and $130.3 million in incremental lifetime costs and 1,419, 1,583, and 3,021 incremental lifetime QALYs would be gained in the point-of-care antibody testing, reflex RNA testing, and point-of-care RNA testing scenarios, respectively.

### Cost effectiveness of the HCV testing strategies

In terms of cost-effectiveness, point-of-care antibody testing (median ICERs ranged from dominant in S1 to $2,751 per QALY gained in S4) and reflex RNA testing (median ICERs ranged from dominant in S1 to $4,879 per QALY gained in S4) would be cost-effective compared to current HCV testing in all four PrEP and HIV treatment scale-up scenarios for the entire MSM population (Table 2). Point-of-care RNA testing would be only cost-effective compared to the current HCV testing if HIV PrEP and treatment coverage remained unchanged (ICER: $24,818 per QALY gained).

Considering the HCV testing strategies alone, most scenarios (except three point-of-care RNA testing strategies in expanded HIV coverage) are cost-effective compared to current HCV testing. When all scenarios of potential changes in HCV testing and HIV services are combined, five most cost-effective scenarios are identified on the cost-effectiveness efficiency frontier (Fig. 3). These are in order of increasing ICER (1) point-of-care antibody testing with the S1 scenario (ICER: dominant), (2) current HCV testing with the S4 scenario (ICER: $75 per QALY gained), (3) point-of-care antibody testing with the S4 scenario (ICER: $2,797 per QALY gained), (4) reflex RNA testing with the S4 scenario (best estimate ICER: $16,517 per QALY gained), and (5) point-of-care RNA testing with the S4 scenario (ICER: $61,500 per QALY gained).

Lifetime costs, QALYs and ICERs for the subpopulation of MSM on PrEP and MSM living with HIV on treatment are shown in Supplementary Materials Tables S5 and S6. Among MSM on PrEP, point-of-care antibody testing, and reflex RNA testing would be cost-effective compared to current HCV testing with the S1, S2 and S4 scenarios. Conversely, point-of-care RNA testing would be cost-effective compared to current HCV testing only in the increased HIV PrEP coverage scenario (S2). Among MSM on HIV treatment, point-of-care antibody testing, and reflex RNA testing strategies would be cost-effective compared to the current HCV testing strategy in all four PrEP and HIV treatment coverage scenarios. However, point-of-care RNA testing would be only cost-effective

| | Lifetime cost (discounted, million) | Lifetime QALY (discounted, thousand) | Incremental lifetime cost (discounted, thousand) | QALY gained (discounted) | ICER |
|---|---|---|---|---|---|
| **S1: PrEP coverage and HIV treatment coverage remains unchanged** | | | | | |
| Current practice | $42.9 ($14.3–$131.3) | 5,262 (3,158–7,652) | NA | NA | NA |
| Point-of-care antibody testing | $35.0 ($12.9–$99.9) | 5,264 (3,159–7,654) | −8,518 (−31,472 to 1,491) | 1,138 (−14 to 2,425) | **dominant (dominant–$124,780)** |
| Reflex RNA testing | $38.7 ($16.2–$76.6) | 5,265 (3,159–7,655) | −4,271 (−62,574 to 9,056) | 1,359 (−1,100 to 3,277) | **dominant (dominant–$166,041)** |
| Point-of-care RNA testing | $117.1 ($45.6–$244.6) | 5,267 (3,160–7,655) | 72,108 (31,074–120,637) | 2,776 (676–5,428) | **$24,818 ($10,501–$105,555)** |
| **S2: PrEP coverage increases to 20% by 2030** | | | | | |
| Current practice | $42.1 ($14.1–$127.6) | 5,267 (3,160–7,653) | NA | NA | NA |
| Point-of-care antibody testing | $40.0 ($15.4–$111.6) | 5,270 (3,161–7,657) | −2,693 (−17,147 to 2,159) | 1,816 (586–3,523) | **dominant (dominant–$767)** |
| Reflex RNA testing | $44.4 ($19.7–$85.2) | 5,270 (3,162–7,657) | 2,250 (−53,079 to 19,854) | 2,030 (−331 to 4,363) | **$1,531 (dominant–$131,325)** |
| Point-of-care RNA testing | $165.7 ($70.4–$315.4) | 5,272 (3,162–7,659) | 120,404 (55,822–195,366) | 3,471 (1,233–6,545) | *$32,974 ($15,781–$104,241)* |
| **S3: HIV treatment coverages increase to 95% by 2030** | | | | | |
| Current practice | $36.3 ($12.3–$116.2) | 5,265 (3,159–7,654) | NA | NA | NA |
| Point-of-care antibody testing | $35.5 ($13.1–$100.9) | 5,266 (3,160–7,655) | −1,229 (−16,044 to 1,346) | 725 (24–1,412) | **dominant (dominant–$2,091)** |
| Reflex RNA testing | $39.2 ($16.5–$77.4) | 5,266 (3,160–7,656) | 2,349 (−47,192 to 15,836) | 942 (−1,060 to 2,208) | **$3,947 (dominant–$141,379)** |
| Point-of-care RNA testing | $121.0 ($47.6–$250.1) | 5,268 (3,161–7,656) | 82,968 (35,606–141,634) | 2,291 (650–4,761) | *$34,239 ($15,821–$141,269)* |
| **S4: PrEP coverage increases to 20% and HIV treatment increased to 95% by 2030** | | | | | |
| Current practice | $35.4 ($12.1–$111.3) | 5,269 (3,161–7,656) | NA | NA | NA |
| Point-of-care antibody testing | $40.3 ($15.6–$112.4) | 5,271 (3,162–7,658) | 3,871 (−1,984 to 6,987) | 1,419 (597–2,486) | **$2,751 (dominant–$3,517)** |
| Reflex RNA testing | $44.7 ($20.0–$85.8) | 5,271 (3,162–7,659) | 8,070 (−36,904 to 27,191) | 1,583 (−323 to 3,258) | **$4,879 (dominant–$86,520)** |
| Point-of-care RNA testing | $169.3 ($72.0–$320.4) | 5,273 (3,163–7,661) | 130,308 (60,514–216,032) | 3,021 (1,135–5,759) | *$41,388 ($21,521–$119,980)* |

The number reported is median with the 95% UI in brackets. Lifetime cost was round to the nearest US$ 10,000. Lifetime QALY, incremental lifetime cost, QALY gained and ICER were round to the nearest whole number. *Bold cells indicate ICERs fell below the cost-effective Threshold (ICERs ≤1Taiwan GDP, $32,811). Italic cells indicate ICERs above the cost-effective threshold and so are not cost-effective.

*Table 2:* **Summary results for cost-effectiveness analysis of simplified HCV testing strategies targeting MSM using HIV PrEP or on HIV treatment.**

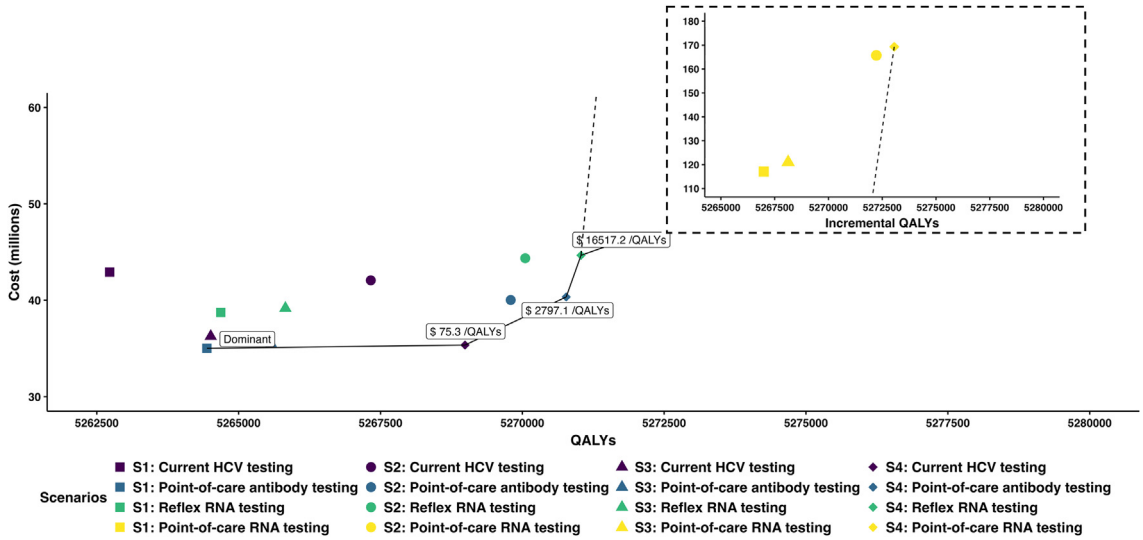


***Fig. 3:*** QALYs and cost for each POC HCV testing strategy compared to current testing strategy with current HIV PrEP and treatment coverage. The dashed line box shows the QALYs and cost for point-of-care RNA testing which has an order of magnitude higher cost compared to the other scenarios. S1: Coverage of PrEP and HIV treatment remains unchanged; S2: PrEP coverage increases to 20% by 2030; S3: HIV treatment coverages increase to 95% by 2030; S4: PrEP coverage increases to 20% and HIV treatment increased to 95% by 2030.

when HIV treatment coverage remained unchanged (scenarios S1 and S2).

### Sensitivity analyses

In Fig. 4, the probability sensitivity analysis shows most simulations fell in the north-east quadrant of the cost-effectiveness plane. This indicates that the testing strategies targeted at MSM on PrEP and HIV treatment, despite requiring more resources, would yield greater benefits in terms of QALYs compared to the current HCV testing scenario in the entire MSM population. While most simulated ICER of the point-of-care RNA testing strategy fell in the north-east quadrants, they are generally above the specified cost-effectiveness threshold, indicating this strategy is unlikely to be cost-effective compared to the current testing strategy. The results of the reflex RNA testing strategy have a high uncertainty with ICERs falling across the north-east, south-east and south-west quadrants. The results for point-of-care antibody testing are in the north-east and south-east quadrants and below the cost-effectiveness threshold, indicating this strategy may require less resources to achieve the same benefits compared to the current testing strategy. Similar distributions are observed in the results for MSM living with diagnosed HIV. In contrast, the probability sensitivity analysis suggested that scaling-up simplified HCV testing strategies among MSM PrEP users is unlikely to be cost-effective (Supplementary Material Figures S17 and S18).

The most influential parameters contributing to the lifetime HCV cost and lifetime QALYs are related to advanced HCV disease progression, HCV-related death, and spontaneous viral clearance and hence are unrelated to HCV testing or the implementation scenarios, shown in Supplementary Material Figures S14–S16.

## Discussion

Our results highlight the critical importance of integrating simplified HCV testing within the framework of HIV PrEP and treatment services, offering pivotal strategies for effectively and cost-effectively addressing the HCV epidemic among MSM. This study suggests point-of-care antibody and reflex RNA testing are consistently cost-effective across all HIV PrEP and treatment coverage scenarios. However, immediate point-of-care RNA testing is generally not a cost-effective strategy. This is likely due to a relatively low HCV prevalence among MSM (2.8% in MSM on PrEP and 12.1% in MSM on HIV treatment in 2022).

Five strategies on the efficiency frontier (point-of-care antibody testing in HIV PrEP and treatment coverage remained unchanged scenario, and all testing strategies under the scenario that both HIV PrEP and treatment coverage expanded) offer the best value for money when integrating HCV testing into PrEP and HIV treatment services among Taiwanese MSM. The integration of services to simplify the care package and expand access to treatment is not uncommon in HCV prevention. A meta-analysis underscores the positive impact of integrating HCV testing and care into harm reduction sites and correctional settings.[45] Additionally, HIV PrEP has been proposed as a gateway to eliminate

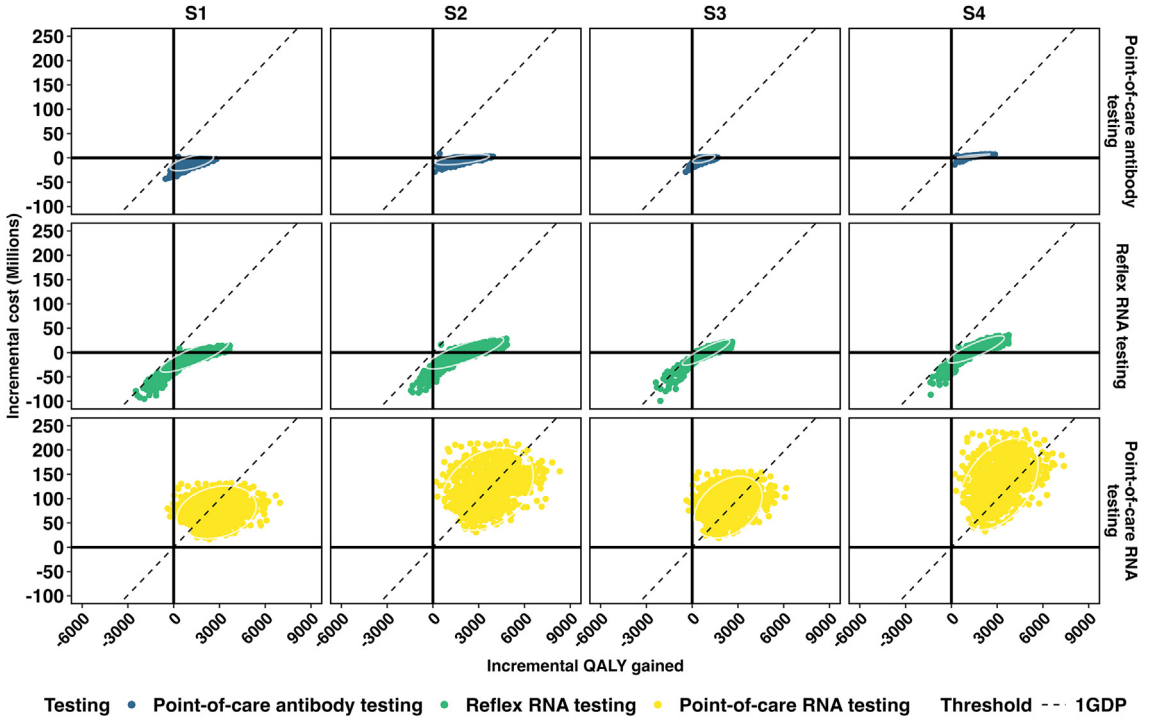


*Fig. 4:* Probability sensitivity analysis cost-effectiveness scatter plot (1000 simulations with threshold $32,811/QALY and 95% 95% joint uncertainty region shown in white ellipse). S1: Coverage of PrEP and HIV treatment remains unchanged; S2: PrEP coverage increases to 20% by 2030; S3: HIV treatment coverages increase to 95% by 2030; S4: PrEP coverage increases to 20% and HIV treatment increased to 95% by 2030.

hepatitis B.[46] In line with these practices, our results indicate that either implementing simplified HCV testing or maintaining current testing while HIV PrEP and treatment coverage are increased would be the most efficient strategies. This finding implies that there is an added cost-effectiveness benefit to simplifying HCV testing and integrating care.

In our analysis, immediate point-of-care RNA testing costs $187.8 (NT$2,640) per test, whereas an HCV antibody test costs $18.3 (NT$257). Given the low prevalence of HCV, prioritizing the cheaper HCV antibody test for initial screening is more economically efficient. Performing immediate point-of-care RNA testing, especially with expanded HIV PrEP and treatment coverage, would significantly increase testing costs. This finding aligns with a previous study suggesting that reflex RNA testing may be more cost-effective in settings with relatively low HCV prevalence setting than point-of-care RNA testing.[47] A more affordable one-step HCV testing (HCVcAg), priced at $20 (approximately NT$600, with exchange rate US$1 = NT$30) per test, has been found to be cost-effective compared to the standard two-step HCV testing approach used for community-based screening among general population in Taiwan.[48] However, we did not include HCVcAg as one of the testing strategies in our study due to its lower sensitivity (87.1%) and positive predictive value (85.1%) compared to the nucleic acid test for HCV RNA, particularly in cases of recently acquired HCV among men who have sex with men.[49] Considering the ongoing risk of HCV transmission in this population and their frequent engagement with HIV services, which could detect HCV acute infections, we chose not to consider HCVcAg as part of a testing strategy in our study.

Several modelling studies have suggested that enhancing HCV screening in MSM living with HIV is cost-effective and cost-saving.[17,19,50–52] Another modelling study suggested that undertaking screening among HIV-negative MSM stratified by PrEP use was cost-effective.[20] Our analysis contributes to this existing body of research by considering what simplified HCV testing strategy is best to implement. Importantly, this study represents one of the first cost-effectiveness analysis of such interventions, filling a crucial gap in the literature.

There are several limitations to our study. Firstly, our model structure represented a trade-off between simplicity and the necessity for comprehensive exploration. Therefore, it may not fully capture the complexity of real-world dynamics, leading to potential misspecification bias. While sensitivity analyses were conducted to explore the impact of varying assumptions and

parameter values to mitigate the misspecification bias, it is possible that some sources of bias remain unaddressed. As such, the interpretation of our model's results should be made with caution. Additionally, we established a range of 0.75 times the point estimate to 1.25 times the point estimate for parameters lacking 95% confidence intervals and for calibrated parameters. Using a uniform distribution to sample parameters served as a practical method for exploring and testing sensitivity in our theoretical scenarios. Nonetheless, its simplicity may not fully capture the complexities of real-world situations. Despite this, our sensitivity analysis demonstrated that parameters with plausible ranges were not the primary influencers of HCV incidence. This suggests that while our approach sufficed for our analysis purposes and did not significantly alter the overarching conclusions derived from the model.

Secondly, it is important to note that we did not attempt to replicate the entire historical HIV epidemic among MSM in Taiwan. Instead, we assumed a stable HIV incidence over time for each population, calibrated to match available data for the HIV epidemic among different MSM sub-populations in Taiwan. Consequently, our model does not account for the impact of increased PrEP and HIV treatment coverage on the HIV epidemic and the associated costs. This implies that our results may be conservative estimations of the benefits of integrating HCV testing into HIV prevention and treatment services.

Lastly, while reflex RNA testing has been reimbursed by Taiwan's National Health Insurance since 2021, it is not mandatory and has not officially become the standard for HCV testing.[53] The information available to us did not include the details on how health facilities integrated reflex RNA testing into their laboratory workflow. As a result, we continued to use the conventional two-step laboratory HCV diagnostic algorithm to represent the current HCV testing in our model. This limitation reflects the gaps that remain in the real-world implementation and effectiveness of simplified HCV testing strategies in Taiwan. Specifically, divers sampling methods, such as capillary blood, fingerstick, or oral samples, have the potential to enhance patient acceptability. Conversely, the acceptance of simplified HCV testing among healthcare providers remains uncertain in Taiwan. To address these gaps, further research is needed to assess these aspects of implementation.

The results of our study provide detailed insights and economics evidence for developing tailored simplified HCV testing interventions for the subpopulation of MSM. These findings could guide decision-makers in shaping HCV prevention policies and planning for MSM, facilitating progress toward HCV elimination targets in Taiwan and the Western Pacific region. In the future, using our dynamic model to simulate more sophisticated screening interventions aimed at optimizing these strategies for HCV diagnosis and treatment among those who are aware of their HCV antibody status would further contribute to shaping HCV testing policies.

## Conclusions

Our analysis shows that integrating simplified HCV testing into HIV prevention and care services would be a cost-effective strategy for Taiwanese MSM. Focusing on the implementation of point-of-care antibody testing and reflex RNA testing could efficiently accelerate progress towards HCV elimination. This study is important for informing the future implementation of HCV testing strategies and optimization of resource allocation for MSM in Taiwan and highlights the economic benefits of integrating simplified HCV testing into existing services for MSM alongside HIV PrEP and treatment.

### Contributors

HJW, SS and RTG conceived the study. HJW developed the model. HJW set up and ran the scenarios. HJW designed the analyses and drafted the manuscript. SS, JG and RTG validated the model input. All authors were involved in writing and revising the manuscript.

### Data sharing statement

Model parameters are available in tables and supplementary materials. The code used to produce the estimates with aggregate data and results for this study are available online at https://github.com/The-Kirby-Institute/Simplified-HCV-testing-model/tree/main/Projects/02.CEA_TWHCVMSM.[21]

### Declaration of interests

RTG has received funding for his research from WHO and has provided non-funded project advice to Gilead and ViiV. JG is a consultant/advisor and has received research grants from AbbVie, Abbott, Cepheid, Gilead Sciences, Hologic and Roche and has received honoraria from AbbVie, Abbott, Cepheid, Gilead Sciences, and Roche. TLA has received research grants from Cepheid, Abbott, Gilead, and SpeeDx, has received travel support to attend a conference from Abbot. All other authors have no conflicts of interest to declare.

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### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101119.

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