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Cascade Analysis of Anonymous Voluntary HIV Counseling and Testing Among Patients with HIV Infection in Taiwan

Chun-Yuan Lee, MD,[1–3] Pei-Hua Wu, MD,[4,5] Jih-Jin Tsai, PhD,[3,4,6] Tun-Chieh Chen, PhD,[3,7] Ko Chang, MD,[1,3] and Po-Liang Lu, PhD[3,4,8]

Abstract

Despite successful implementation of anonymous voluntary human immunodeficiency virus (HIV) counseling and testing (aVCT) in Taiwan, the trend of late HIV presentation in sexually active populations has remained unchanged in Taiwan over the past decade. We evaluated the effect and acceptance of an aVCT cascade program among Taiwanese individuals by surveying 572 participants (mean age: 29.6 years; 99.3% men; and 79.5% same-sex sexual contact) diagnosed with HIV/acquired immune deficiency syndrome (AIDS) from 2015 to 2019. We designed a five-stage continuum based on acceptance of the program before HIV diagnosis: at high risk of HIV infection (Stage 1), heard of aVCT (Stage 2), wants to receive aVCT (Stage 3), has received aVCT (Stage 4), and regularly receives aVCT (Stage 5). Four domains established from exploratory factor analysis described reasons for inability to reach the next aVCT stage: low perceived HIV risk, fear of testing positive because of discrimination/stigmatization, and structural barriers to aVCT. Regular aVCT (vs. never receiving aVCT) protected against AIDS on diagnosis ($p < 0.001$). There were no significant differences in program acceptance across 2015–2019. However, uptake reduced markedly across the program; the largest reduction (37.4.0–61.0%) occurred from Stage 4 to Stage 5. Fear of testing positive because of discrimination/stigmatization was the main reason for not proceeding to the next aVCT stage. Although the findings indicate the benefits of regular aVCT for early HIV diagnosis, additional strategies to reduce fear of negative social consequences of HIV infection are prioritized to optimize aVCT in Taiwan.

Keywords: cascade, discrimination, human immunodeficiency virus, stigmatization, HIV testing

Introduction

Human immunodeficiency virus (HIV) infection diagnosis is essential for ''the first 90'' of the 90-90-90 continuum of HIV care advocated by the World Health Organization (WHO). People who are aware of their HIV-positive status display a low frequency of risky behaviors, which could cause further HIV transmission.[1–3] Further, early entry into HIV care reduces morbidity and mortality among people living with HIV (PLWH).[4–6] Improving ''the first 90'' involves HIV testing in individuals having HIV infection risk. Several strategic combinations of HIV testing services (HTSs) have been advocated, which primarily comprise routine or opt-out testing,[7,8] indicator condition (IC)-guided HIV testing [patients presenting to any health care setting with conditions indicating acquired immune deficiency syndrome (AIDS)-defining diseases or higher prevalence of undiagnosed HIV, or significant adverse implications for the patient, would be routinely recommended a HIV testing],[9,10] and voluntary HIV counseling and testing (VCT).[11]

[1]Department of Internal Medicine, Kaohsiung Municipal Siaogang Hospital, Kaohsiung City, Taiwan.
[2]Graduate Institute of Medicine, Kaohsiung Medical University, Kaohsiung City, Taiwan.
[3]Department of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung City, Taiwan.
[4]Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung City, Taiwan.
[5]Department of Public Health, College of Health Science, Kaohsiung Medical University, Kaohsiung City, Taiwan.
[6]Tropical Medicine Center, Kaohsiung Medical University Hospital, Kaohsiung City, Taiwan.
[7]Infection Control Office, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung City, Taiwan.
[8]Department of Laboratory Medicine, Kaohsiung Medical University Hospital, Kaohsiung City, Taiwan.

The US Centers for Disease Control and Prevention (CDC) advocates a universal opt-out and routine HTS for all individuals at the point of contact with a health care system in areas with local HIV seroprevalence ≥0.1%.[8] Except in specific situations (pregnancy, military recruitment, and imprisonment), involuntary routine HIV testing in at-risk individuals is prohibited by law in Taiwan. The IC-guided HTS has been advocated in many European countries since 2016,[12] and these HTSs can alleviate the shame surrounding HIV infection risk assessment.[9] However, their implementation remains low in numerous countries[13–15] because of a lack of awareness and experienced physician.[16] Moreover, IC-guided HTSs do not facilitate testing for asymptomatic HIV.

Considering the limitations of the aforementioned HTSs, VCT remains a crucial strategy for encouraging at-risk individuals to test regularly to ensure early diagnosis. VCT reportedly leads to a reduction in risky sexual behaviors[2,3] and a reduction in the incidence of HIV infection.[17] In Taiwan, a nationwide program of free anonymous VCT (aVCT) for HIV infection among the at-risk population was initiated in 1997 at several hospitals, clinics, and nongovernmental organizations. According to the 2005–2016 annual reports from the Taiwan CDC (TW-CDC), the annual number of visits for free aVCT services increased from 5350 to 37,244 and percentage of PLWH diagnosed through aVCT increased from 5.16% to 29.34%; moreover, HIV seropositivity detection rate remained between 1.9% and 3.0% over 2005–2016.

Despite successful implementation of aVCT in Taiwan, the rate of late HIV infection presentation in the sexually active population has remained unchanged since 2000s,[18–20] which indicates that numerous at-risk individuals are unaware of aVCT or are unwilling to undergo aVCT until late-stage HIV infection is diagnosed by routine or IC-guided HTS. In 2019, the WHO HTS guidelines recommended annual HIV testing for individuals with ongoing HIV-related risks in all settings.[21] Engagement in annual aVCT can be conceptualized as a continuum-aVCT care cascade, which begins with ''patients at high risk of HIV infection'' and progresses through to ''patients receiving aVCT at least annually,'' but many patients at high risk of HIV infection may disengage from annual aVCT across the span of the care cascade. However, relevant studies related to the uptake of each step of aVCT care cascade are scarce.[13] The only study conducted in Taiwan revealed that over 2006–2008, only 57.4% of PLWH had received aVCT, with an even smaller number (26.0%) receiving regular aVCT, before HIV infection diagnosis.[13] Better understanding of the magnitude and reasons of loss at different stages of aVCT care cascade could aid in promoting regular access to aVCT before HIV diagnosis for at-risk individuals.[22]

To address this gap in the literature, in this study, we administered questionnaires to PLWH diagnosed from 2015 to 2019 at three HIV referral centers in Taiwan to collect data for a cascade analysis of aVCT. The aim of this study was to collect data that would assist in devising strategies encouraging patients with a high HIV infection risk to receive aVCT at least annually.[8,21] To that end, we evaluated the effect of aVCT on AIDS diagnosis at presentation and then investigated the care cascade of aVCT program. Finally, we explored the causes of losses at each step of the aVCT care cascade.

Methods

Study design and setting

A multicenter, cross-sectional, questionnaire-based investigation was conducted at Kaohsiung Medical University Chung-Ho Memorial Hospital, the largest referral center for the treatment of patients with HIV in Southern Taiwan, and Kaohsiung Municipal Siaogang Hospital and Kaohsiung Municipal Ta-Tung Hospital, two regional hospitals in Southern Taiwan, from April 1, 2017, to December 31, 2019. The health care staff at each hospital had extensive experience in treating PLWH. This study was approved by the ethics committee of Kaohsiung Medical University Hospital [KMUHIRB-SV(II)-20170056], and it adhered to the principles of the Declaration of Helsinki. Because the data were analyzed anonymously, the ethics committee waived the need for written informed consent.

Development of questionnaire assessing opinions and acceptance of aVCT before HIV infection diagnosis

The questionnaire was designed to (1) understand the evolution of HIV-related risk assessment, (2) determine participants' opinions on HIV-related issues and on the use of aVCT before HIV infection diagnosis, (3) determine the factors associated with stage of HIV infection at presentation, (4) develop an aVCT cascade and examine the acceptance of the cascade among different categories of participants, and (5) examine the reasons for the inability to proceed to the next step of the aVCT program cascade.

An expert group—comprising an HIV case manager, consultants working in aVCT programs, HIV specialists, and researchers working in the participating hospitals—developed the preliminary questionnaire used in this study. Questions used in studies related to the perception of HIV infection and the reasons for the inability to access VCT were modified for this study.[23–26] We performed a pretest in 30 PLWH using the preliminary questionnaire and discussed ambiguous responses and participant comments with the expert group. After the pretest, we modified the preliminary questionnaire, tested it again on 20 PLWH, and then modified the questionnaire further.

The final questionnaire consisted of five sets of variables: sociodemographics, HIV-related risk assessment, thoughts on HIV-related issues, thoughts regarding the use of aVCT before HIV infection diagnosis, and reasons for the inability to proceed to the next step of the aVCT cascade. Variables related to thoughts on HIV-related issues included perceived risk of HIV infection, perceived stigma associated with HIV infection, perceived discrimination against PLWH, and perceived severity of HIV infection; these variables were measured using a 5-point Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree).

Sixteen questions initially designed to evaluate the reasons for the inability to proceed to the next step of the aVCT cascade were also rated using a 5-point Likert scale (strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree).

Participants and study procedure

A trained investigator screened patients diagnosed as having HIV infection between January 1, 2015, and

December 31, 2019. Patients who were younger than 20 years, were dead at screening, or were lost to follow-up during the screening period (over April 1, 2017–December 31, 2019) were excluded from the study. The trained investigator then explained the goal and procedure of the study to the eligible patients in the outpatient departments in the participating hospitals. If the eligible patients agreed to participate in the study, verbal informed consent for enrollment was obtained by trained investigators. Participants were then asked to recall their circumstances at HIV infection diagnosis, while doing the self-completed questionnaires on Google forms.

Each participant was categorized into one of five groups according to the calendar year of their HIV infection diagnosis: 2015 (Group 1), 2016 (Group 2), 2017 (Group 3), 2018 (Group 4), and 2019 (Group 5). Each calendar group was then stratified into a continuum of five stages (the ''aVCT cascade'') based on their acceptance of aVCT before HIV infection diagnosis (Fig. 1): patients at high risk of HIV infection (Stage 1), heard of aVCT (Stage 2), want to receive aVCT (Stage 3), have received aVCT (Stage 4), and regularly receive aVCT (Stage 5).

Each participant was subsequently categorized into one of five subgroups based on the loss from preceding stage to the next of the aVCT cascade: high HIV infection risk, but never heard of aVCT (Subgroup 1), heard of aVCT, but do not want to receive aVCT (Subgroup 2), want to receive aVCT, but do not receive aVCT (Subgroup 3), have received aVCT, but do not regularly receive aVCT (Subgroup 4), and have regularly receive aVCT (Subgroup 5; Fig. 1).

Finally, participants in Subgroup 2–4 were asked the reasons for the inability to proceed to the next step of the aVCT cascade.

Definitions

The stage of HIV infection at presentation was retrieved from medical records, and was recorded on a 0–3 scale by using the US CDC 2014 case definition of HIV infection.[27] Baseline $CD4^+$ cell count, HIV viral load, and other laboratory test results (hepatitis A virus antibody, hepatitis B virus surface antigen, and hepatitis C virus antibody titers) were measured as soon as possible or within 6 months at HIV infection diagnosis.[28]

The five stages of aVCT cascade (Fig. 1) are defined below. Stage 1 comprised patients who should receive HIV testing at least annually.[8,21] The Stage 1 criterion was modified to include injection-drug users, individuals who exchanged sex for money or drugs, sexual partners of people with HIV infection, men who had male sexual partners (MSM), and people who had multiple sexual partners or condomless sex before HIV infection diagnosis.[8] Stage 2 comprised patients who met the Stage 1 criteria and had heard of aVCT before HIV infection diagnosis. Stage 3 comprised patients who met the Stage 2 criteria and wanted to receive aVCT before HIV infection diagnosis. Stage 4 comprised patients who met the Stage 3 criteria and had received aVCT before HIV infection diagnosis. Stage 5 comprised patients who met the Stage 4 criteria and received aVCT at least once a year.

Participants were categorized into five subgroups (Fig. 1). Subgroup 1 comprised patients who met the Stage 1 criteria, but had never heard of aVCT. Subgroup 2 comprised patients who met the Stage 2 criteria, but did not want to receive aVCT. Subgroup 3 comprised patients who met the Stage 3 criteria, but did not receive aVCT. Subgroup 4 comprised patients who met the Stage 4 criteria, but did not receive aVCT at least once a year. Subgroup 5 comprised patients who met the Stage 5 criteria. Subgroups 1, 2, and 3 were collectively termed ''no VCT,'' Subgroup 4 was termed ''irregular VCT,'' and Subgroup 5 was termed ''regular VCT.''

Outcomes of interest

The primary outcome was the effect of aVCT (no, irregular, or regular VCT) on the diagnosis of AIDS at presentation. The

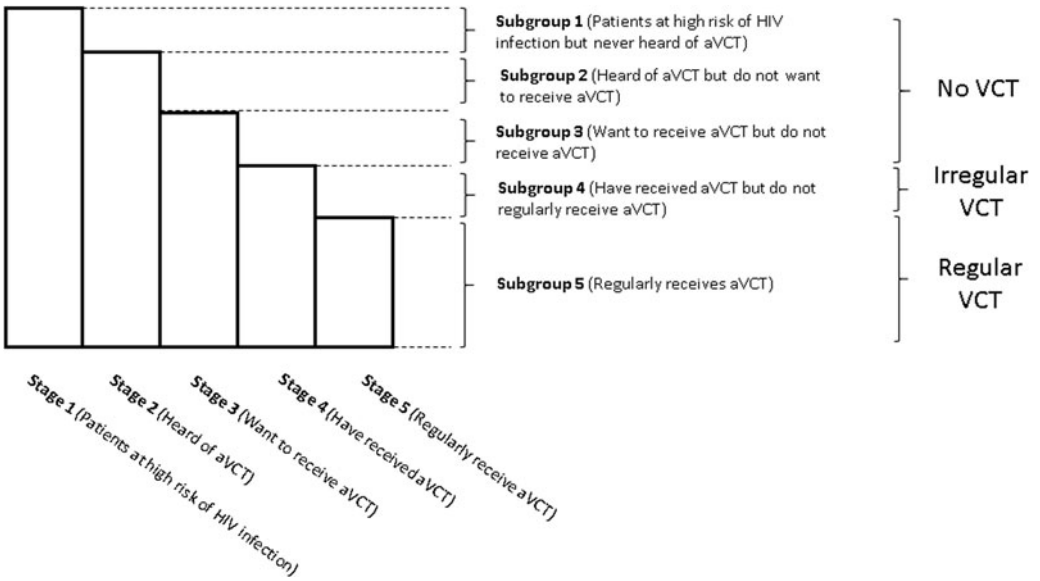

FIG. 1. Schematic description of aVCT. aVCT, anonymous voluntary human immunodeficiency virus counseling and testing.

Table 1. Demographics, Human Immunodeficiency Virus-Related Variables, and Anonymous Voluntary Human Immunodeficiency Virus Counseling and Testing Status of Enrolled Patients 2015–2019

	Total N = *572*	*2015* N = *114*	*2016* N = *117*	*2017* N = *139*	*2018* N = *111*	*2019* N = *91*	p
Sociodemographic characteristics							
Male, *n* (%)	568 (99.3)	114 (100)	114 (97.4)	138 (99.3)	111 (100)	91 (100)	0.089
Mean age at HIV presentation, years (SD)	29.6 (7.9)	28.0 (7.2)	28.6 (6.7)	30.5 (8.3)	29.9 (7.4)	31.0 (9.5)	0.020
Subgroup of age (years) at presentation, *n* (%)							0.727
30	369 (64.5)	77 (67.5)	79 (67.5)	85 (61.2)	70 (63.1)	58 (63.7)	
31–40	148 (25.9)	30 (6.3)	29 (24.8)	37 (26.6)	31 (27.9)	21 (23.1)	
≥41	55 (9.6)	7 (6.1)	9 (7.7)	17 (12.2)	10 (9.0)	12 (13.2)	
HIV diagnosis in Kaoping area, *n* (%)	490 (85.7)	93 (81.6)	86 (73.5)	117 (84.2)	105 (94.6)	89 (97.8)	<0.001
HIV stage at presentation by 2014 CDC definition,[27] *n* (%)							0.148
Stage 0 (Acute HIV)	46 (8.0)	4 (3.5)	11 (9.4)	9 (6.5)	10 (9.0)	12 (13.2)	
Stage 1 (CD4 count ≥500 cells/μL)	84 (14.7)	17 (14.9)	12 (10.3)	22 (15.8)	17 (15.3)	16 (17.6)	
Stage 2 (CD4 count 200–499 cells/μL)	265 (46.3)	64 (56.1)	59 (50.4)	65 (46.8)	44 (39.6)	33 (36.3)	
Stage 3 (AOIs or CD4 cell count <200 cells/μL)	177 (30.9)	29 (25.4)	35 (29.9)	43 (30.9)	40 (36.0)	30 (33.3)	
Comorbidities, *n* (%)							
Chronic kidney disease	1 (0.2)	1 (0.9)	0 (0)	0 (0)	0 (0)	0 (0)	0.403
Diabetes mellitus	12 (2.1)	2 (1.8)	1 (0.9)	5 (3.6)	3 (2.7)	1 (1.1)	0.540
Hypertension	19 (3.3)	3 (2.6)	1 (0.9)	8 (5.8)	5 (4.5)	2 (2.2)	0.215
Depression disorder	24 (4.2)	5 (4.4)	4 (3.4)	8 (5.8)	3 (2.7)	4 (4.5)	0.799
Insomnia	30 (5.2)	7 (6.1)	2 (1.7)	10 (7.2)	5 (4.5)	6 (6.6)	0.326
Marriage, *n* (%)	15 (2.6)	4 (3.5)	1 (0.9)	5 (3.6)	2 (1.8)	3 (3.4)	0.600
Employment, *n* (%)	464 (81.1)	100 (87.7)	106 (90.6)	111 (79.9)	80 (72.1)	67 (73.6)	0.001
Education above college level at presentation, *n* (%)	316 (55.2)	68 (59.6)	65 (55.6)	69 (49.6)	65 (58.6)	49 (53.8)	0.520
History of sexually transmitted diseases, *n* (%)	280 (49.0)	55 (48.2)	51 (43.6)	78 (56.1)	59 (53.2)	37 (40.7)	0.111
Multiple sexual partners, *n* (%)	437 (76.4)	85 (74.6)	94 (80.3)	104 (74.8)	84 (75.7)	70 (76.9)	0.834
History of unprotected sex, *n* (%)	548 (95.8)	107 (93.9)	113 (96.6)	137 (98.6)	107 (96.4)	84 (92.3)	0.150
History of chemosex, *n* (%)	191 (33.4)	44 (38.6)	36 (30.8)	42 (30.2)	40 (36.0)	29 (31.9)	0.588
HIV-related risk assessment							0.576
Same-sex sexual contact, *n* (%)	455 (79.5)	92 (80.7)	92 (78.6)	115 (82.7)	90 (81.1)	66 (72.5)	
Different-sex sexual contact, *n* (%)	35 (6.1)	6 (5.3)	7 (6.0)	8 (5.8)	4 (3.6)	10 (11.0)	
Same- and different-sex sexual contact, *n* (%)	78 (13.6)	14 (12.3)	17 (14.5)	16 (11.5)	16 (14.4)	15 (16.5)	
IDU, *n* (%)	4 (0.7)	2 (1.8)	1 (0.9)	0 (0.0)	1 (0.9)	0 (0.0)	
Laboratory profiles							
Mean CD4 count at presentation, cells/L (SD)	313 (223)	330 (183)	304 (197)	311 (236)	294 (224)	335 (275)	0.643
Subgroup of CD4 cell count at presentation, *n* (%)							0.192
≤200 cells/μL	185 (32.3)	30 (26.3)	36 (30.8)	44 (31.7)	42 (37.8)	33 (36.3)	
201–350 cells/μL	151 (26.4)	27 (23.7)	35 (29.9)	38 (27.3)	29 (26.1)	22 (24.2)	
351–500 cells/μL	140 (24.5)	40 (35.1)	31 (26.5)	33 (23.7)	20 (18.0)	16 (17.6)	
≥501 cells/μL	96 (16.8)	17 (14.9)	15 (12.8)	24 (17.3)	20 (18.0)	20 (22.0)	
Mean VL (log) (SD)	4.82 (0.78)	4.73 (0.71)	4.84 (0.92)	4.84 (0.74)	4.90 (0.71)	4.77 (0.85)	0.496
HIV VL >100,000 copies/mL, *n* (%)	228 (39.9)	36 (31.6)	52 (44.4)	60 (43.2)	46 (41.4)	34 (37.4)	0.260
RPR titer 1:8, *n* (%)	176 (31.3)	35 (31.5)	32 (28.1)	49 (36.0)	30 (27.0)	30 (33.0)	0.552
HAV Ab seropositivity, *n* (%)	131 (23.1)	27 (23.7)	25 (21.6)	30 (21.7)	27 (24.5)	22 (24.7)	0.965
HBs Ag seropositivity, *n* (%)	44 (7.7)	9 (7.9)	12 (10.3)	9 (6.5)	7 (6.3)	7 (7.7)	0.794
HCV Ab seropositivity, *n* (%)	40 (7.0)	6 (5.3)	10 (8.5)	8 (5.8)	11 (9.9)	5 (5.5)	0.549

(*continued*)

Table 1. (Continued)

	Total N = *572*	*2015* N = *114*	*2016* N = *117*	*2017* N = *139*	*2018* N = *111*	*2019* N = *91*	p
Thoughts on HIV-related issues							
Heard of HIV before HIV diagnosis, *n* (%)	551 (96.3)	109 (95.6)	111 (94.9)	133 (95.7)	110 (99.1)	88 (96.7)	0.482
Perceived risk for HIV transmission, *n* (%)							0.382
Do not positively agree	423 (74.0)	92 (80.7)	85 (72.6)	100 (71.9)	83 (74.8)	63 (69.2)	
Positively agree	149 (26.0)	22 (19.3)	32 (27.4)	39 (28.1)	28 (25.2)	28 (30.8)	
Recognize HIV as a severe illness, *n* (%)							0.817
Do not positively agree	221 (38.6)	44 (38.6)	44 (37.6)	50 (36.0)	43 (38.7)	40 (44.0)	
Positively agree	351 (61.4)	70 (61.4)	72 (62.4)	89 (64.0)	68 (61.3)	51 (56.0)	
Perceived stigma of HIV infection, *n* (%)							0.799
Do not positively agree	147 (25.7)	28 (24.6)	28 (23.9)	41 (29.5)	29 (26.1)	21 (23.1)	
Positively agree	425 (74.3)	86 (75.4)	89 (76.1)	98 (70.5)	82 (73.9)	70 (76.9)	
Perceived discrimination of HIV infection, *n* (%)							0.977
Do not positively agree	103 (18.0)	20 (17.5)	23 (19.7)	23 (16.5)	20 (18.0)	17 (18.7)	
Positively agree	469 (82.0)	94 (82.5)	94 (80.3)	116 (83.5)	91 (82.0)	74 (81.3)	
Subgroup according to acceptance of aVCT cascade upon HIV diagnosis, *n* (%)							0.139
Never heard of aVCT	55 (9.6)	14 (12.3)	11 (9.4)	13 (9.4)	8 (7.2)	9 (9.9)	
Does not want to receive aVCT	89 (15.6)	21 (18.4)	20 (17.1)	21 (15.1)	11 (9.9)	16 (17.6)	
Does not receive aVCT	82 (14.3)	15 (13.2)	20 (17.1)	22 (15.8)	18 (16.2)	7 (7.7)	
Does not regularly receive aVCT	170 (29.7)	39 (34.2)	28 (23.9)	31 (22.3)	43 (38.7)	29 (31.9)	
Regularly receives aVCT	176 (30.8)	25 (21.9)	38 (32.5)	52 (37.4)	31 (27.9)	30 (33.0)	

Categorical variables among the five groups were compared using the χ^2 test or Fisher's exact test, and continuous variables were compared using the independent *t*-test or one-way analysis of variance. Data are *n* (%), unless indicated otherwise; percentages were calculated for all individuals for a given calendar year.

AIDS, acquired immune deficiency syndrome; AOI, AIDS-defining opportunistic illness; aVCT, anonymous voluntary HIV counseling and testing; CDC, Centers for Disease Control and Prevention; HAV, hepatitis A virus; HBs Ag, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU, intravenous drug user; RPR, rapid plasma reagin; SD, standard deviation; VL, viral load.

secondary outcomes were acceptance of the aVCT cascade from 2015 to 2019 and reasons for the inability to proceed to the next step of the aVCT cascade.

Statistical analysis

A descriptive analysis of the characteristics of the participants in five calendar-based groups was performed. For variables in the set ''thoughts on HIV-related issues,'' the responses ''agree'' and ''strongly agree'' were classified as ''positively agree.'' Categorical variables in the five groups were compared using χ^2 or Fisher's exact tests, and continuous variables were compared using one-way analyses of variance followed by a Tukey *post-hoc* test.

Univariable and multivariable analyses were performed to examine the associations between the study variables and AIDS at presentation. Binary logistic regression analysis for AIDS at presentation was performed using backward selection. In the multivariable analysis, a history of sexually transmitted diseases was used instead of Rapid Plasma Reagin titer ≥1:8 because of the marked collinearity between these two variables. The effects of each variable were estimated using odds ratios. Trend analyses of each stage in the aVCT cascade from 2015 to 2019 were performed using the Cochran-Armitage trend test with modified ridit scores.

To test the validity of the 16 reasons provided for the inability to proceed to the next step of the aVCT cascade, an item analysis was performed to assess item discrimination and an exploratory factor analysis to investigate the structural domain of the variables. Principal axis factor analysis with varimax rotation extraction was performed. Cronbach's alpha was employed to measure reliability for questions in each structural domain generated from the exploratory factor analysis. Finally, the mean scores of each structural domain within Subgroup 2, 3, and 4 were compared using one-way analyses of variance followed by a Tukey *post-hoc* test. All tests were two tailed, and $p < 0.05$ was considered significant. Statistical analyses were performed using SPSS (version 25.0; IBM Corp., Armonk, NY).

Results

Patients who were excluded from analysis

In total, 838 participants met the screening criteria for new diagnosis of HIV infection from January 1, 2015, to December 31, 2019. Among them, 266 patients were excluded because they were lost to follow-up ($n = 170$), were unwilling to participate in the study ($n = 74$), or died ($n = 22$). The remaining 572 enrolled participants were divided into Groups 1 ($n = 114$), 2 ($n = 117$), 3 ($n = 139$), 4 ($n = 111$), and 5 ($n = 91$).

Table 2. Risk Factors for Acquired Immune Deficiency Syndrome at Presentation Among Patients with Newly Diagnosed Human Immunodeficiency Virus Infection 2015–2019

	Number of patients, n = *572*	*Number of AIDS cases* n = *177*	*%*	*Univariable analysis, crude OR (95% CI)*	*Multivariable analysis, adjusted OR (95% CI)*
Demographic variables					
Age group (years), *n* (%)					
≤30	369	96	26	1.0 (Reference)	1.0 (Reference)
31–40	148	52	35.1	1.54 (1.02–2.32)*	1.61 (1.03–2.51)*
≥41	55	29	52.7	3.17 (1.78–5.66)***	2.81 (1.49–5.29)**
Sex, *n* (%)					
Female	4	4	100	1.0 (Reference)	1.0 (Reference)
Male	568	173	30.5	N/A	
Period of HIV diagnosis, *n* (%)					
2015	114	29	25.4	1.0 (Reference)	
2016	117	35	29.9	1.25 (0.70–2.23)	
2017	139	43	30.9	1.31 (0.75–2.29)	
2018	111	40	36.0	1.65 (0.93–2.93)	
2019	91	30	33.0	1.44 (0.78–2.65)	
Region of HIV diagnosis, *n* (%)					
Non-Kaoping area	82	17	20.7	1.0 (Reference)	
Kaoping area	490	160	32.7	1.85 (1.05–3.27)*	
HIV transmission route, *n* (%)					
Same-sex sexual contact	455	130	28.6	1.0 (Reference)	
Different-sex sexual contact	35	19	54.3	2.97 (1.48–5.95)**	
Same- and different-sex sexual contact	78	28	35.9	1.40 (0.85–2.32)	
IDU	4	0	0	N/A	
Laboratory profiles					
HAV Ab seropositivity, *n* (%)					
Seronegativity	436	132	30.3	1.0 (Reference)	
Seropositivity	131	44	33.6	1.17 (0.7–1.77)	
HBs Ag seropositivity, *n* (%)					
Seronegativity	528	164	31.1	1.0 (Reference)	
Seropositivity	44	13	29.5	0.93 (0.48–1.83)	
HCV Ab seropositivity, *n* (%)					
Seronegativity	532	163	30.6	1.0 (Reference)	
Seropositivity	40	14	35.0	1.22 (0.62–2.40)	
Social and behavioral variables					
Education level, *n* (%)					
Below college	256	86	33.6	1.0 (Reference)	
College and above	316	91	28.8	0.80 (0.56–1.14)	
Marital status, *n* (%)					
Not married	557	167	30.0	1.0 (Reference)	
Married	15	10	66.7	4.67 (1.57–13.87)**	
Employment status, *n* (%)					
Employed	464	144	31.0	1.0 (Reference)	
Not employed	108	33	30.6	0.98 (0.62–1.54)	
History of sexually transmitted diseases, *n* (%)					
No	292	106	36.3	1.0 (Reference)	1.0 (Reference)
Yes	280	71	25.4	0.60 (0.42–0.85)**	0.64 (0.43–0.94)*
Multiple sexual partners, *n* (%)					
No	135	52	38.5	1.0 (Reference)	
Yes	437	125	28.6	0.64 (0.43–0.96)*	
History of unprotected sex, *n* (%)					
No	24	11	45.8	1.0 (Reference)	
Yes	548	166	30.3	0.51 (0.23–1.17)	
History of chemosex, *n* (%)					
No	381	130	34.1	1.0 (Reference)	
Yes	191	47	24.6	0.63 (0.43–0.93)*	

(*continued*)

TABLE 2. (CONTINUED)

	Number of patients, n = *572*	*Number of AIDS cases* n = *177*	*%*	*Univariable analysis, crude OR (95% CI)*	*Multivariable analysis, adjusted OR (95% CI)*
Variables related to HIV issues					
Heard of HIV before HIV diagnosis, *n* (%)					
No	21	11	52.4	1.0 (Reference)	
Yes	551	166	30.1	0.39 (0.16–0.94)	
Perceived risk for HIV transmission, *n* (%)					
Do not positively agree	423	136	32.2	1.0 (Reference)	
Positively agree	149	41	27.5	0.39 (0.16–0.94)*	
Recognize HIV as a severe illness, *n* (%)					
Do not positively agree	221	55	24.9	1.0 (Reference)	1.0 (Reference)
Positively agree	351	122	34.8	1.61 (1.10–2.34)*	1.52 (1.01–2.28)*
Perceived stigma of HIV infection, *n* (%)					
Do not positively agree	147	46	31.3	1.0 (Reference)	
Positively agree	425	131	30.8	0.98 (0.65–1.47)	
Perceived discrimination of HIV infection, *n* (%)					
Do not positively agree	103	37	35.9	1.0 (Reference)	
Positively agree	469	140	29.9	0.76 (0.49–1.19)	
aVCT status					
No aVCT	226	99	43.8	1.0 (Reference)	1.0 (Reference)
Irregular aVCT	170	54	31.8	0.60 (0.39–0.91)*	0.67 (0.43–1.04)
Regular aVCT (every 6–12 months)	81	14	17.3	0.27 (0.14–0.51)***	0.29 (0.15–0.57)***
Regular aVCT (every 1–3 months)	95	10	10.5	0.15 (0.07–0.31)***	0.17 (0.08–0.36)***

Binary logistic regression analysis for AIDS at presentation was performed using the enter strategy for sex and age and the stepwise strategy for other variables. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

CI, confidence interval; N/A, not available; OR, odds ratio.

Characteristics of study participants in five groups

The baseline sociodemographic characteristics, HIV-related risk assessments, laboratory profiles, thoughts on HIV-related issues, and aVCT status before HIV infection diagnosis of the five calendar groups are summarized in Table 1.

The mean (±standard deviation) age at HIV infection presentation of all participants was 29.6 (±7.9) years and 99.3% of participants were men. The routes of HIV transmission were same-sex sexual contact (79.5%), same- and different-sex sexual contact (13.6%), different-sex sexual contact (6.1%), and drug injection (0.7%). The overall prevalence of AIDS at presentation was 30.9%.

Significant differences were observed between the five groups regarding age at HIV infection presentation, site of HIV infection diagnosis, and employment status. The groups did not differ significantly in other sociodemographic characteristics, HIV-related risk assessments, laboratory profiles, thoughts on HIV-related issues, and aVCT status at HIV infection diagnosis.

Factors associated with AIDS at presentation

Table 2 lists the factors associated with AIDS at presentation. Older age (≥41 and 31–40 years vs. ≤30 years) and recognizing HIV as a severe illness were risk factors associated with AIDS at presentation. History of sexually transmitted diseases and regular aVCT (every 1–3 months or every 6–12 months vs. no aVCT) were associated with reduced AIDS at presentation.

Trend analysis of each stage and losses for each preceding stage in aVCT cascade across five calendar groups

Figure 2 illustrates participants' acceptance of the aVCT cascade from 2015 to 2019. Overall, the acceptance of each stage across 2015 to 2019 was 100% in Stage 1, 87.7–92.8% in Stage 2, 69.3–82.9% in Stage 3, and 56.1–66.7% in Stage 4. Only 21.9–37.4% of the participants reached Stage 5. *p* Values for the trends in each of the five stages from 2015 to 2019 were all >0.05.

The percentages of losses from the preceding stage to the next stage across 2015 to 2019 were 7.2–12.3% from Stage 1 to 2, 10.7–21.0% from Stage 2 to 3, and 9.2–23.3% from Stage 3 to 4. The largest reduction occurred from Stage 4 to 5 (37.4–61.0%).

In summary, only 21.9–37.4% of patients engaged in Stage 5 (aVCT at least annually), with the largest reduction in participant numbers occurring in the transition from Stage 4

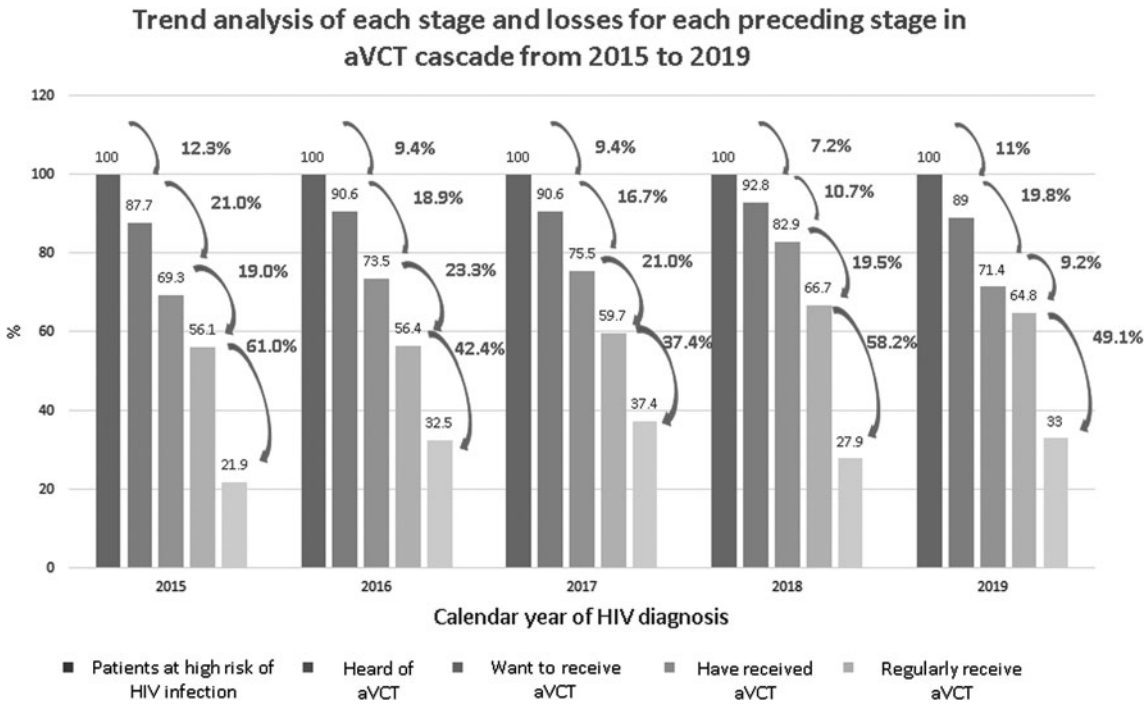

FIG. 2. Acceptance of aVCT cascade from 2015 to 2019. No significant difference was exhibited in any of the five aVCT stages from 2015 to 2019, and losses were revealed in each preceding step in the aVCT continuum from patients at high risk of HIV infection to patients regularly receiving aVCT. The largest drop in the cascade occurred in the transition from Stage 4 to 5. A Cochran-Armitage trend test with modified ridit scores was used for the trend analyses of each stage in the VCT cascade from 2015 to 2019.

to 5 (37.4–61.0%). Overall, the trend of acceptance did not differ significantly from 2015 to 2019 in any of the five stages.

Validation of the 16 questions on inability to proceed to the next step of the aVCT cascade

The item analysis initially revealed satisfactory discrimination of the original 16-item measure. In the exploratory factor analysis, the Kaiser–Meyer–Olkin measure of sampling adequacy was 0.79 and Bartlett's test of sphericity was $\chi^2 = 1650.149$ (degree of freedom = 120, $p < 0.001$), suggesting that the items were suitable for factor analysis. The varimax rotation categorized these 16 items into five domains: low perceived risk of HIV infection, high perceived risk of HIV infection, fear of testing positive (for discrimination), fear of testing positive (for stigmatization), and structural barriers to aVCT. Cronbach's alpha revealed poor reliability of two items in the domain of high perceived risk of HIV infection and they were subsequently omitted from further analysis. Domains 1 (perceived low risk of HIV infection), 2 (fear of testing positive, discrimination), 3 (fear of testing positive, stigma), and 4 (structural barrier to aVCT) were further analyzed (Table 3).

Comparison of mean scores of four domains within each subgroup

Across the three subgroups, fear of negative effects because of discrimination or stigma (Domains 2 and 3) were the two principal factors that dissuaded participants from reaching the next stage of the aVCT cascade (Table 4).

Discussion

Our findings revealed uptake of aVCT at least annually is a protective factor of AIDS at presentation. Therefore, the goal of an aVCT cascade should be to encourage the HIV at-risk population to have aVCT at least annually. Our results highlighted two problems in the implementation of an aVCT cascade in Taiwan. First, only one-quarter of participants reached the final stage of the aVCT cascade, with the greatest losses occurring from Stage 4 to 5 (Fig. 2). Second, the annual rate of regular aVCT uptake was constant throughout the five study periods (Fig. 2). The low rate of regular access to aVCT among PLWH (29.9%) in the study is similar to the report for PLWH in 2006–2008 in Taiwan (26.0%),[13] which indicates no improvement of regular aVCT among this at-risk population in a decade, despite the Taiwan government's great efforts to implement aVCT.[18] Although the aVCT program is the most effective in reaching the at-risk population for HIV and sexually transmitted diseases,[29] aVCT promotion should identify and address the concerns of the at-risk population to increase usage of aVCT and maximize early diagnosis of HIV infection.

PLWH are not only confronted with medical problems but also the social problems associated with HIV infection.[30,31] In this study, fear of the negative consequences of discrimination or stigma was the principal obstacle across three subgroups that prevented them from progressing to the next stage in the aVCT cascade (Table 4). The perceived negative

Table 3. Validation of Original 16 Questions on Inability to Proceed to the Next Step of the Anonymous Voluntary Human Immunodeficiency Virus Counseling and Testing Cascade

	Item analysis	*Exploratory factor analysis*	*Cronbach's alpha*	*Final established domain*
1. HIV infection is nothing to worry about	Good discrimination	Low perceived risk of HIV	Good reliability	Domain 1
2. The risk of HIV infection is low	Good discrimination			
3. The risk of HIV infection is high, but I do not care and do not want diagnostic confirmation	Good discrimination	High perceived risk of HIV	Poor reliability	
4. The risk of HIV infection is high, but I am afraid to receive diagnostic confirmation	Good discrimination			
5. I am afraid that people would avoid me if they knew that I had HIV	Good discrimination	Fear of testing positive (for discrimination)	Good reliability	Domain 2
6. I am afraid that the relationship among my family, friends, and partners would change if they knew that I had HIV	Good discrimination			
7. I am afraid that my patient rights would be compromised if I were diagnosed with HIV	Good discrimination			
8. I am afraid of losing my job as a result of being diagnosed with HIV	Good discrimination			
9. I am afraid that people will think that the cause of HIV infection is excessive sexual activity	Good discrimination	Fear of a positive result (for stigmatization)	Good reliability	Domain 3
10. I am afraid that people will think that HIV infection only results from same-sex sexual behavior	Good discrimination			
11. I am afraid that people will think that the cause of HIV infection is drug abuse	Good discrimination			
12. The location where anonymous testing is offered is inconvenient to access	Good discrimination	Structural barriers to aVCT	Good reliability	Domain 4
13. The method of anonymous testing is inconvenient	Good discrimination			
14. The times at which anonymous testing is offered are inconvenient	Good discrimination			
15. The process of anonymous testing is unclear	Good discrimination			
16. Anonymous testing will invade my privacy	Good discrimination			

consequences of HIV infection were the disruption of social and sexual relationships, medical mistrust, and loss of employment (Table 3). These findings are consistent with those of previous studies conducted with MSM[32,33] and adult women.[34] Further, homosexuality-related stigma among MSM community is especially an important obstacle to HIV testing in Chinese society.[35,36] A recent nationwide study of MSM community in China revealed 26.1% of participants regarded homosexuality-related stigma as a barrier of HIV testing.[35] In this study, if ''agree'' and ''strongly agree'' for the one question in Domain 3 (fear of a positive result due to stigma, Table 3) were to be reclassified as a casual result in this study, 53.2–58.9% across Subgroups 2–4 classified ''I am afraid that people will think that HIV infection only results from same-sex sexual behavior'' as reasons for dropping out of the aVCT cascade (data not shown). Although several anti-HIV stigma campaigns have been implemented in Taiwan, homosexuality remains sensitive issues in traditional Taiwanese families. Therefore, concerted efforts to reduce homosexuality- and HIV-related discrimination and stigmatization should be the first priority to optimize participation in aVCT cascade.

With the successful introduction of aVCT in Taiwan in 1997, most of the population at high risk of HIV infection in

Table 4. Comparison of Mean Scores of Four Domains Within Each Subgroup

	Domain 1 (perceived low risk of HIV)	*Domain 2 (fear of testing positive [discrimination])*	*Domain 3 (fear of testing positive [stigmatization])*	*Domain 4 structural barriers to aVCT*	p	*Tukey* post-hoc *test*
Subgroup 2 (does not want to receive aVCT), $N=88$	2.76 (0.92)	3.64 (0.87)	3.35 (0.93)	2.88 (0.82)	<0.001	Domain 2 > 1 Domain 3 > 1 Domain 2 > 4 Domain 3 > 4
Subgroup 3 (does not receive aVCT), $N=82$	2.52 (0.99)	3.84 (0.88)	3.61 (0.97)	2.95 (0.84)	<0.001	Domain 2 > 1 Domain 3 > 1 Domain 2 > 4 Domain 3 > 4
Subgroup 4 (does not regularly receive aVCT), $N=170$	2.71 (0.94)	3.71 (0.93)	3.55 (1.03)	2.65 (0.72)	<0.001	Domain 2 > 1 Domain 3 > 1 Domain 2 > 4 Domain 3 > 4

Continuous variables were compared using independent *t*-tests or one-way analysis of variance followed by *post-hoc* Tukey test. Scores are means (SDs).

this study had heard of aVCT (87.7–92.8% in Stage 2; Fig. 2). However, several aVCT sites are still located in health care settings in Taiwan, which are structural barriers for accessing aVCT due to inconvenience (e.g., wait times and sites of aVCT) and concerns about confidentiality (Table 3). These structural barriers can discourage the at-risk population from receiving aVCT.[32,35,37] Different delivery approaches could be complementary to aVCT in Taiwan, such as HIV self-testing (HIVST).[38–40] The HIVST has the potential to increase HIV testing frequency by overcoming the aforementioned structural barriers associated with voluntary facility-based attendance.[32,40,41] A recent randomized controlled trial among MSM in Australia revealed a higher frequency of HIV testing among users of self-testing kits and facility-based confirmatory testing than among users of facility-based testing only.[38] Further, with active follow-up from a counselor, HIVST even more likely benefits from being linked with other prevention (e.g. risk reduction counseling and pre-exposure prophylaxis [PrEP] referrals) compared with HIVST without active follow-up.[40] The first rapid kit for HIVST, OraQuick® In–home rapid HIV test, was approved by the US Food and Drug Administration in 2012. In 2016, TW-CDC implemented a self-testing program using OraQuick plus facility-based confirmatory testing; the program has a positive rate of 1% and a late presentation rate of 18%. Implementation of HIVST may supplement Taiwan's aVCT program. Although the privacy feature of OraQuick increased preference for using the test, concerns about its accuracy and its costs might impede its adoption.[42]

In contrast to these results, an internet-based survey conducted in 2007 indicated that low perceived risk was the primary reason preventing participants from being tested for HIV,[32] rather than the fear of negative consequences of HIV infection (low perceived risk of infection, 32.2%, and fear of testing positive, 18.1%). These differences of primary reason may stem from differences in the enrolled populations because in our study, 100% of participants met the criteria of high HIV infection risk,[8,21] whereas in the internet-based survey, criterion for inclusion was MSM who had sexual relationships in the preceding 12 months.[32] However, if ''agree'' and ''strongly agree'' for the two questions in Domain 1 (low perceived risk of HIV infection, Table 3) were classified as ''positively agree,'' 14.6–21.8% and 18.3–22.7% of the participants across Subgroups 2–4 still considered ''HIV infection is nothing to be concerned over'' and ''the risk of HIV infection is low'' as reasons for dropping out of the aVCT cascade, respectively (data not shown). Therefore, interventions to increase understanding of their vulnerability to HIV infection are also crucial. However, an intervention to increase the perceived vulnerability to HIV infection may threaten an individual's self-image and cause defensive avoidance.[43–45] Therefore, interventions that preserve self-image and consider functional outcomes may be effective in reducing high-risk behavior and improving acceptance of aVCT among at-risk population.[46,47]

Although these findings demonstrated that irregular use of aVCT services was not sufficient to reduce the prevalence of AIDS at presentation (Table 2), irregular use of aVCT

(Subgroup 4) accounted for the largest dropout in the aVCT cascade (Fig. 2). Therefore, more efforts are needed to link patients with ongoing risk of HIV infection, who were previously tested HIV negative, to visit aVCT at least annually. Text message reminders may be an effective and acceptable means of enhancing patient usage of and attendance at VCT.[48–50]

A mathematical model suggested that the frequency of HIV testing should be based on the level of risk of HIV infection: every 2.4 years for low-risk individuals (0.01% annual incidence), every 9 months for moderate-risk individuals (0.1% incidence), and every 3 months for at-risk individuals (1.0% incidence).[1] The US CDC 2017 HIV testing guidelines recommended frequent HIV testing among at-risk populations, such as MSM, of two to four times per year.[51] The WHO 2019 HTS guideline also recommended more frequent retesting (every 3–6 months) based on individual risks (e.g., individuals taking PrEP or from a key population group presenting with an sexually transmitted infection).[21] However, the case numbers in our study may be too small to demonstrate the protection of more frequency of regular aVCT on AIDS at presentation (every 1–3 months vs. every 6–12 months, $p = 0.593$, data not shown). Moreover, other benefits, which may accompany the increased frequency of aVCT among the at-risk population, such as improved short-term and long-term outcomes[5] and reduced onward transmission,[52] are not measured in this study. Therefore, further direct evidence is required to overall evaluate the effect of increasing frequency of aVCT among at-risk populations on early diagnosis of HIV infection and HIV prevention.

This is the first study to analyze the evolving acceptance of an aVCT cascade among PLWH. Cascade analysis was used to understand the trend at each stage of the aVCT cascade and explore the causes of losses across the aVCT continuum of care. However, there were several study limitations. First, 74 patients were not willing to participate, which might have caused selection bias. However, the enrolled and unwilling patients did not differ on demographic characteristics, HIV-related risk, and HIV stage at presentation. Second, participants were PLWH and thus most likely comprised a higher rate of the population with the highest HIV infection risk. Therefore, the findings cannot be generalized to the at-risk population, some of whom have a relatively low risk of HIV infection. Future studies should use a population characterized by varying HIV infection risk stratified by demographic characteristics, such as exact HIV infection risk, region, and age, to monitor the acceptance and effectiveness of the aVCT cascade. Third, participants' responses may have reflected their knowledge of the socially desirable or perceived ''correct'' responses. Finally, although the trained investigator asked participants to recall their situation before HIV infection diagnosis, inaccurate recalling could not be avoided.

In conclusion, this was the first study to analyze the acceptance of an aVCT cascade among HIV-infected patients. Our findings clarified the role of regular access to aVCT in promoting early diagnosis of HIV infection. However, the examination of the aVCT cascade revealed two problems: a low rate of HIV-infected patients engaged in regular aVCT at least annually and an unchanged trend of acceptance of each stage in the aVCT cascade in 2015–2019. Strategies to avoid fear of negative social consequences of HIV infection should be prioritized. Other interventions, such as HIVST, preservation of self-image with the incorporation of effective outcomes, and text message reminders, may improve acceptance of aVCT.

Availability of Data and Materials

All data containing relevant information to support the study findings are provided in the article.

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Authors' Contributions

C.Y.L.: study inception and design, data collection and analysis, and drafting of article. P.H.W.: study design, data collection and analysis, and critical review of article. J.J.T.: study design and data collection and analysis. T.C.C.: study design and data collection and analysis. K.C.: study design and data collection and analysis. P.L.L.: study inception and design, data collection and analysis, and critical review of article. All authors approved final article.

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Address correspondence to:
Po-Liang Lu, PhD
Division of Infectious Diseases
Department of Internal Medicine
Kaohsiung Medical University Hospital
No. 100, Tzyou 1st Road
Kaohsiung City 807
Taiwan

E-mail: d830166@gmail.com