C型肝炎病毒抗體快篩試劑的運用

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慢性C型肝炎病人可能在沒有症狀或是沒有特異性症狀的狀態下持續數十年，等到症狀出現，病情往往已惡化到威脅生命的肝硬化或是肝癌階段。及早發現C型肝炎病毒（HCV）感染，對於防治後續併發症是十分重要的。傳統先經實驗室檢驗C肝抗體（anti-HCV）陽性，再以核酸檢驗來確認C肝病毒是否存在的兩階段檢定步驟，被認為是發掘及診斷HCV病毒感染的關鍵挑戰。除了傳統實驗室的血清抗體檢驗外，世界衛生組織亦建議以快篩試劑作為anti-HCV檢驗分析方法之一，並認為快篩將可改善篩檢到後續照護與治療的連結。2020年以來，C肝抗體快篩試劑的敏感度及特異度已有提升；目前我國已有3項C肝抗體快篩試劑取得上市許可證，依據文獻回顧結果，其敏感度及特異度分別至少都在92.8%及92.6%以上。本文蒐集文獻並彙整C肝抗體快篩試劑的檢驗效能和國際運用情境文獻，希望有助於提升國人對C肝快篩檢試劑的認識，並討論其在台灣推動C肝消除的可能應用。（台灣衛誌 2023；**42(6)**：594-611）

關鍵詞：C肝篩檢、C肝抗體快篩試劑、快篩、敏感度、特異度

前　言

世界衛生組織（World Health Organization, WHO）估計全球約有7千多萬的慢性C型肝炎病人，每年恐有70萬人死於C型肝炎（簡稱C肝）相關的合併症，包括肝硬化及肝癌[1]。2016年5月第69屆世界衛生大會（World Health Assembly, WHA）上，194個會員國承諾要在2030年前消除病毒性肝炎，使其不再成為公共衛生的威脅，以期阻斷病毒性肝炎傳播，並使病毒性肝炎病人能獲得安全、可負擔、有效的照護和治療[2]。

WHO在「2016-2021年病毒性肝炎全球衛生部門戰略」報告指出，為了快速地擴大病毒性肝炎檢驗服務、確保準確可靠的診斷、臨床評估及病人監測，改善診斷的技術、策略及方法至關重要；若能發展簡單的診斷技術方法，對於偏遠地區和困難觸及的族群便能有更多的機會獲得檢驗服務。為了優化檢驗及診斷程序，該份報告還指出幾項建議應優先開發的檢驗診斷方法，包括(1)可在短時間內即獲知C肝抗體（anti-HCV）或病毒量（HCV RNA）結果的快速診斷檢驗法（rapid diagnostic test, RDT）；(2)可監測C肝抗體及病毒量的定點照護（point-of-care, POC）檢驗模式，即在病人接受採檢的同一地點，直接進行檢驗分析，在病人離開前即能快速獲知檢驗結果；(3)能有效評估肝纖維化及肝硬化的簡易方法[3]。2016年10月WHO在一份聚焦於克服C肝消除障礙的全球報告中指出，先檢驗出C肝抗體陽性，然後再以核酸檢驗來確認病毒是否已經清除的這種兩階段檢定步驟是診斷慢性C肝的關鍵挑戰。而快速診斷、定點照護檢驗、去中心化、以病人為中心等檢驗服務特性，將可

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有效提升民眾獲得適當診斷及連結至所需照護與治療的機會[1]。

「依據衛生福利部國家消除C肝辦公室的推估，我國的慢性C肝人數約為32-40.5萬人[4,5]。慢性C肝病人可能在沒有症狀或是沒有特異性症狀的狀態下持續數十年[6]，直到出現肝硬化或肝癌等嚴重併發症時才發現。研究顯示只有近50%的人知道自己是C肝病毒感染者[7]，若能及早發現C肝病毒感染，將可減少傳播及降低併發症的風險。為辨別出無症狀的病人，WHO建議應提供檢驗服務及檢驗工具。通常想在實驗室處理大量樣本，也必須考量實驗室的負荷能力，有時需要投資額外的基礎設施及設備，及具備操作能力的專業人員；反之，RDT不需要額外投資實驗室設備，只要由培訓過的醫療人員，甚至一般人員就可以執行[8]，惟必須視當地對執行RDT人員的相關規範而訂。C肝抗體RDT不需靜脈穿刺集血後送實驗室分析的過程，它僅需將指尖血或是唾液滴入卡匣，當場30分鐘內即可獲知C肝抗體篩檢結果。歐洲肝臟研究學會在2016年便建議以C肝抗體RDT取代傳統酵素免疫分析法，將可促進篩檢，以及改善後續照護的連結狀況，加速肝炎的消除[9]。美國肝病研究學會及感染症醫學會在2019年則是建議傳統實驗室或快速POC的檢驗模式皆可用於C肝抗體篩檢，檢測方法只要是經美國食品藥物管理局核准的即可[10]。

為了加速發掘潛在C肝病人，RDT在國際已有許多運用經驗，本文除介紹WHO針對RDT運用的建議，及已取得WHO認證及我國上市許可證的RDT試劑外，也應政策需求，快速回顧文獻中有關醫療人員應用指尖血anti-HCV RDT試劑的敏感度及特異度，及國際上使用anti-HCV RDT的運用情境，以供其規劃篩檢工具及提供台灣各界在運用RDT做為C肝抗體篩檢工具時之參考。

運用C肝抗體快篩試劑之WHO建議

2017年2月WHO公布的「B型及C型肝炎檢驗指引」，針對C肝抗體RDT有三點建議[11]。由建議可知C肝抗體RDT已為國際認可之檢驗方法，各國藥證單位審查通過並核發許可證的產品即為適用的工具。

1. C肝抗體RDT為anti-HCV血清檢驗分析方法之一。
2. 為了檢驗成人、青少年及兒童（18個月以上）過去或現在感染的血清學證據，建議使用滿足最低安全性、品質及效能標準的C肝抗體RDT或實驗室操作之免疫分析方式，滿足WHO體外診斷醫療器材（in vitro diagnostic, IVD）認證（prequalification）或是藥證單位IVD法規審查之最低允收基準（acceptance criteria）即可。
3. 對於處於實驗設施及檢驗受限的環境或地區，以及/或對於使用快速檢驗有助於連結到照護與治療的族群，建議可使用C肝抗體RDT。

為了簡化C肝的診治流程，2022年6月WHO於「簡化服務提供流程及HCV診斷政策」指出：對於anti-HCV檢驗結果呈現陽性者，建議進行反射式病毒量檢測（reflex HCV RNA testing）；除可藉由實驗室已經保存anti-HCV陽性者的檢體來達到reflex HCV RNA testing，也可在衛生機構以RDT檢驗anti-HCV呈現陽性時，立即採集檢體進行HCV RNA檢驗來實現流程簡化[12]。

取得WHO認證的C肝抗體快篩試劑

為協助中低收入國家改善公共衛生，WHO會針對常見流行疾病的診斷試劑、藥物及疫苗進行審查認證，以協助這些國家本身或提供援助的國際組織有可用的工具控制疾病[13]。在anti-HCV快篩方面，截至2023年2月3日，WHO公告已取得認證者共有4種anti-HCV RDT試劑[14,15]，請見表一。

WHO指出與檢驗效能有關的常見測量指標包括下列5項，可供衛生單位評估自費醫材或採購評估時參酌：

1. 臨床/診斷敏感度（clinical/diagnostic sensitivity）
   檢驗可正確識別有感染或罹有疾病之能力，亦即真陽性/(真陽性+假陰性)。通常以伴隨信賴區間（confidence intervals）的點估計呈現。
2. 臨床/診斷特異度（clinical/diagnostic specificity）

表一　取得WHO認證之C肝抗體快篩試劑

試劑名稱	製造商
Standard Q HCV Ab Test	SD Biosensor, Inc., Korea
Rapid Anti-HCV Test	InTec Products, Inc., China
OraQuick HCV Rapid Antibody Test Kit	OraSure Technologies Inc., USA
SD Bioline HCV	Abbott Diagnostics Korea Inc., Korea

檢驗可正確識別沒有感染或沒有疾病之能力，亦即真陰性/(真陰性+假陽性)。通常以伴隨信賴區間的點估計呈現。

3. 陽性預測值（positive predictive value, PPV）
   當一個人的檢驗結果為陽性時，實際真有感染或罹病的機率。預測值會受到母群體疾病盛行率（prevalence）的影響。
4. 陰性預測值（negative predictive value, NPV）
   當一個人的檢驗結果為陰性時，實際真沒有感染或沒有罹病的機率。預測值會受到母群體疾病盛行率的影響。
5. 分析敏感度/偵測極限（analytical sensitivity/limit of detection, LoD）
   在常規實驗室的條件下，檢體可被偵測到的最低濃度。

取得我國上市許可證之C肝抗體快篩試劑

自2016年第4季已有單獨測試C肝抗體的RDT試劑引進我國，迄2023年11月共有3種試劑取得食品藥物管理署（Taiwan Food and Drug Administration, TFDA）上市許可證（請見表二），可供專業人員利用指尖血來進行檢驗。在此三種試劑各自的仿單上所報告，相比於實驗室酵素免疫分析法之敏感度及特異度，分別達99.08%及96.77%以上。

C肝抗體快篩試劑的敏感度及特異度

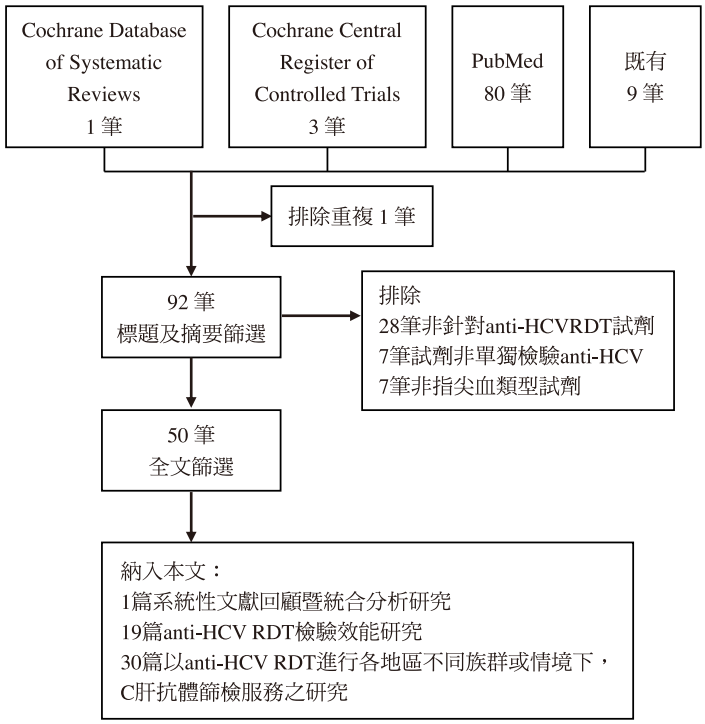
為了解我國已上市RDT的敏感度及特異度，以及國際上運用RDT的範疇，2023年3月20日分別以RDT、"rapid diagnostic test"、"Rapid Diagnostic Tests"[Mesh]、"Point of care testing"、"Point-of-Care Testing"[Mesh]、anti-HCV、"HCV Antibodies"、"Hepatitis C Antibodies"[Mesh]等作為關鍵字，蒐尋Cochrane及PubMed文獻資料庫，分別從Cochrane Database of Systematic Reviews（Issue 3 of 12, March 2023）及Cochrane Central Register of Controlled Trials（Issue 2 of 12, February 2023）各得1筆及3筆文獻，從PubMed得80筆文獻，另納入作者掌握之既有文獻9篇[16-24]。首先由作者楊及吳檢視這93筆文獻之標題及摘要，排除1筆重複、28筆非針對anti-HCVRDT試劑、7筆試劑非單獨檢驗anti-HCV、7筆非指尖血類型。再經楊及吳檢視內文後，保留1篇系統性文獻回顧暨統合分析研究[25]，及19篇與實驗室酵素免疫分析法相比的C肝抗體RDT檢驗效能研究[15,26-43]，另保留30篇以anti-HCV RDT進行各地區不同族群或情境下，C肝抗體篩檢服務或探討盛行率的研究[16-24,44-64]，文獻篩選流程圖請見圖一。

前述系統性文獻回顧暨統合分析研究共納入5篇發表在2000年至2011年之間的RDT研究，受測人數介於197人至2,754人，其中一款RDT非單獨檢驗C肝抗體，而是可檢驗HIV、HCV及梅毒的複合式試劑。經統合分析，C肝抗體RDT相較於酵素免疫分析法的敏感度為98%（95% CI: 98%-100%）；特異度為100%（95% CI: 100%-100%），試驗間存在有異質性（p<0.001）[25]。

有關C肝抗體RDT檢驗效能的19篇研究[15,26-43]，共納入74項C肝抗體RDT試劑與實驗室酵素免疫分析法的結果，各篇研究中提及之試劑名稱、執行地點、樣本採集時間及來源、人數、敏感度及特異度、陽性預測值及陰性預測值等資料，擷錄於表三。這些研究的論文發表時間介於2013至2022年；研究執行的地點包括：坦尚尼亞、喀麥隆、奈及利亞、比利時、法國、德國、喬治亞、伊朗、印度、柬埔寨、泰國、中國、蒙古、韓國、巴西、美國等；檢體採集的對象或是來源包括 HIV感染者、靜脈藥癮者、矯正機關收容人、血液透析病人、參加健檢者、參加篩檢者、捐血者、或一般民眾；檢測樣本數介於79至1,788人；研究結

表二　我國已取得食品藥物管理署許可證之C肝抗體快篩試劑

試劑名稱	安倍多標的C肝病毒抗體快速檢驗套組 MP Diagnostics Multisure HCV Antibody Assay	圖優C型肝炎抗體快篩 TOYO Anti-HCV Test, WB/S/P	詩丹C型肝炎抗體快篩 Standard Q HCV Ab Test
許可證字號	衛部醫器輸字第028922號	衛部醫器輸字第035674號	衛部醫器輸字第035896號
製造國	新加坡	土耳其	韓國
許可證效能	本產品使用定性免疫層析分析法，快速體外檢驗人類含抗凝劑之全血、指尖採血全血、血漿或血清中C肝病毒抗體	本產品利用層析免疫分析方法，定性檢測人類全血/血清/血漿中HCV抗體	本產品是一種快速免疫層析法，可針對人類血清、血漿或全血中所存在的HCV特異性抗體作定性檢測。本檢測用於體外專業診斷用途，目的是幫助有HCV感染臨床症狀患者早期診斷出HCV感染症。而它僅提供初步篩檢結果。還應施以更具特定性的替代診斷方法，以確認HCV的感染。本產品並不適用於自我檢測
敏感度	99.31% 總樣本2,643份	100% （95% CI: 99.22-100) 總樣本數472份	100% （95% CI: 99.08-100.00） 總樣本413份
特異度	99.22% 總樣本數4,556份	100% （95% CI: 99.8-100） 總樣本數1,882份	97.67% （95% CI: 96.77-98.32） 總樣本1,500份
結果讀取時間	15分鐘	15分鐘	5-20分鐘



圖一　文獻篩選流程圖

表三　C肝抗體快篩試劑的敏感度、特異度、陽性預測值及陰性預測值

第一作者	發表年	執行地點	樣本時間	對象或場所情境	RDT試劑(製造廠)	人數	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Vetter [27]	2022	Nigeria Georgia Cambodia Belgium	September 2018-March 2019	HIV-infected, HIV-uninfected populations	Standard Q HCV Ab (SD Biosensor, Korea)	1,500	94.8% (92.8-96.2)	100% (99.6-100)	100%	96.0%
					HCV Hepatitis Virus Antibody Test (Antron Laboratories, Canada)	1,500	94.9% (92.9-96.4)	99.1% (98.2-99.5)	99.0%	96.0%
					HCV-Ab Rapid Test (Beijing Wantal Biological Pharmacy Enterprise, China)	1,511	96.8% (95.1-97.9)	97.2% (95.8-98.1)	96.0%	96.0%
					Rapid Anti-HCV Test (InTec, China)	1,500	95.7% (93.8-97.0)	99.2% (98.3-99.6)	99.0%	97.0%
					First Response HCV Card Test (Premier Medical Corporation, India)	1,500	95.8% (94.0-97.1)	99.8% (99.2-99.9)	100%	97.0%
					Signal HCV Version 3.0 (Arkray Healthcare, India)	1,499	94.3% (92.2-95.8)	97.1% (95.7-98.0)	96.0%	96.0%
					TriDot HCV (J. Mitra & Co., India)	1,494	95.7% (93.8-97.0)	99.4% (98.6-99.8)	99.0%	97.0%
					Modified HCV-only Ab Test (Biosynex SA, France)	1,500	96.3% (94.6-97.5)	99.1% (98.2-99.5)	99.0%	97.0%
					SD Bioline HCV (Abbott Diagnostics, US)	1,500	95.1% (93.1-96.5)	99.7% (99.0-99.9)	100%	96.0%
					OraQuick HCV (OraSure, US)	1,500	95.4% (93.5-96.7)	99.4% (98.6-99.8)	99.0%	97.0%
Wasitthankasem [26]	2022	Thailand	August-September 2018	test-to-treat program at point-of-care; 117 subdistricts (primary healthcare centers)	Abon (Abon Biopharm, Hangzhou, China)	200	83.0% (74.2-89.8)	100% (96.4-100)	100%	85.5%
Chen [42]	2021	Yunnan and Gansu, China	not available	intravenous drug users; blood donors	Brand A approved by CFDA	100	100% (91.5-100)	98.0% (88.5-100)	98.0%	100%
					Brand B approved by CFDA	100	100% (91.5-100)	96.0% (85.8-99.7)	96.2%	100%
					Brand C approved by CFDA	100	100% (91.5-100)	100% (91.5-100)	100%	100%
					Brand D approved by CFDA	100	94.0% (83.2-98.6)	100% (91.5-100)	100%	94.3%
					Brand E approved by CFDA	100	100% (91.5-100)	98.0% (88.5-100)	98.0%	100%
					Brand F approved by CFDA	100	96.0% (85.8-99.7)	98.0% (88.5-100)	98.0%	96.1%
					Brand G approved by CFDA	100	100% (91.5-100)	96.0% (85.8-99.7)	96.2%	100%

表三　C肝抗體快篩試劑的敏感度、特異度、陽性預測值及陰性預測值（續）

第一作者	發表年	執行地點	樣本時間	對象或場所情境	RDT試劑(製造廠)	人數	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Chevaliez [40]	2021	Créteil, France	September 2012-November 2013;	French National Reference Center;	SD Bioline (Abbott)	456	97.2% (94.6-98.8)	100% (97.9-100)	100%	96.0%
		Yaounde, Cameroon	April 2016-April 2018	Centre Pasteur of Cameroon	Hexagon HCV (Human Diagnostics)	498	98.3% (96.0-99.4)	100% (98.3-100)	100%	98.0%
					First Response HCV card test (Premier Medical Corporation)	498	97.2% (94.6-98.8)	100% (98.3-100)	100%	96.0%
					Multisure HCV antibody assay (MP Diagnostics)	493	100% (98.7-100)	96.1% (92.6-98.0)	97.0%	100%
					Anti-HCV card (Cypress Diagnostics)	498	97.6% (95.1-99.0)	100% (98.3-100)	100%	97.0%
					TOYO anti-HCV test (Turklab)	498	97.9% (95.5-99.2)	99.5% (97.4-100)	100%	97.0%
					OraQuick HCV rapid antibody test (OraSure)	498	99.0% (97.0-100)	100% (98.3-100)	100%	99.0%
Jargalsaikhan [38]	2020	Ulaanbaatar, Mongolia	April-July 2015	blood donors (healthy controls); positive participants from screening registry of the Liver Center	One step HCV antibody rapid test (Abon Biopharm, Hangzhou, China)	270	100% (95.9-100)	86.1% (80.3-90.4)	40.1% (31.0-49.0)	100% (99.5-100)
					Onsite HCV Ab plus combo rapid test (CTK Biotech, San Diego, US)	270	100% (95.9-100)	96.7% (92.9-98.5)	73.6% (56.0-86.0)	100% (99.6-100)
					Anti-HCV dipstick test (Cypress Diagnostics, Belgium)	270	96.7% (90.7-98.9)	97.8% (94.5-99.1)	80.2% (60.0-91.0)	99.7% (99.1-99.9)
					Genedia HCV rapid LF (Green Cross Life Sciences Corp, Korea)	270	96.7% (90.7-98.9)	98.9% (96.1-99.7)	89.0% (68.0-97.0)	99.7% (99.1-99.9)
					Hexagon HCV test (Human, Wiesbaden, Germany)	270	98.9% (94-99.8)	97.8% (94.5-99.1)	80.5% (61.0-91.0)	99.9% (99.4-100)
					Humasis HCV card (Humasis, Gyeonggi-do, Korea)	270	100% (95.9-100)	93.9% (89.4-96.6)	60.3% (46.0-73.0)	100% (99.6-100)
					One step HCV test card (InTec Products, Xiamen, China)	270	100% (95.9-100)	97.8% (94.5-99.1)	80.7% (62.0-91.0)	100% (99.6-100)
					OraQuick HCV rapid antibody test (OraSure technologies, Bethlehem, PA, US)	270	100% (95.9-100)	100% (97.9-100)	100% (81.0-100)	100% (99.6-100)
					SD Bioline HCV test (SD Standart Diagnostics Ltd, Kyonggi-do, Korea)	270	96.7% (90.7-98.9)	98.9% (96.1-99.7)	89.0% (68.0-97.0)	99.7% (99.1-99.9)
					One step Hepatitis C Virus (Wondfo Biotech, Guangzhou, China)	270	100% (95.9-100)	96.7% (92.9-98.5)	73.6% (56.0-85.0)	100% (99.6-100)

表三　C肝抗體快篩試劑的敏感度、特異度、陽性預測值及陰性預測值（續）

第一作者	發表年	執行地點	樣本時間	對象或場所情境	RDT試劑(製造廠)	人數	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Vetter [28]	2020	Tbilisi, Georgia Phnom Penh, Cambodia	July 2019-December 2019	general outpatient clinic (Phnom Penh, Cambodia); HCV screening facility (Tbilisi, Georgia); opioid substitution treatment facility (Tbilisi, Georgia)	HCV-Ab Rapid test (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd, Beijing, China)	1,529	86.5% (83.2-89.2)	99.2% (98.4-99.6)	98.1%	93.6%
					First Response HCV card test (Premier Medical Corporation Ltd., Mumbai, India)	1,529	91.4% (88.6-93.6)	99.8% (99.2-99.9)	99.6%	95.8%
Mahajan [34]	2019	Delhi, India	March-May 2018	clinically suspected cases of HCV infection with deranged liver function tests from the department of Clinical Virology in a tertiary liver-care hospital	Alere Trueline (SD Bioline; Haryana, India)	86	65.3%	100%	100%	29.7%
					Benesphera HCV Rapid card test (Avantor Performance Materials India Limited; Uttarakhand, India)	86	77.3%	100%	100%	39.4%
					AccuTest HCV (Accurex Biomedical Pvt. Ltd.; Mumbai, India)	86	68.0%	100%	100%	31.4%
Mane [33]	2019	India Atlanta, US	2015-2017	Panel Indian/ Panel US-CDC	Alere Truline	360/100	99.4% (96.6-99.9)	100% (98.8-100)	100%	99.7%
					Flaviscreen	360/100	86.3% (79.9-91.2)	100% (98.8-100)	100%	93.2%
					Advanced Quality	360/100	96.3% (91.9-98.6)	100% (98.8-100)	100%	98.0%
					SD Bioline	360/100	99.4% (96.6-99.9)	100% (98.8-100)	100%	99.7%
					OraQuick	360/100	99.4% (96.6-99.9)	100% (98.8-100)	100%	99.7%
Sharafi [29]	2019	Karaj, Alborz, Iran	September 2017-January 2018	Central Prison of Karaj	Advanced Quality Rapid anti-HCV test (InTec)	1,788	100% (94.8-100)	98.89% (98.3-99.3)	78.7% (70.2-85.2)	100% (99.8-100)
Barbosa [43]	2018	Southeast and Northeast region, Brazil	not available	3 private hemodialysis clinics	Wama Imuno-Rápido HCV (Wama Diagnostica, Brazil)	286	84.8% (71.1-93.7)	99.6% (97.7-99.9)	97.5% (84.6-99.6)	97.1% (94.5-98.5)
					Doles HCV Teste Rápido (Doles reagents, Brazil)	286	86.9% (73.7-95.1)	99.2% (97.0-99.9)	95.2% (83.3-98.7)	97.5% (94.9-98.8)
Fondjo [39]	2018	Cameroon	November 2016-February 2017	Centre Pasteur of Cameroon	Multisure HCV Antibody Assay	200	99.0% (97-100)	83.0% (77.7-88.2)	85.0% (80.0-89.9)	99.0% (97.6-100)
					First Response HCV Card Test	200	96.0% (92.7-99.2)	90.0% (85-94.9)	96.0% (92.7-99.2)	90.0% (85.0-94.9)
					TOYO Anti HCV Test	200	96.0% (92.8-99.1)	78.0% (71.3-84.6)	89.7% (83.9-94)	90.7% (86.0-95.3)

表三　C肝抗體快篩試劑的敏感度、特異度、陽性預測值及陰性預測值（續）

第一作者	發表年	執行地點	樣本時間	對象或場所情境	RDT試劑(製造廠)	人數	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Poiteau [31]	2018	Tanzania	September 2012-November 2013	Henri Mondor Hospital; Muhimbili National Hospital OST clinic in Dar-es-Salaam	Advanced Quality Rapid Anti-HCV Test (InTec Products, Inc., Xiamen, China)	396	99.0% (96.5-99.7)	99.0% (96.3-99.7)	99.0%	99.0%
Barbosa [15]	2017	Southeast and Northeast region, Brazil	January 2013-November 2014	HIV clinics	Bioeasy Teste Rápido HCV serum	355	88.8% (72.5-96.7)	100% (98.8-100)	100% (88.4-100)	98.8% (96.9-99.6)
					Wama Imuno-Rapido HCV serum	355	82.3% (65.5-93.2)	100% (98.8-100)	100% (87.6-100)	98.7% (95-99.3)
Chevaliez [41]	2016	France	September 2012-November 2013	Henri Mondor university hospita; Centre Hospitalier Intercommunal de Créteil	OraQuick HCV Rapid Antibody Test (OraSure Technologies, Bethlehem, Pennsylvania, US)	513	99.4% (97.9-99.8)	100% (97.9-100)	100%	99.7%
					TOYO anti-HCV test (Türklab Medical Devices, Izmir, Turkey)	513	95.8% (93.0-97.5)	98.8% (95.8-99.7)	97.6%	98.0%
					Labmen HCV test (Türklab Medical Devices).	513	63.1% (55.8-69.8)	100% (94.4-100)	100%	84.7%
Kosack [36]	2016	Langen, Germany	January 2014-August 2015	Panel 1 (IDU, n = 82) from ZeptoMetrix, New York, USA	OraQuick (OraSure)	80	100% (93.5-100)	100% (86.3-100)	100%	100%
					Multisure (MP Diagnostics)	79	100% (93.5-100)	96% (79.6-99.9)	98.2%	100%
				Panel 2 (n = 198) from University of Frankfurt, Germany	OraQuick (OraSure)	191	99.0% (96.3-99.9)	-	100%	-
					Multisure (MP Diagnostics)	192	99.5% (97.1-100)	-	100%	-
Poiteau [30]	2016	Cameroon	November 2016-February 2017	Henri Mondor University Hospital; Centre Hospitalier Intercommunal de Cr eteil	OraQuick HCV Rapid Antibody Test (OraSure Technologies, Inc, Bethlehem, Pennsylvania, US)	207	100% (97.3-100)	100% (94.6-100)	100%	100%
					First Response HCV Card Test (Premier Medical Corporation Ltd, Watchung, New Jersey, US)	207	99.3% (96.0-99.9)	100% (94.6-100)	100%	98.6%
					Assure HCV Rapid Test (MP Diagnostics, Santa Ana, California, US)	207	98.6% (94.9-99.6)	100% (94.6-100)	100%	97.1%
					Multisure HCV Antibody Assay (MP Diagnostics, Santa Ana, California, US)	207	98.6% (94.9-99.6)	100% (94.6-100)	100%	97.1%

表三　C肝抗體快篩試劑的敏感度、特異度、陽性預測值及陰性預測值（續）

第一作者	發表年	執行地點	樣本時間	對象或場所情境	RDT試劑(製造廠)	人數	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Kosack [35]	2014	Langen, Germany	September-October 2011	panel 1 (IDU, n=82) from ZeptoMetrix, NewYork, USA	ImmunoFlow HCV test (Core Diagnostics)	81	100% (93.5-100)	100% (86.8-100)	100%	100%
				panel 2 (n=199) from University of Frankfurt, Germany	ImmunoFlow HCV test (Core Diagnostics)	193	99.0%	-	100%	-
Kim [37]	2013	Korea	April-August 2012	HCV negative samples from hospital for routine health screening	GENEDIA HCV Rapid LF (Green Cross Medical Science Corp., Chungbuk, Korea)	100	69.7% (61.1-78.9)	99.3% (97.0-100)	97.9%	62.3%
					SD Bioline HCV (Standard Diagnostics, Kyounggi-do, Korea)	100	78.8% (71.2-86.8)	100%	100%	70.8%
O'Connell [32]	2013	Colmar, PA, US	2004-2008	blood donors from Biological Specialty Corporation	OraQuick HCV Rapid Test (OraSure Technologies, Bethlehem, PA, US)	168	98.8% (94.3-99.9)	98.8% (94.3-99.9)	98.8%	98.8%
					Instant View Cassette (Alfa Scientific Designs, Inc., Poway, CA, US)	168	81.0% (71.5-88.3)	96.4% (90.6-99.1)	95.8%	83.5%
					FirstVue HCV (AT First Diagnostic LLC, Woodbury, NY, US)	168	78.6% (68.8-86.4)	100% (96.5-100)	100%	82.4%
					Axiom HCV Card (Axiom Diagnostics, Burstadt, Germany)	168	91.7% (84.2-96.3)	97.6% (92.4-99.6)	97.5%	92.1%
					Core HCV (Core Diagnostics, Birmingham, UK)	168	34.5% (25.0-45.1)	98.8% (94.3-99.9)	96.7%	60.1%

註：CFDA: China Food and Drug Administration; HCV: hepatitis C virus; HIV: human immunodeficiency virus; IDU: intravenous drug users; NPV: negative predictive value; PPV: positive predictive value; US-CDC: US Centers for Disease Control and Prevention

果顯示C肝抗體RDT試劑相較於實驗室酵素免疫分析法的敏感度介於25.0%至100%，特異度介於71.3%至100%；論文發表年代愈晚，敏感度及特異度則越高。若僅觀察2020年（含）以後發表的6篇研究[26-28,38,40,42]，C肝抗體RDT試劑敏感度介於74.2%至100%，特異度介於86.1%至100%；在前述文獻中，我國上市的3項產品[27,40]之敏感度介於92.8%至100%，特異度介於92.6%至100%。

國際運用C肝抗體快篩試劑的可能情境

前一節所述文獻蒐尋結果中，30篇是描述以RDT進行各地區不同族群或情境下，C肝抗體篩檢服務或探討盛行率的研究[16-24,44-64]，各篇研究提供的試劑名稱、執行時間、進行場域或對象、篩檢人數及年齡等資訊彙整於表四。這30篇研究共涉及25個國家：冰島、英國、丹麥、葡萄牙、西班牙、羅馬尼亞、立陶宛、喬治亞、伊朗、貝南、迦納、盧安達、剛果、衣索比亞、埃及、馬來西亞、緬甸、泰國、越南、馬來西亞、新加坡、香港、美國、加拿大、紐

西蘭等。執行篩檢的人數從86人至埃及的4,960萬人，篩檢超過1萬人的國家包括馬來西亞、羅馬尼亞、盧安達、泰國、喬治亞、埃及；其中埃及在1年半的時間以C肝抗體RDT篩檢將近5千萬人[16]，喬治亞除捐血中心使用實驗室檢驗方式外，其餘對象則使用C肝抗體RDT篩檢[17]。

各文獻涉及之篩檢對象或場所情境相當多樣化，包括針具交換服務站、戒毒中心、定點減害中心、流動毒品消費站、靜脈藥癮者收容中心、美沙冬診所、庇護所、中途之家、愛滋病組織、監獄、美國聯邦認證健康中心（Federally Qualified Health Centers）、藥局、零售連鎖藥妝店、農村、綜合門診中心、醫院及診所、初級保健中心、捐血者、定點照護站、初級及農村衛生單位、健康中心、外展站、HIV病人、男男間性行為者、難民、住院病人、有風險因子的急診病人、肝病病人等。其中埃及是動員所有衛生部醫院、初級及農村衛生單位、健康保險特約診所、大學醫院、軍醫院及警察醫院，以及所有青年中心來提供C肝抗體RDT篩檢服務[16]。喬治亞則是在其國家疾病控制中心（National Centers for Disease Control）總部及區域中心、國家篩檢中心、HCV管理中心、監獄及徵兵站、減害網絡站等提供免費的RDT篩檢服務，也為產前診所的所有孕婦、醫院所有的入院及住院病人、門診及所有鄉村醫師的病人、HIV病人等提供免費RDT篩檢[17,65,66]。馬來西亞一般係在初級保健中心提供篩檢服務[22]，另利用世界肝癌月宣傳並動員醫院及診所提供篩檢服務[57]。對於靜脈藥癮者等較難觸及的對象，從文獻可觀察到需要外展到這些族群較可能出入的地點，無論是定點或移動式的戒毒、減害、毒品消費站、藥局、收容中心、美沙冬診所、中途之家或庇護所等，透過這些場所主動提供RDT篩檢服務將有助於發掘C肝病毒感染者。

我國運用C肝抗體快篩試劑的建議情境

WHO對C肝抗體RDT的建議適用情境主要有二[11]，其一為用於實驗設施及檢驗受限的環境或地區以提高C肝抗體檢驗的受檢率，其二為利用快速獲知檢驗結果來提高後續接受HCV RNA檢驗及治療的比例。

提高C肝抗體受檢率

在提高C肝抗體檢驗的受檢率部份，自國民健康署2020年9月27日起擴大提供45-79歲(原住民提早到40歲)民眾終身一次免費B、C型肝炎篩檢（以下簡稱為成健擴大B、C肝篩檢）迄今，目前約有5,600家成健特約醫事機構實際提供成健B、C型肝炎篩檢服務，普及性高，且自2022年3月1日起成健B、C型肝炎檢查醫師資格鬆綁，不限專科別之成健特約醫事機構專科醫師都可提供篩檢服務，又更提高了C肝抗體篩檢的可近性。在實驗室的anti-HCV檢驗分析能力方面，除醫院具有酵素免疫分析部門外，醫院評鑑暨醫療品質策進會公布的檢驗所也有222家[67]。無論醫師資格的放寬或是酵素免疫分析實驗室的普及，對C肝篩檢的推廣都有所助益。在此前提下，我國多數情境對C肝抗體RDT的需求較低，因此衛生福利部國家消除C肝辦公室於2022年11月22日召開之流行病學組專家會議即決議，在不方便進行抽血檢驗C肝抗體時，例如不易抽血的美沙冬或丁基原啡因替代療法者或其他靜脈藥癮者、愛滋匿名篩檢者、部份矯正機關等，C肝抗體RDT是良好的篩檢工具選擇。此外，其他因受限於醫療資源、地理位置、身分或工作型態較困難觸及的族群，以至於不方便進行抽血檢驗C肝抗體的族群，亦可考慮以C肝抗體RDT來進行篩檢，例如部份偏鄉、山地或離島地區、街友、無固定工作場域之勞工、或參加毒品講習處分者等。

目前我國食品藥物管理署許可的C肝抗體RDT試劑尚無民眾可自行操作的試劑，皆需由專業人員操作。雖然部份國家如美國[55]、英國[24]及紐西蘭[48]可由藥局人員提供C肝抗體RDT服務，但依據我國相關醫療法規，除醫師、醫檢師及在醫師指示下執行醫療輔助行為的護理師可進行採血檢驗外，藥師則不在可採血檢驗的專業人員之列。因此在執行C肝抗體RDT檢驗時，需考量操作採血檢驗的人員資格；例如，常見的清潔針具交換處包括清潔針具販賣機和藥局，雖然是方便讓靜脈藥癮者接受到C肝抗體RDT檢驗的場所，但受限於目前TFDA許可的C肝抗體RDT尚不允許民眾自採自驗或由藥師執行採血檢驗，使得C肝抗體RDT在清潔針具

表四　C肝抗體快篩試劑的運用情境

第一作者	發表年	地點	執行時間	對象或場所情境	RDT試劑（製造廠）	篩檢人數	年齡
Kabamba-Tshikongo [51]	2023	Lubumbashi, Democratic Republic of Congo	November 1, 2017-December 30 2019	blood donors in 2 hospitals (Hôpital Jason Sendwe and Cliniques Universitaires de Lubumbashi)	One Step Hepatitis C Virus Test Strip (Accurate, China)	1,512	18-65
Pratedrat [60]	2023	Phetchabun province, Thailand	September 2020-December 2021	at the point of care	SD Bioline HCV (Abbott, North Chicago, IL)	170,163	35-69
Ciupkeviciene [21]	2022	Lithuania	November 2020-February 2022	Jurininku Health Care Center located in seaport Klaipeda	TOYO rapid test (Turklab Tibbi Malzemeler A.S., Turkey)	4,867	1945-1994世代
Curado [46]	2022	Lisbon, Portugal	March 2018-March 2020	a fixed location harm reduction center, a mobile drug consumption room, and outreach testing (using a mobile unit)	RDT	176	≥18
Hsiang [23]	2022	Singapore	February 2017-September 2018	halfway house residents	OraQuick HCV Rapid Antibody test (OraSure Technologies, Bethlehem, PA, US)	351	≥21
Kamali [53]	2022	Rwanda	September 2019	2 rural Rwandan districts (Kirehe and Southern Kayonza)	SD Bioline (Abbott Diagnostics Korea Inc.)	1,725	≥15
Wong [20]	2022	Hong Kong	May 2021-January 2022	methadone clinics	SD Bioline HCV antibody testing	86	not available
Draper [47]	2021	Yangon, Myanmar	30 January-30 September 2019	two sites: PWID; people with liver disease	SD Bioline	633	≥18
Hedayati-Moghaddam [50]	2021	Mashhad, Iran	March-December 2019	drug treatment and harm reduction centers	SD Bioline HCV (Standard Diagnostics Inc., South Korea)	390	15-74
Kamali [52]	2021	Mahama Camp, Eastern Rwanda	February-March 2020	Burundian refugees	SD Bioline rapid diagnostic tests (Abbott Diagnostics Korea Inc, Giheung-gu, Korea)	26,498	≥15
Kpossou [54]	2021	Benin	July 2016	4 big cities of 4 different departments	ImuMed HCV Rapid Diagnostic Test (Healgen Scientific LLC, US)	2,809	all age
Markby [22]	2021	Malaysia	December 2018-October 2019	25 primary healthcare clinics	SD Bioline HCV RDT (Standard Diagnostic, Korea)	15,366	adult
Nguyen [19]	2021	Vietnam	since 2017	PWID and/or MSM	OraQuick HCV Rapid Antibody Test (OraSure Technologies Inc., Bethlehem, PA, US)	282	≥18
Olafsson [18]	2021	Iceland	first 3 years since Feb 10, 2016~	harm reduction facilities, homeless shelters	Oraquick (Orasure Technologies, Bethlehem, PA, US)	1,248	≥18
Wentworth [63]	2021	Denmark	May-August 2020	patients with one or more risk factors in the emergency department at Odense University Hospital	Rapid Anti-HCV Test (InTec Products, INC)	489	18-79
Birjandi [44]	2020	Accra, Ghana	July- September 2019	outpatients of the polyclinic	RDT	728	≥18
Gauld [48]	2020	Waitemata District Health Board in West and North Auckland, New Zealand	7: late July 2018-2 November 2019 3: April 2019-2 November 2019	10 participating pharmacies	SD Bioline HCV rapid kit	192	≥16 with ≥1 risk factors; 35-69

表四　C肝抗體快篩試劑的運用情境（續）

第一作者	發表年	地點	執行時間	對象或場所情境	RDT試劑（製造廠）	篩檢人數	年齡
Gheorghe [49]	2020	Romania	March 2019-March 2020	all admitted patients from >20 medical institutions (from 4 Romanian cities: Bucharest, Iasi, Timisoara, Cluj-Napoca)	RDT	25,141	≥18
Lee [56]	2020	Alabama, US	November 2016-November 2018	shelters, drug treatment centers, AIDS organizations, Federally Qualified Health Centers	OraQuick HCV testing kits (Orasure Technologies)	4,293	adult
Md Said [57]	2020	Malaysia	July 15-21, 2019	49 hospitals and 38 health clinics (one-week nationwide hepatitis C screening campaign)	SD Bioline HCV rapid test	11,382	adult
Mohamed [58]	2020	West London, England	September 2017-December 2018	remand prison	Xpert HCV VL Fingerstick	162	not available
NHS Publishing [24]	2020	UK	August 2020	PWID (pharmacy store)	InTec Rapid Anti-HCV Test	-	≥18
Noller [59]	2020	South Island, New Zealand	not available	3 NEX services (needle exchanges)	OraQuick Rapid HCV Rapid Antibody Test (OraSure Technologies)	204	≥16
Ragan [61]	2020	Calgary, Alberta, Canada	April-July 2018	patients who self-reported one or more high-risk criteria at the community hospital ED	Oraquick HCV Rapid Antibody Test	144	≥18
Rodríguez-Tajes [62]	2020	Catalonia, Spain	October 2016-October 2018	38 primary care centers	Quickview (Lumiquick Diagnostics)	3,328	≥18
Shadaker [17]	2020	Georgia	November 1, 2016-October 31, 2017	270 hospitals	RDT or enzyme immunoassay	252,848	≥18
Waked [16]	2020	Egypt	October 1, 2018-April 30, 2019	all Ministry of Health hospitals; all primary and rural health units; Egyptian Health Insurance Organization-managed clinics, university hospitals, and military and police hospitals; all youth centers	SD Bioline HCV (Abbott)	49,630,319	≥18
Kugelmas [55]	2017	US	September 2015-February 2016	45 Walgreens retail pharmacies in 9 US cities (Chicago, Dallas, Houston, Miami, New York, Oakland, Philadelphia, Phoenix, and San Antonio)	OraQuick HCV Rapid Antibody Test (OraSure Technologies)	1,296	birth cohort (1945-1965) or ≥18 years with CDC-defined high-risk factors
Shimelis [64]	2017	Southern Ethiopia	October-November 2015	HIV-infected clients at Hawassa University Hospital	CTK Biotech, Inc, San Diego, CA, US	477	≥15
Bouscaillou [45]	2014	Tbilisi, Georgia	October 2012	PWID (drop-in centre)	SD-Bioline HCV RDT	217	≥18

註：AIDS: acquired immunodeficiency syndrome; ED: emergency department; MSM: men who have sex with men; NHS: UK National Health Service; PWID: people who inject drugs; RDT: rapid diagnostic test.

交換處，或其他無相關專業人員在場的場域上推動，可能會遇到執行面的困難。

提高C肝抗體陽性者之HCV RNA受檢率

我國要達成C肝消除的目標，除了繼續努力提高C肝抗體檢驗的受檢率外，另一個關鍵阻礙是C肝抗體陽性者接受HCV RNA檢驗的比例仍偏低。以成健擴大B、C肝篩檢為例，在初期HCV RNA檢驗率僅不到5成。為了能有效提升HCV RNA檢驗率，WHO建議可進行HCV reflex testing（反射式檢驗）來簡化C肝診斷的兩階段檢定步驟，即當民眾接受C肝抗體篩檢時，先抽取足夠的血液檢體，待C肝抗體分析結果顯示為陽性後，民眾無須再次回診，醫療院所即可直接以預先收集的血液檢體執行HCV RNA檢驗。在國民健康署及中央健康保險署的合作下，我國自2021年10月起增加成健C肝篩檢的HCV reflex testing申報方式，供醫療院所選擇。至2022年年底之統計資料顯示，HCV RNA檢驗率雖已有提升，但仍未達70%。究其原因，可能由於HCV reflex testing除了需申報方式的配合外，仍需在實際檢驗流程上作協調才能達成，包括在執行C肝抗體篩檢時，即預先抽取較多的血液檢體，並在C肝抗體檢驗結果為陽性後，再將該檢體送至可執行HCV RNA檢驗的單位進行檢驗，因此牽涉到採檢單位、抗體檢驗單位和HCV RNA檢驗單位之間的協調合作及成本分攤。

在HCV RNA檢驗資源方面，雖然醫院評鑑暨醫療品質策進會公布全國檢驗所達222家[67]，但其中取得財團法人全國認證基金會（Taiwan Accreditation Foundation, TAF）認證具HCV RNA檢驗能力之實驗室僅有34家[68]，且各區域分布並不均等，許多偏鄉，例如馬祖、澎湖等離島，都必須將血液檢體送回臺灣本島才能完成HCV RNA檢驗。WHO建議另一種可提升HCV RNA檢驗率的方式，即是推動C肝抗體RDT篩檢。由於C肝抗體RDT可在5-20分鐘內快速獲知結果，當場再針對抗體陽性民眾抽血作後續HCV RNA檢驗，如此將可大幅簡化醫療端及民眾端的程序及時間，提高HCV RNA檢驗率[12]，並可減少血液檢體保存及銷毀之成本；若由此觀點思考，C肝抗體RDT的適用族群或可考慮再加以放寬。參酌2023年2月屏東縣琉球鄉推動C肝抗體快篩的經驗，透過衛生局及衛生所針對45-79歲C肝抗體未篩名單進行篩檢邀約，10天期間有約1,000位居民參加C肝抗體RDT篩檢，其中14位結果為陽性，14人全數皆完成採血進行後續HCV RNA檢驗。就琉球鄉的例子而言，C肝抗體RDT篩檢既省去醫療人力及檢體處置成本，也省去民眾傳統第一階段需回診確認C肝抗體報告結果的資源耗用。

因此對於醫療院所及實驗室檢驗分析資源較為不足的偏鄉、山地及離島地區，受限於交通運輸不便，無論是anti-HCV酵素免疫分析或是HCV RNA分子生物學分析，民眾取得報告的時間相較於都會區通常需要更長的天數；例如僅能仰賴衛生室提供醫療服務的山地居民、外島居民，縱使檢體被收集，可能也得累積到一定的量，或是恰逢有進都會的車船才能將檢體送檢。若民眾再因工作性質或是交通因素無法取得結果報告，陽性結果的民眾恐有延宕診治的可能。在這些地區，或可考慮推動C肝抗體RDT篩檢。

結　語

簡化診斷流程[12]及診斷即治療（test-and-treat）策略是國際趨勢[69]，特別是對於一些特殊族群[70-73]。雖然我國尚未引進WHO建議之HCV RNA乾血點（dried blood spot, DBS）診斷檢驗[11]，相較於傳統實驗室檢驗更快獲知結果的HCV RNA定點照護（POC）檢驗模式[11]，亦鮮少為醫療院所使用；但C肝抗體RDT對於不方便進行靜脈穿刺取血檢驗的特殊族群，例如血管脆弱不易抽血的美沙冬或丁基原啡因替代療法者或其他靜脈藥癮者、愛滋匿名篩檢者、部份矯正機關收容人等，應是有助於提升C肝抗體篩檢率的良好選擇。且C肝抗體RDT是除了HCV reflex testing以外，另一個可有效提升HCV RNA檢驗率的方式，對於醫療院所及實驗室檢驗分析資源較為不足的偏鄉、山地及離島地區，或可優先考慮推動C肝抗體RDT篩檢。

我國以2025年消除C肝為重要政策目標，在剩下的2年內，如何加強各目標族群的C肝抗體篩檢率及HCV RNA檢驗率，將是能否順利達成目標的重要關鍵。C肝抗體RDT的檢驗效能已在國際獲得認可，也有諸

多使用經驗，在我國亦有通過上市許可的產品，若能善用C肝抗體RDT的長處，相信對我國加速C肝篩檢及提升HCV RNA檢驗率將帶來不小助益。

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Rapid diagnostic tests for detection of antibodies to hepatitis C virus

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Most patients with chronic hepatitis C often remain asymptomatic or experience nonspecific symptoms for decades, and by the time symptoms manifest, the disease has deteriorated to life-threatening stages such as cirrhosis or liver cancer. Early detection of hepatitis C virus (HCV) infection is crucial for preventing and managing subsequent complications. The conventional two-step diagnostic process, involving initial enzyme immunoassay testing for HCV antibodies (anti-HCV) followed by nucleic acid testing in the laboratory to confirm the presence of HCV, presents a significant challenge in the discovery and diagnosis of HCV virus infection. In addition to traditional laboratory-based serum antibody testing, the World Health Organization recommends the use of rapid diagnostic tests (RDTs) as one of the methods for analyzing anti-HCV antibodies, with the potential to improve access and linkage to care and treatment. Since 2020, the studies have shown that both the specificity and sensitivity of the anti-HCV RDTs have been improved. Three anti-HCV RDTs in Taiwan have received market approval, each demonstrating a sensitivity and specificity of at least 92.8% and 92.6%, respectively, as indicated by literature reviews. This article collects and summarizes existing literature on the diagnostic performance of anti-HCV RDTs and their implementation scenarios. It aims to enhance awareness across various sectors regarding the utility of anti-HCV RDTs and to discuss their potential applications in accelerating hepatitis C elimination efforts in Taiwan. (*Taiwan J Public Health. 2023;**42(6)**:594-611*)

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