Pay-it-forward incentives for hepatitis virus testing in men who have sex with men: a cluster randomized trial

Author lists:

Ye Zhang[1,2]*, Jianjun Li[3]*, Yewei Xie[4], Dan Wu[2,5], Jason Ong[6,7], Gifty Marley[4], Adeeba Kamarulzaman[8,9], Haidong Lu[10], Fei Zou[11], Jennifer S. Smith[12], Joseph D. Tucker[4,5], Gengfeng Fu[3#], Weiming Tang[4,13#]

Affiliations:

1. Kirby Institute, UNSW Sydney, Sydney, NSW, Australia
2. School of Public Health, Nanjing Medical University, Nanjing, China
3. Department of HIV/STI Prevention and Control, Jiangsu Provincial Center for Diseases Prevention and Control, Nanjing, Suzhou, China
4. University of North Carolina Project-China, Guangzhou, Guangdong, China
5. Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK
6. Central Clinical School, Monash University, Melbourne, VIC, Australia
7. Melbourne Sexual Health Centre, Alfred Health, Carlton, VIC, Australia
8. University of Malaysia, Kuala Lumpur, Malaysia
9. International AIDS Society (IAS), Geneva, Switzerland
10. Department of Epidemiology of Microbial Diseases, Yale School of Public Health, Yale University, New Haven, CT, USA
11. Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA
12. Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA
13. Guangdong Second Provincial General Hospital, Guangzhou, China

Corresponding authors:
Dr. Weiming Tang, Guangdong Second Provincial General Hospital; and the University of North Carolina at Chapel Hill Project-China, Guangzhou, 510095, China. Weiming_tang@med.unc.edu

Dr. Gengfeng Fu, Department of HIV/STI Prevention and Control, Jiangsu Provincial Center for Diseases Prevention and Control, Nanjing, China, fugf@jscdc.cn

Abstract

Pay-it-forward incentives involve having a person receive a free test with community-generated messages and then asking if those who received a free test would like to donate money to support others to receive free testing. We undertook a two-arm cluster-randomized trial to evaluate pay-it-forward incentives with active community participation to promote HBV and HCV testing among men who have sex with men (MSM) in China. Men randomized to the pay-it-forward arm received free HBV and HCV testing and were offered a chance to pay-it-forward by donating money to support the testing of another anonymous person. Each participant paid for their HCV and HBV test at $7.7/test in the standard-of-care arm. The primary outcome was the proportion of men who tested for HBV and HCV. Between 28 March and 6 October 2021, 32 groups (10 men per group) of men were randomized to the pay-it-forward (n=160, 16 clusters) and standard-of-care (n=162, 16 clusters) arms, respectively. HBV and HCV rapid testing were higher in the pay-it-forward arm (59.4%) than in the standard-of-care arm (25.3%) (proportion difference 35.2%, 95% CI 24.1%-46.3%). No adverse events were reported. The community-led pay-it-forward incentives improved HBV and HCV testing among MSM . Clinical Trial registration: ChiCTR 2100046140.

Background

Hepatitis B virus (HBV) and Hepatitis C virus (HCV) can cause chronic hepatitis, a major cause of morbidity and mortality globally, especially in Asia [1-3]. A mathematical modeling study estimated that, without global intensification to control chronic hepatitis, HBV and HCV infections would cause more deaths by 2040 than the sum of deaths from HIV, malaria, and tuberculosis combined [4]. In 2016, the World Health Organization (WHO) set ambitious goals for HBV and HCV elimination by 2030: to diagnose 90% of people with HBV and HCV infections globally, to provide treatment to 80% of people diagnosed, and to achieve a 65% of reduction in related mortality by 2030 [5].

China has a considerable HBV and HCV disease burden accounting for approxiamtely 33% and 17% of all infection cases recorded worldwide, respectively [6,7]. According to the WHO data for China, an estimated 87 million people live with chronic HBV, and around 8 million live with chronic HCV [8]. Effective prevention depends on regular testing of HBV and HCV among those who test negative and early treatment for those who test positive. With such a large population co-infected with HBV and HCV, researchers have advocated for universal HBV and HCV testing among adults in China [9,10]. However, HBV and HCV testing rates in China are far from optimal, with the majority of people with infection being unaware of their infection status (82% for HBV and >70% for HCV), resulting in missed opportunities to refer them to effective treatment [11]. In addition, many studies have shown that sexual transmission has become the most common route of acute HBV infection in many countries [12-14]. A previous modeling study in China estimated that more than a third of new HBV infections in China (35%) were attributed to sexual transmission[15]. Although, the HBV vaccination program to prevent mother-to-child transmission has resulted in decreased incidence of new HBV infections in China[16]. The total prevalent cases of chronic hepatitis B among persons over 15 years of age in China are still increasing [17].

There are several challenges to scaling up HBV and HCV testing in China. First, the cost of testing, especially in the absence of insurance subsidies or coverage, deters people from seeking HBV and HCV testing in clinics [18]. Like many low- and middle-income countries (LMICs), China's primary efforts to control HBV focus on pregnant women and premarital couples to prevent mother-to-child transmission. The number of hepatitis testing promotion programs among other populations in China is limited [1]. Consequently, the lack of awareness of the infection, low perceived risk, and low motivation to seek preventive screening were commonly cited as the main factors contributing to low hepatitis testing uptake among key populations, such as men who have sex with men (MSM) [19-21]. Second, even when free testing is available in some settings, testing uptake is often low due to hepatitis-related stigma and macro-social determinants [22,23]. Many MSM could experience double discrimination against their sexual orientation and hepatitis status, which limits their motivation to seek care in health facilities [24,25]. Until now, hepatitis testing programs in China have been centralized and focused on clinics within secondary and tertiary hospitals [1,26,27]. Therefore, innovative strategies are needed to overcome both person-centered barriers (i.e., testing costs) and system-level barriers (e.g., stigma) hindering people from accessing HBV and HCV testing in China [28].

A pay-it-forward incentive provides a person with an opportunity to receive an anonymous gift, such as HBV and HCV testing, and a chance to pay forward the kindness by anonymously giving a similar offering to another person [29]. Implementing a pay-it-forward incentive in community-based organizations has successfully improved chlamydia and gonorrhea testing among Chinese MSM and community engagement, which can positively affect health service uptake and decrease stigma [30,31]. Community-led testing services provided by lay health workers outside of traditional hospital settings could help increase testing uptake and overcome system and societal barriers to health services [32,33]. Studies have found that a community-led testing model could attract more untested MSM at increased risk of infection than traditional health facility testing [34-36]. A community-led pay-it-forward approach may be a promising solution to improve testing uptake and address macro-social factors that hinder HBV and HCV testing uptake, such as mistrust in doctors, long waiting time, and lack of privacy among high-at-risk populations like Chinese MSM[30,31].

In collaboration with local community-based organizations, we conducted a cluster randomized control trial (RCT) to investigate the impact of integrating pay-it-forward incentive with HBV and HCV testing services within established community-led HIV testing programs. We chose to utilize a cluster RCT for the following reasons. First, participants were recruited from existing HIV/syphilis testing services in real-life settings. Hence, adopting a cluster randomized trial design could help reduce the potential bias due to between-group contamination. Second, it is common during community outreach activities that some men are accompanied by friends to receive tests together. Third, because community staff from each site were primarily responsible for the intervention recruitment and implementation, the implementation of cluster RCT had greater potential to simplify project management and improve adherence to intervention protocols than an individual-based RCT. In addition, many testing behaviors are related to group characteristics. We have used a similar procedure in our previous studies among Chinese MSM [31].

This cluster RCT aimed to assess the effectiveness of a community-led pay-it-forward intervention in increasing HBV and HCV testing uptake among MSM in Nanjing and Suzhou of Jiangsu Province, China. The primary outcome of this study is to measure the proportion of dual HBV and HCV testing uptake. The secondary outcomes include assessing the updatke of dual HBV and HCV within subgroups, examining donation rates and amounts, and evaluating the cost-effectiveness of the interventions as compared to the standard of care.

Results

A total of 431 people were screened for recruitment from 28 March 2021 to 6 November 2021. Among them, 109 were ineligible for the following reasons: 94 participants had tested for HBV or HCV in the past 12 months, 3 did not meet inclusion criteria, and 12 did not provide consent (Figure 1). The 322 eligible participants were categorized into 32 cluster (average cluster size (number of participants) =10)), and were randomized to two study arms, including 16 clusters (in the pay-it-forward arm (160 participants) and 16 clusters in the standard-of-care arm (162 participants). Of these 322 participants, 241 and 81 were recruited by office-based and outreach sites.

Participant disposition

Figure 1 shows the trial profile of the participants. The median age of recruited participants was 29 years old (interquartile range [IQR], 25 to 37). Most participants were unmarried (73.6%), highly educated (81.3%), and self-identified as gay (71.1%). About a third of men (34.5%) self-reported drug use in the previous 12 months. 82.0% of self-reported used amylnitratate (poppers), 2.7% used cannabis, and 2.7% reported injection drug use. Demographic characteristics of participants were similar across the study arms, except that more people use drugs (pay-it-forward: 65 [40.6%], standard-of-care: 46 [28.4%]) and more men engaged in high-risk sexual behavior (pay-it-forward: 80 [50.0%], standard-of-care: 46 [28.4%]) in the pay-it-forward arm (Table 1).

Primary outcome

For the primary outcome – rate of HBV and HCV testing among study participants - overall, 59.4% (95 of 160) of men in the pay-it-forward arm and 25.3% (41 of 162) in the standard-of-care arm received HBV and HCV testing (adjusted proportion difference 35.2%, 95% CI 24.1%-46.3%, p <0.001) (Figure 2).

Secondary outcomes

The secondary outcomes were rate of HBV and HCV testing across subgroups, donation rates and amounts, and economic evaluation.

Among those recruited at the outreach sites, 62.9% (27 of 43) of men in the pay-it-forward arm and 13.1% (5 of 38) of men in the standard-of-care arm received HBV and HCV testing (adjusted proportion difference 51.3%, 95% CI 33.4%-69.2%, p<0.001). Among those recruited at the office-based sites, 58.1% (68 of 117) of men in the pay-it-forward arm and 29.0% (36 of 124) of men in the standard-of-care arm received HBV and HCV testing (adjusted proportion difference of 29.8%, 95% CI 17.5%-42.1%, p<0.001).

Across the subgroups defined by high-risk characteristics for HBV or HCV infection, the proportions of MSM testing for HBV and HCV in the pay-it-forward arm were significantly higher than the standard-of-care arm. The most significant increase in testing uptake was among men who had used drugs in the last 12 months (adjusted proportion difference 50.3%, 95% CI 34.6%-66.0%, p<0.001). The following significant increase in testing uptake was among MSM who self-identified as gay (adjusted proportion difference 42.7%, 95% CI 30.9%-54.5%, p<0.001). Similarly, the pay-it-forward intervention was associated with a 41.0% (95% CI 25.3%-56.7%, p<0.001) and 36.9% (95% CI 20.7%-53.2%, p<0.001) absolute increase in the proportion of men receiving a dual HBV and HCV test among men aged 30 or above and men who had engaged in risky sexual behavior in the past three months, respectively. The effect estimates suggested that the pay-it-forward intervention was superior to standard-of-care in promoting HBV and HCV testing among all subgroups at a higher risk of HBV and HCV infection (Figure 2). The pay-it-forward intervention effects were numerically similar among subgroups at a lower risk of HBV and HCV infection but not superior to standard-of-care. The adjusted absolute proportion differences between the pay-it-forward intervention and standard-of-care arm were: 30.6% among younger men (pay-it-forward: 50/88 men, standard-of-care: 24/84 men, 95% CI 14.9%-46.2%, p<0.001); 18.9% among MSM who self-identified as heterosexual or bisexual men (pay-it-forward: 21/50 men, standard-of-care: 19/53 men, 95% CI 1.4%-26.5%, p<0.001); 27.0% among MSM who had never used any drugs in the last 12 months (pay-it-forward: 54/95 men, standard-of-care: 35/116 men, 95% CI 11.2%-42.7%, p<0.001); and 32.2% among MSM who had never engaged in risky sexual behavior in the past three months (pay-it-forward: 45/80 men, standard-of-care: 25/75 men, 95% CI 18.5%-45.9%, p<0.001). Details are in Figure 2.

The evaluation of cost-effectiveness is a secondary outcome. Among 160 men in the pay-it-forward arm, 63.1% (101/160) chose to donate some amount to the future participants, including 69 (68.3%) men who received HBV and HCV testing and 32 (31.7%) men who did not test. In addition, the proportions of men who donated were similar among men recruited in the outreach and office-based sites (67.4% vs. 61.5%, p=0.49). The total donation amount was $498.9 among MSM in the pay it forward arm, and the median donation amount per donor was about $3.1 (Interquartile range [IQR]:1.5-7.7). The largest donation was $15.4, and the lowest was $1.9. No difference in donation status was found by study site and income level (Table 3). The incremental cost for each treatment arm and the incremental cost-effectiveness ratios (ICERs) based on financial and economic costs, respectively, are shown in Table 2. Considering economic or financial costs, the pay-it-forward incentive was more effective and cheaper than the standard-of-care.

Safety

Of the 136 MSM who received testing, 10 men (7.4%) tested positive for HBV, among whom 6 tested through the pay-it-forward arm. 4 (3.7%) tested positive for HCV, of whom 3 tested through the pay-it-forward arm. All positive cases (identified during the course of the study) were referred to local hospitals for further diagnostics, treatment, and clinical management. No adverse events associated with the pay-if-forward intervention were identified in the study.

Post-hoc sensitivity analyses

Using parameters from Extended Table 1, we created a decision-tree model using TreeAge Pro 2020 (TreeAge Software Inc) to explore the cost-effectiveness of pay-it-forward and the standard of care (Extended Figure 1). The results from the univariate sensitivity analyses are presented as tornado plots in Extended Figure 2. For ICERs of financial cost per additional person tested, the biggest drivers of cost-effectiveness were the donation amount in the pay-it-forward arm when comparingwith standard-of-care arm (Extended Figure 3). Despite changing input parameters to their plausible extremes, pay-it-forward remains cost-saving compared to standard-of-care. In addition, we performed a one-way sensitivity analysis toward the donation amount. We found out that the pay-it-forward is not cost-saving when the donation amount was $1.03. For ICERs of financial cost per additional case identified, the biggest drivers of cost-effectiveness were the probability of positive cases identified in the standard of care group when comparing pay-it-forward with standard-of-care (Extended Figure 4). Probabilistic sensitivity analyses with 100,000 runs were conducted and presented as cost-effectiveness acceptability curves (Extended Figure 5). They confirm that PIF dominates the standard of care when considering economic or financial costs. Figure S7 shows that the probability of pay-it-forward being more cost-effective than standard-of-care may decrease as the willingness to pay increases from $0 to $2000 per identified case.

Discussion

HBV and HCV testing among high-risk populations is the cornerstone of case identification and treatment initiation for those with infection, and a prerequisite for the "Treatment as Prevention" strategy to end HBV and HCV epidemics [37,38] . Our study found that a community-led pay-it-forward incentives to testing among MSM resulted in significant increased HBV and HCV testing uptake among Chinese MSM (35.2%, 95% CI 24.1%-46.3%). This finding is similar and consistent with previous intervention studies adding support to the evidence-based for that pay-it-forward incentives increasing testing of sexually transmitted diseases among Chinese MSM who attend sexual health clinics [30,31].

A strength of our study is the rigorous investigation of the effect of the pay-it-forward incentives with 'bottom-up' community empowerment efforts. Community-led interventions are a critical component of community empowerment. We believe that the high level of community participation from study design to implementation enabled our pay-it-forward intervention to be contextually appropriate and as inclusive as possible. The effect of pay-it-forward on HBV and HCV testing uptake was greater in outreach settings where peer staff provided the testing service more proactively with more flexible services in a gay-friendly environment than waiting for people to present at the community-based organizations.

Additionally, the pay-it-forward incentives is known as a way of fostering community engagement [40] and participatory approaches like pay-it-forward could be positively received within the community and promote HBV and HCV testing uptake [29].

We observed a significantly higher effect of pay-it-forward among MSM who used any drugs, which was associated with a 50% increase in testing uptake probability compared to standard-of-care. People who use drugs are an important group that require targeted efforts for HBV and HCV prevention considering they carry higher risk burdens of HBV and HCV and face more barriers to testing due to the double stigma associated with their sexual and drug use behaviors [41-43]. Unsurprisingly, testing rates among people who use drugs in the standard-of-care arm were among the lowest across all subgroups. Studies have shown that pay-it-forward incentives with small gifts and generosity can cement community identity [30]. Peer support intervention can also reduce stigma and facilitate health behavior change [44,45]. The findings of our study suggest that community-led pay-it-forward incentives may be effective for marginalized populations, such as people who use drugs. This pay-it-forward intervention helped set up a system that allowed accessing healthcare with cheaper costs for financially disadvantaged individuals, which might be another vital facilitator for hepatitis testing uptake among people who use drugs.

Critical challenges for programs that hinge upon free or subsidized testing are the high test cost and limited ability to sustain the program in the long term[50]. About two-thirds of participants (63.1%) who received HBV and HCV testing in the pay-it-forward arm chose to donate some money to support other MSM to get HBV and HCV tests. These donations successfully helped offset the total financial costs for testing participants in the pay-it-forward arm. We did not solicit details on participants' refusal to donate. In addition, 32 study participants were randomized to the pay-it-forward arm and declined to get tested for HBV and HCV but still donated some money to their peers in the MSM community. This finding was consistent with a previous study showing that pay-it-forward intervention could successfully promote a sense of belonging and increase community solidarity [21]. Evidence accumulated during the COVID-19 pandemic indicates that community solidarity plays a vital role in bridging the social distance and provoking altruism to shift the focus from self-protection to social integration[51,52]. Why those participants chose to not get a free test for HBV and HCV is unknown.

The study has several limitations to consider. In the cluster randomised trial, the randomisation process was conducted at the group-level, where a group of ten eligible participants was randomised and assigned to one of the trial arms based on a pre-determined allocation sequence. As a result, there is a possibility that the recruiter may decide consciously, or sub-consciously, about recruiting certain types of participants into each of the trial arms. This may lead to potential selection bias from recruiting participants within clusters, for example, more people use drugs, and more men engage in high-risk sexual behavior in the pay-it-forward arm. We designed the primary and secondary outcomes to mitigate recruitment bias from the lack of blinding. Additionally, we included additional variables in the regression model (i.e. individuals who had previously used illicit drugs and high-risk sexual behaviours), which can help assess baseline imbalances in individual-level characteristics across arms.

Another limitation is that the sample size of this study was designed to examine the primary outcome in the study population overall. Therefore, the subgroup analyses are likely underpowered. Furthermore, participants in the pay-it-forward arm were only asked to decide whether to be tested and donate money to other peers at the sites. Without subsequent follow-up, our study could not assess HBV and HCV test uptake or donation behaviors after the intervention. In addition, to align with previous practice [53], we did not make proper adjustments to correct the potential multiplicity across subgroups. Therefore, our model interpretation focused on estimating the intervention effect within and between subgroups rather than the subgroup-specific statistics to avoid misleading [54]. The community-based organizations in Nanjing and Suzhou of Jiangsu province were busy during different periods by an influx of COVID-19 patients and related COVID-19 prevention activities. This caused a variation in implementation time across the various study sites (Extended Figure 6). However, we have adjusted for the recruitment sites in our model, and the difference in testing uptake between the two arms did not change significantly.

All participants were recruited through community-based organization staff at community-based HIV and syphilis testing sites, which may have contributed to potential selection bias [55]. Hence, our findings may not be directly generalizable to the overall MSM population in China, especially MSM who are not yet linked to community-based HIV and syphilis testing services. However, by integrating HBV and HCV testing services with HIV, our study reflected an opportunity to improve HBV and HCV testing uptake among marginalized populations. The generalizability of our findings may also be limited due to the lack of a sample representative of the larger population of interest. Nanjing and Suzhou represent relatively more open and inclusive cities with less stigma toward homosexual behavior and sexually transmitted infections than other cities in China. This observation might be reflected in our study, as MSM participants randomized to the control group displayed higher HBV and HCV testing rates compared to their counterparts recruited from other settings within China [23]. It remains an open question whether settings without robust community-based organizations could achieve similar effects, particularly among conservative culture settings with high stigma toward sexually transmitted infections and MSM.

In summary, the result of this cluster RCT demonstrate the effectiveness of community-led pay-it-forward strategy in promoting HBV and HCV testing among high-risk populations in communities. To eliminate HBV and HCV by 2030, it is important to get all populations at high risk of infection to be tested for HBV and HCV at least once in their life. Future studies should further explore the potential pathways that can connect these initial programs to the widespread implementation of universal testing.

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Authorship Contributions

This manuscript is an original research paper that has not been published previously, nor is it under review with any other journal. WT and GF conceived the initial idea and designed this clinical trial. WT oversaw the study design, implementation, data analysis, results generation, and manuscript write-up. JL, YX, GM, and GF implemented the study and collected data.

WT, GF, and JL had access to the study's raw data. YZ, JL, YX, and HL were responsible for data cleaning and data analysis and generated the final analysis outputs. JJO and FZ provided advice for data analysis. YZ, JL, and YX wrote the first draft of the paper, and JDT, JJO, DW, AK, and JSS contributed to the interpretation of the results and provided expert advice on the draft. All co-authors provided constructive comments and approved the final draft of the submission.

Competing Interests Statement

The authors declare no competing interests.

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Figures and Tables

Figure 1: Consort Flowchart

Figure 2 Multivariable logistic regression to compare HBV &HCV test uptake rates of two arms

The data presents estimated from the adjusted GEE model, represented as adjusted probability differences with +/- two-sided 95% confidence interval. The overall GEE model adjusted for age, study sites, education level, income, marital status, and HBV vaccine history. Subgroups models adjusted for age, study sites, education level, income and HBV vaccination history to achieve convergence; * due to sampling limitation, illicit drug user model, community-based organization model, and heterosexual or bisexual model only adjusted for age to achieve convergence.

Table 1 Descriptive Statistics Showing the Sociodemographic Characteristics of MSM Participants.

	Total (n=322)	SC arm (n=162, 16 clusters)	PIF arm (n=160, 16 clusters)	P value†
Age (median, IQR)	29 (25-37)	30 (25-36)	29 (25-39)	0.85
Education				0.38
Middle school or lower	27 (8.3%)	15 (9.3%)	12 (7.4%)	
High school or technical school	33 (10.3%)	12 (13.6%)	11 (6.7%)	
Undergraduate or above	262 (81.3%)	128 (79.0%)	134 (83.7%)	
Marriage status				0.50
Unmarried	237 (73.6%)	116 (71.6%)	121 (75.6%)	
Married or engage	50 (15.5%)	29 (17.9%)	21 (13.1%)	
Divorced or widowed	35 (10.9%)	17 (10.5%)	18 (11.3%)	
Employee				0.50
Yes	263 (81.7%)	130(80.3%)	133 (83.1%)	
No	59 (18.3%)	32(19.8%)	27 (16.9%)	
Student				0.80
Yes	54 (16.8%)	28 (17.3%)	26 (16.3%)	
No	268 (83.2%)	134 (82.7%)	134 (83.7%)	
Monthly salary (USD)				0.70
0-150	34 (10.6%)	18 (11.1%)	16 (10%)	
150-800	103 (32.0%)	53 (32.7%)	50(31.3%)	
801-1550	123 (38.2%)	64 (39.5%)	59 (36.9%)	
>1550	62 (19.3%)	27 (16.8%)	35 (21.9%)	
Sexual Orientation				0.13
Gay	229 (71.1%)	109 (67.3%)	120 (75.0%)	
Heterosexual or bisexual	93 (28.9%)	53 (32.7%)	40 (25%)	
People who had used drugs in the past 12 months				0.02
Yes	111 (34.5%)	46 (28.4%)	65 (40.6%)	
No	211 (65.5%)	116 (71.6%)	95 (59.4%)	
Ever involved in any sexual behavior in the past three months*				0.04
Yes	142 (44.1%)	62 (38.3%)	80 (50.0%)	
No	180 (55.9%)	100 (61.7%)	80 (50.0%)	

Note: SC: standard-of-care; PIF: pay-it-forward; IQR: interquartile range.
*Sexual risk behaviors include- reported engagement in condomless anal sex, group sex, or more than two sexual partners in the preceding three months.
† Chi-square and Wilcoxon rank-sum tests were used to compare the sociodemographic characteristics of participants between the standard-of-care and pay-it-forward arms.

Table 2: Distribution of donation status by study site and income level, N (%)

Characteristics	Donation status (n=160)		P value
	Yes	No	
Study site			0.49
Office-based site	72 (61.5%)	45 (38.5%)	
Outreaching site	29 (67.4%)	14 (32.6%)	
Monthly salary (USD)			0.68
0-150	11 (68.8%)	5 (31.3%)	
150-800	30 (60%)	20 (40%)	
801-1550	40 (67.8%)	19 (32.2%)	
>1550	20 (57.1%)	15 (42.9%)	

† Chi-square tests were used to compare the donation status of participants.

Table 3. Outcome Analyses for the CostsTesting for Each Group

Treatment group	Economic cost (USD)	Incremental cost	Probability per person tested	Probability per case identified (HBV/ HCV)	ICER (USD per person tested for HBV/HCV)	ICER (USD per case of HBV/HCV identified)
SOC (n=162, 16 clusters)	3.99	-	0.25	0.10	-	-
PIF (n=160, 16 clusters)	3.78	-0.21	0.59	0.08	Dominated*	10.50
Treatment group	**Financial cost (USD)**	**Incremental cost**	**Probability per person tested**	**Probability per case identified (HBV/HCV)**	**ICER (USD per person tested for HBV/HCV)**	**ICER (USD per case of HBV/HCV identified)**
SOC (n=162, 16 clusters)	2.04	-	0.25	0.10	-	-
PIF (n=160, 16 clusters)	0.66	-1.38	0.59	0.08	Dominated*	69.00

ICER = incremental cost-effectiveness ratio; PIF = pay-it-forward; SOC = standard-of-care; USD = United States Dollars.
* A dominated strategy is cheaper and more effective than the comparator (SOC).

Methods

Study design

We conducted a two-arm cluster-randomized controlled trial in Nanjing and Suzhou of Jiangsu Province, a province with one of the highest liver cancer incidences in China[60]. Two cities (Nanjing and Suzhou) were selected for study inclusion given their 1) relatively large MSM populations and 2) presence of at least one MSM-led community-based organizations ith experience in providing regular HIV and syphilis testing services for MSM. We selected one MSM-led community-based organization in each city that provided comprehensive sexual health services (i.e., HIV and syphilis testing, pre- and post-counseling, and care services) for the MSM community by MSM peers.

Community-led intervention

Before recruitment, the research team held separate interactive capacity-building sessions to share their knowledge and thoughts on the trial procedures with community staff. The modules for the capacity building workshop included providing information about HBV and HCV testing, rapid testing procedures, data collection, and results reporting. Individuals who had implemented a pay-it-forward incentives for other infectious diseases were invited to share their strategies for effective public health messaging, explaining the pay-it-forward process using plain language and promoting donation and engagement.

Community-based organization staff were also encouraged to design tailored operating procedures to ensure the trial was culturally sensitive and responsive in their local settings (Extended Figure 7). Initially, the community-based organizations in Suzhou recruited participants through outreach activities in convenient locations with flexible schedules (e.g., gay clubs and KTVs). Secondly, telling real-world pay-it-forward stories about the power of kind actions were applied to improve the connection. Thirdly, participants who donated money were encouraged to write a postcard for future participants. The MSM volunteers from the community-based organizations piloted the study procedures with the research team. These volunteers were committed to all aspects of the pilot study, including ethics, training, engagement strategies, resource management plan, and continuous process monitoring. After the pilot phase, the community-based organizations carried out the designed study independently. Our study's HBV and HCV testing was conducted with an HIV, syphilis, HCV, and HBsAg multiplex rapid test (Wondfo, Guangzhou, China).

Our study is reported according to the CONSORT guidelines for cluster-randomized controlled trials (Supplementary document 1. CONSORT Checklist).

Study participants

Participants were recruited when they sought HIV or/and syphilis tests at the study or outreach sites. The inclusion criteria included: 1) 18 years old or above; 2) self-identified as MSM; 3) assigned a male gender at birth; 4)neither tested for HBsAg nor HCV antibody in the past 12 months. Men with a chronic HBV or HCV infection diagnosis, who have ever participated in the pay-it-forward program, and those who did not provide informed consent were excluded. In addition, since the HCV vaccine is unavailable in China, even MSM vaccinated for HBV were included in the study, as we used dual HBV and HCV testing.

Randomization and masking

This randomized controlled trial (RCT) was designed as a cluster RCT in which a group (cluster) of ten men was randomized into the pay-it-forward or control arms in a 1:1 ratio. We defined a cluster in this study as a group of ten eligible men who arrived at the study site and agreed to participate. We used block randomization and stratified the randomization by study sites. We recruited 8 clusters from Nanjing (for the officed-based model) and 24 from Suzhou (for the outreaching-based model). In each study site, the clusters were randomized with a block of four independently, while two clusters in each block were randomly assigned to the intervention arm and another two clusters to the control arm. We included two blocks in Nanjing and six blocks in Suzhou. The research staff pre-designed the randomization, and community staff enrolled participants at each study site according to a pre-determined allocation sequence (Supplementary document 4). The pre-determined allocation sequence was sealed in a envelope, and the study site only can open it when they recruit the first participant. This was a single-blinded cluster RCT, and only the study team member who performed the data analyses was blinded.

Procedures

Our study used a two-arm cluster randomized control trial to evaluate the effectiveness of the pay-it-forward intervention model (pay-it-forward arm) against a standard-of-care model (standard-of-care arm) on HBV and HCV testing uptake among MSM. The study recruited participants at office-based sites between Aug 20 2021 and Nov 6 2021, and from outreach site between March 2021 to October 2021. This trial is registered with Clinical Trial registration, ChiCTR 2100046140.

In the intervention arm, eligible participants were informed about the importance of HBV, HCV testing, and hepatitis transmission routes at enrollment. In the intervention arm, trained MSM peers from the office-based and outreach sites introduced the pay-it-forward concept. Subsequently, participants were offered HBV and HCV testing as a gift courtesy of the generosity of previous participants, which cost RMB 50 (~$7.7) or more at hospitals in China. At the end of the introduction session, each participant (regardless of whether they accepted or rejected testing) could choose to donate any amount of money to support other men in the community to receive the same HBV and HCV tests. All donations were voluntary, with no fixed amounts required. In addition, in the control arm, MSM received the same information about HBV and HCV testing in the control arm but needed to pay for their tests ($7.7), as is the standard at the clinic.

Data collection

In both arms, participants completed a brief, self-administered questionnaire covering socio-demographics, sexual behaviors, previous history of drug use, testing history for HIV, and vaccination history for HBV. A staff of each community-led organization was responsible for the daily reporting of data gathered in a standard administration log, which included the number of participants who gave consent to recruitment, the number of participants who completed HBV and HCV testing, the number of participants in the pay-it-forward arm who donated, and the amount of money donated by participants.

Participants were sub-categorized based on age (>30 years old vs. ≤30 years old), sexual behavior (those involved in any high-risk sexual behaviors in the past three months vs. those not), sexual orientation (gay or heterosexual/ bisexual), and history of drug use (used any injection or non-injection recreational drugs in the past 12 months vs. those not). These characteristics are all known to be high-risk factors for HBV or HCV infection [61-64]. We defined high-risk sexual risk behaviors as reported engagement in the following: condomless anal sex, group sex, or more than two sexual partners in the preceding three months. One project staff at the Jiangsu CDC updated all outcome data and double-checked with the original records weekly into a secure, password-protected web-based database. The lead investigator overseeing the research progress had full access to the de-identified data.

Outcomes

The primary outcome of this trial was the proportion of men in each arm who tested for HBV and HCV. The dichotomous outcome was determined by HBV and HCV test uptake verified by the community-based organization members. The secondary outcomes were; (1) the proportion of HBV and HCV testing uptake across each subgroup was compared to determine the heterogeneity in the intervention effect, (2) the proportion of participants who donated to others for HBV and HCV testing and the total amount donated (3) the cost-effectiveness of the community-led pay-it-forward model to the standard-of-care arm. The exploratory outcome was the proportion of men who tested positive for HBV and HCV.

Sample size calculation

The sample size was calculated based on a superiority cluster randomized trial design. We hypothesize that the community-led pay-it-forward model would increase testing rates more than the standard-of-care model. To detect the differences in testing uptake proportions between the two arms, we estimated the need for 100 participants per arm based on a superiority margin of 0.2 on a 5% level with a power of 80%. The intraclass correlation coefficient is 0.02, and the significance level of the test is 0.05. The superiority margin of 0.2 for the primary efficacy was considered clinical significance per a previous modeling study [65]. In addition, we also increased the sample size by 60% to allow for subgroup analyses of different types of study sites, leading to a sample size of 160 for each arm. Detailed sample size calculation and statistical analysis plan can be found in the study protocol.

Statistical analysis

We used descriptive analyses to summarize the sociodemographic and sexual behaviors of participants, the donation amount, and the proportion of donation of participants. We used a generalized estimating equation model (GEE) with a binomial distribution and an identity link function to estimate the absolute proportion difference as a measure of effect. The sandwich estimator and Kauermann-Carroll small sample correction have been used to correct the potential bias caused by the small number of clusters [66]. We adjusted for intraclass confounding factors, including study sites and baseline individual-level covariates (age, sex, education, marital status, income, study site, and previous HBV vaccination history). In addition, to address any existing imbalances between arms, we added additional factors into the GEE model, including the history of illicit drug use and high-risk sexual behaviours. Subgroup analyses were performed to investigate the potential effect modification using a relatively simpler model to avoid the problems of collinearity and convergence across the subgroup variable and adjustments [54]. Subgroup analyses were based on study site, age, sexual risk behaviors, and drug use patterns. Adjusted absolute proportion differences and corresponding 95% confidence intervals (CIs) were estimated with a GEE model adjusted for age, education, marital status, income, and recruited cities. All *P*-values reported are, and $P < 0.05$ was deemed statistically significant. Statistical analyses were performed with STATA software version 14.1 (StataCorp LP, TX, USA).

Economic evaluation

We used a micro-costing approach to assess the financial and economic costs (i.e., the cost of all resources needed to implement the testing models) from the perspective of a health provider, the Jiangsu Provincial CDC. We recorded the resources utilized throughout the trial from on-site observation and invoices. The cost items were further classified as fixed or variable. We categorized the start-up (training) and equipment fees as fixed costs (i.e., regardless of the number of tests completed). The cost of supplies used for HBV/HCV testing was considered 'variable costs (i.e., based on the number of tests completed). All expenses are expressed in USD using OANDA currency conversion rates in 2021 (1 USD = 6.50 Yuan). We conducted a cost analysis in Excel 2019 (Microsoft, USA), and the cost-effectiveness analysis was performed using TreeAge Pro 2021 (TreeAge Software, Inc., Williamstown, MA). This trial was registered with China Clinical Trial (identifier: ChiCTR2100046140) and was reported following the CONSORT 2010 checklist (Supplementary document 1).

Safety and adverse events

The study safety monitoring focuses on captuting negative event resulting from interventions, including anxiety, depression, and suicidal tendencies, as well as negative events arising from blood draws, such as physical discomfort, illness, and overall physical discomfort.

Per the protocol, no data monitoring committed was not established for this cluster RCT due to potential for harm to participants in minimal. Participants who tested positive during the study were referred to the designed hospital that have partnered with local community-based organizations. Any participants who feel they have experienced adverse events or unwanted effects during their involvement in the cluster RCT can withdraw at any time.

Inclusion and ethics statement

This research project was initiated by the University of North Carolina Project China, in collaboration with MSM-led community-based organizations in Nanjing and Suzhou of Jiangsu province, namely the Rainbow Group and Zhinanzhen Group, along with the Jiangsu Center for Diseases Prevention and Control, the Social Entrepreneurship to Spur Health Global. The research team co-led the study design with community-based organizations. The draft study protocol was shared with all partner organizations, ensuring each entity had a voice in the study design. The recruitment and implementation phases were led by the local Rainbow Group and Zhinanzhen Group staff in two study cities, further ensuring local relevance and commitment.

We fully adhere to the Nature Portfolio journals' guidance on Low and Middle-Income Countries (LMICs) authorship and inclusion. Of our research team, three authors (GF, JL &DW) are local researchers, and five authors (YZ, YX, HL, FZ, WT) are originally from the study country and are now based in high-income countries.

Ethics approval

The study was approved by the Jiangsu Center for Diseases Prevention and Control (IRB number JSLK-2020-B014-2) (Supplementary document 3). All participants provided written informed consent to participate in the trial before any study-specific procedures. Designated staff at each site confirmed participants' eligibility and obtained written informed consent. No compensation has been provided for participation in the study.

Data availability

The data are not publicly available for everyone because making the data publicly available without additional consent. If other investigators are interested in performing additional analysis, data requests can be submitted to the corresponding author, explaining the analyses planned. Access to data will be provided upon application, with a timeline of one month determined in accordance with the request.

Code availability

All codes are available on Github. The code is freely accessible at https://github.com/PIFHepstudy/code.git

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