Pay-it-forward gonorrhea and chlamydia testing among men in China: The PIONEER pragmatic randomized controlled trial

Study Protocol Version 4.0

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Background: Gonorrhea is one of the most common sexually transmitted diseases (STDs) among men who have sex with men in China. Past studies have shown that pay-it-forward (PIF) approaches premised on upstream reciprocity theory have been associated with a substantial increase in gonorrhea test uptake compared to standard of care. We propose the Pay-It-forward gONorrhEa tEsting randomized controlled trial (PIONEER) to examine the effectiveness of two implementation strategies involving different levels of community engagement to translate the generosity created by the pay-it-forward approach into test-taking action.

Methods: PIONEER will be a three-arm, programmatic cluster randomized controlled trial (RCT) to compare effectiveness of the three implementation strategies, followed by a mixed-methods implementation evaluation study. For the cluster RCT, we will enroll 12 diverse clinics which will be randomly assigned to one of the intervention arms for delivering gonorrhea testing: a standard pay-it-forward implementation strategy with minimal encouragement to get tested, a community-engaged pay-it-forward strategy, and a control arm in which men pay for their own STD test. The primary outcome of the RCT will be gonorrhea test uptake and secondary outcomes will include chlamydia testing, syphilis testing, STD treatment among those with infection, amount donated, 100% condom use, and antimicrobial resistance. A sequential explanatory mixed methods design will be used to evaluate the implementation process. Data sources will include survey data on acceptability of intervention, intervention appropriateness, feelings and attitudes towards interventions among participants, administrative data about test uptake, treatment rate, and donations, as well as qualitative data to gain insights about men's perceptions and attitudes towards the pay-it-forward interventions strategies, mechanisms driving uptake and donating behaviors. Both survey and qualitative interviews with implementers and organizers about fidelity and adherence to protocol, intention to continue and maintain a pay-it-forward intervention, and barriers and facilitators of implementing the intervention will be conducted.

Discussion: PIONEER will substantially increase gonorrhea testing among MSM in China, providing an innovative new financial mechanism to sustain STD screening among sexual minorities in low- and middle-income countries. This study will answer compelling scientific questions about how best to implement pay-it-forward and the individual and organization characteristics that moderate it.

Contributions to the literature

- This cluster randomized controlled trial aims to examine the effectiveness of two implementation strategies involving different levels of community engagement to translate the generosity created by the pay-it-forward approach into test-taking action.
- A sequential explanatory mixed methods design will be used to evaluate the implementation process to determine mechanisms by which pay-it-forward motivates testing and donations across the two intervention arms, and how these are moderated by individual and organizational characteristics.

- This study will answer compelling scientific questions about how best to implement pay-it-forward and the individual and organization characteristics that moderate it.

Background

Gonorrhea is common among MSM in China. Gonorrhea is one of the most common sexually transmitted diseases (STDs) worldwide and in China. The World Health Organization estimated that there were 87 million new cases of gonorrhea among people 15-49 years old based on a global systematic review[5]. The prevalence of gonorrhea among MSM in southern China has been reported as high as 12.5%[6-7]. Gonorrhea is known to increase the risk of HIV acquisition and transmission, but is often asymptomatic at extragenital sites.

Gonorrhea testing rates among MSM are low. World Health Organization[9] and United States Centers for Disease Control and Prevention guidelines[10] recommend routine gonorrhea testing for sexually active MSM. Studies in different provinces of China consistently report less than half of MSM have ever been tested for gonorrhea[11-12]. Low testing rates are problematic because this allows onward gonorrhea transmission

Low testing rates likely related to fees and minimal community engagement. User fees are common in many low and middle-income countries for STD testing and discourage test uptake[12], decreasing opportunities for prompt treatment and public health interventions[11,13]. Gonorrhea testing in China is expensive, not covered by health insurance, and not covered by other social support systems. This decreases access to routine gonorrhea testing[14]. Some young MSM may opt to self-pay for STD services in order to decrease the risk of parents, insurance providers, or others knowing about their need for services[15]. In addition to financing problems, community engagement in STD testing is often weak.58 Many MSM campaigns for STD testing are driven by public health authorities and have limited authentic input from local end-users[16]. This limited participation may then diminish STD test uptake. In response to these financial and community barriers to STD testing, our team developed a pay-it-forward approach to gonorrhea testing for MSM.

Pay-it-forward has a person receive a free gonorrhea test from the local community and then decide to donate money to support subsequent testers (**Figure 1**)[17,18]. Pay-it-forward fits within the broader field of behavioral economics which uses multiple disciplines to understand human decision making. Pay-it-forward chains of giving are sometimes driven by unconnected generous individuals[18], but more often organized by a group with a common purpose[19,20]. Studies have shown that pay-it-forward can be sustainable and promote generosity[21].

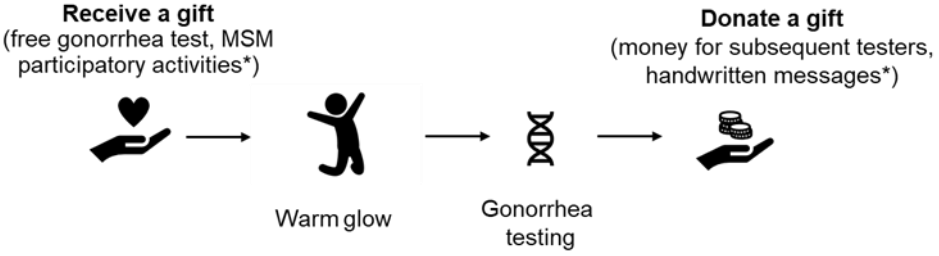

Figure 1. Overview of pay-it-forward. *Participatory activities such as open calls to create handwritten messages in the community-engaged implementation strategy. Warm glow refers to

a positive feeling after receiving a gift.

Our previous pay-it-forward research showed that it was associated with a substantial increase in gonorrhea test uptake compared to standard of care[22,23]. However, these studies have several limitations. First, the projects were mostly, although not entirely, implemented at MSM-led clinics. These clinics serve MSM who are more likely to disclosure their sexual orientation compared to MSM who present to public clinics. Alongside the MSM volunteers at MSM-led clinics, these sites are likely in a better position to organize MSM community engagement activities[15]. In addition to MSM-led clinics, public clinics also provide gonorrhea testing and treatment for MSM. Public clinics include HIV testing sites and STD clinics that receive support from public health authorities. Public clinics have higher rates of linkage to care and are more likely to have antibiotic therapy on-site. Second, MSM included in these two studies were mostly younger, better educated, higher income, and more willing to donate. The pay-it-forward intervention needs to be evaluated in additional cities and different types of clinic (i.e., both MSM-led and public clinics). Last, the previous study showed that pay-it-forward was effective compared to standard of care, but for scale up, explicit and intentional support for implementation is needed. Lack of implementation evaluation limits our understanding of the implementation process and community-engaged strategies are needed to maximize the efficiency and effectiveness. These underscore the importance of implementation research to inform contextually appropriate strategies to implement pay-it-forward most effectively at scale.

We propose the Pay-It-forward gONorrhEa tEsting randomized controlled trial (PIONEER) to examine the effectiveness of two implementation strategies involving different levels of community engagement to translate the generosity created by the pay-it-forward approach into test-taking action. In the standard approach, men receive the gift of a free test and view messages promoting testing. In the community-engaged approach, men receive gifts, view tailored messages, are encouraged to create tailored messages of their own and are invited to become part of a community of collaborators engaged in promoting gonorrhea testing. Community-engaged approaches are important for enhancing contextual appropriateness of public health interventions and possibility of success.[1] The objectives of the study are threefold:

1) To compare point-of-care gonorrhea test uptake in a standard pay-it-forward implementation strategy arm, a community-engaged pay-it-forward implementation strategy arm, and a control arm using a three-arm cluster randomized controlled trial.
2) To determine mechanisms by which pay-it-forward motivates testing and donations across the two intervention arms, and how these are moderated by individual and organizational characteristics.

Theories informing the PIONEER intervention

Our trial design and pay-it-forward strategies were informed by two theories/principles. First,

the pay-it-forward is a novel concept embedded in upstream reciprocity theory. Upstream reciprocity is defined as individuals helped by someone are more likely to help other unspecified people.

Upstream reciprocity theory has been used to understand the mechanism of pay-it-forward within a community. The idea is that if someone is generous to you, it generates a "warm glow" that encourages you to be generous to others. In the context of pay-it-forward, the hypothesis is that someone receiving a gift feels an obligation to be generous to the community by getting tested, and also by contributing a gift in return.

Principles guiding the design of community engagement elements

Our implementation strategies were developed based on community -based participatory research (CBPR)[26.] Community participation is essential to the acceptance and contextual appropriateness of an intervention strategy.[1] This is especially important for hard-to-reach sexual minority groups. CBPR involves having the target community participating in several phases of the research process to address a health research question[26]. CBPR is appealing as it generates community engagement and amplifies voices of neglected populations in service delivery strategy designs. It is a bottom-up, user-centered approach which leads to the development of culturally appropriate intervention strategies. Evidence has shown community engagement in developing intervention strategies is associated with better acceptance, adherence, and effectiveness of the interventions in changing behaviors in a favorable way. We will use CBPR to guide following activities: 1) organizing a co-creation group to co-create the community-engaged pay-it-forward strategy and forming shared leadership; 2) guiding the design of community engagement elements of the community-engaged strategy; 3) involving key stakeholders in various stages of the project to enhance appropriateness, acceptability and feasibility.

Effectiveness-implementation (EI) hybrid trial design

Hybrid effective-implementation study designs are emerging as a useful research method to examine not only the intervention outcomes but also the implementation process that may affect the intervention effectiveness to various degrees. Evaluating the implementation outcomes collects evidence about the intervention delivery process which can inform future evidence-based practices, facilitate replication or scale-up, and translate research findings to routine practices. We define our trial as a hybrid implementation-effectiveness design in which we aim to identify an optimal pay-it-forward delivery strategy (ie, community-engaged pay-it-forward versus standard pay-it-forward strategies and a control arm without pay-it-forward components) by comparing effectiveness of these three strategies, and in the meantime, examine the implementation process of the two pay-it-forward strategies guided by RE-AIM framework.

Implementation evaluation framework

Finally, we used the RE-AIM evaluation framework to define outcomes in the five key domains for evaluating the implementation process and how different factors may affect intervention effectiveness. The RE-AIM framework is one of the most commonly used

frameworks to evaluate implementation of an intervention. It guides the development of implementation-focused outcomes to better understand mechanisms and factors influencing behavioral changes as a result of the interventions. Evaluation of the five key domains of the implementation process will provide evidence for future scale up of the intervention and facilitate evidence-based practices. These domains are reach of the three implementation strategies within the target MSM population, effectiveness of the intervention itself and of the strategies that aim to enhance and optimize intervention delivery, factors affecting adoption of the implementation strategies, fidelity and adherence to standard operation protocol for implementation, maintenance and sustainability.

Methods/design

Design overview

Our trial will use a hybrid effectiveness-implementation study design which values both intervention effectiveness and implementation process. Specifically, the PIONEER trial will be a three-arm, programmatic cluster randomized controlled trial (RCT), followed by a mixed-methods implementation evaluation study. The cluster RCT aims to compare effectiveness of the three implementation strategies and the implementation evaluation will look into other domains of the implementation process guided by the RE-AIM framework.

For the cluster RCT, we will enroll 12 diverse clinics (i.e., MSM-led and public sexual health clinics) and the clinics will be randomly assigned to one of the intervention arms for delivering gonorrhea testing: a standard pay-it-forward implementation strategy with minimal encouragement to get tested, a community-engaged pay-it-forward strategy, and a control arm in which men pay for their own STD test. The standard strategy, which was developed through our previous pay-it-forward research, will have men who enter the clinic be provided a free gonorrhea test alongside handwritten postcards from other MSM in the local community. The community-engaged strategy will include all elements of the standard strategy, in addition to the following key community engaging activities, which may include gift recipients will be invited to submit handwritten postcards of their own, print images from instant cameras, or create videos promoting gonorrhea testing (to be viewed at the same clinic); men who agree to participate will be invited to a hybrid digital and in-person pay-it-forward event where they meet other people who have donated and to related participatory activities organized by the local clinic to promote gonorrhea testing.

Mixed methods will be used to evaluate the implementation process with project implementers, organizers, and participants. Data sources will be multiple which will include survey data on acceptability of intervention, intervention appropriateness, feelings and attitudes towards interventions among participants, administrative data about test uptake, treatment rate, and donations, as well as qualitative data to gain insights about men's perceptions and attitudes towards the pay-it-forward interventions strategies, mechanisms driving uptake and donating behaviors. Both survey and qualitative interviews with implementers and organizers about fidelity and adherence to protocol, intention to continue and maintain a pay-it-forward intervention, and barriers and facilitators of implementing the

intervention will be conducted.

Study setting and population

We will implement the study in Guangdong cities that have either (or both) public STD and MSM-led clinics. Examples include Zhuhai, Foshan, Jiangmen, Shenzhen, Zhanjiang, Dongguan, and Yunfu. These clinics were chosen because respective cities have a higher burden of STDs, and findings would be potentially relevant in many cities. Each of the clinics sees both MSM and non-MSM and only MSM who meet screening criteria will be approached to learn more about the study. Each of the clinics have dual chlamydia/gonorrhea point-of-care testing available.

The study settings between public clinics and MSM-led clinics would be different. One key obstacle for recruiting MSM at public STD clinics is that MSM usually may not want to disclose their sexual identities due to justifiable fears about risks of stigma and discrimination from other men and health workers. Therefore, in order to avoid indirect sexual orientation disclosure and feeling of discrimination, public STI clinic recruitment will be extended to include all men regardless sexual orientation visiting the public clinic setting. This will lower the risk of being unnecessarily 'targeted' and accidental sexual orientation disclosure.

The inclusion criteria at public clinics include men who at least 18 years old; have had sex over the past year; have not been tested for gonorrhea and chlamydia in the past year; reside in the city in the past three months; speak Mandarin Chinese or Cantonese; mentally capable to provide informed consent to test for gonorrhea and chlamydia; and owning a mobile phone.

The inclusion criteria at MSM-led clinics include men who had anal sex with another man; at least 18 years old; have had anal sex over the past year; have not been tested for gonorrhea and chlamydia in the past year; reside in the city in the past three months; speak Mandarin Chinese or Cantonese; mentally capable to provide informed consent to test for gonorrhea and chlamydia; and owning a mobile phone. In China, over 90% of MSM own a mobile phone.

Development of intervention and formative research

Approach and study team

A key innovation of this trial study, relative to past pay-it-forward research, is the development and evaluation of the community-engaged approach as an additional intervention arm. While upstream reciprocity is hypothesized to promote the pay-it-forward mechanism in our proposed trial, simulation models of the upstream reciprocity process show that by itself, the "warm glow" does not guarantee sustainability. In contrast, there is evidence to show that when combined with network reciprocity where acts of altruism are reinforced by a community of collaborators, the probability of cooperation increases.72 The two arms of our trial are designed to test these two hypotheses. The standard pay-it-forward arm evaluates the hypothesis that the upstream reciprocity created by a pay-it-forward approach will increase testing adoption with minimal implementation support, while the community-engaged arm tests the hypothesis that pay-it-forward needs to be reinforced by an

implementation strategy based on network reciprocity to enhance its effectiveness.

The study will be managed through a consortium involving two academic centers, the University of North Carolina in Chapel Hill and the Southern Medical University Dermatology Hospital in Guangzhou, as well as a non-profit community-based organization who will organize community engagement activities, the Social Entrepreneurship to Spur Health (SESH). The SESH team has strong track record of community engagement and organizing research studies focused on sexual health, including pay-it-forward programs in Beijing and Guangzhou. The study team comprises representatives from the academic centers and SESH who have complementary expertise in community mobilization, implementation science, epidemiology, health economics, biostatistics, and social science.

A co-creation group will be appointed and will comprise MSM representatives, clinicians and nurses, communication officer, co-chaired by members of SESH and a local MSM community-based organization. Co-creation groups serve as a source of shared leadership in CBPR-premised research, and its members typically reflect the community of interest. This co-creation group will be consulted on a quarterly basis to provide input on the study design, implementation, and dissemination activities.

Site Selection, training and trial registration

We will implement the study in Guangdong cities that already have MSM-led clinics: Guangzhou, Shenzhen, Zhuhai, Jiangmen, Foshan, and Dongguan. These clinics were chosen because respective cities have a higher burden of STDs, they include the two major service delivery approaches (MSM-led clinics and public clinics) in China, and findings would be potentially relevant in many cities have dual chlamydia/gonorrhea point-of-care testing available in addition to ceftriaxone and azithromycin. These clinics have also been selected to ensure that there is a stable supply chain for ceftriaxone and azithromycin.

Each of the clinical sites will receive Good Clinical Practice (GCP) training for new personnel, regulatory assessment, and related trial requirements. Representative from each of the participating clinics will be invited to attend a single training workshop in Guangzhou to introduce the study protocol, local implementation workflows, point-of-care diagnostics, gonorrhea treatment, and resistance testing processes. We will register the RCT on ClinicalTrials.gov prior to the commencement of the trial.

Developing standard strategy and the community-engaged strategy

This three-arm cluster randomized controlled trial will compare gonorrhea test uptake in a standard pay-it-forward implementation strategy arm, a community-engaged pay-it-forward implementation strategy arm, and a control arm. Our implementation strategies are summarized in Table 1.

Table 1. Overview of the three study arms.

Trial Arm	**Financial Component of Gonorrhea Testing***	**Community Engagement**

Standard Pay-it-forwardarm	Free point-of-care gonorrhea testing	Passive: viewing postcards and materials written by others encouraging gonorrhea testing
Community-engagedPay-it-forward arm	Free point-of-care gonorrhea testing	Active: multi-stakeholder co-creation activities to develop essential components of the intervention and implementation strategies; writing postcards; opportunity to donate to support others
Control arm	Fee-based point-of-care gonorrhea testing(approximately 20 USD	None

*Note that all MSM found to have gonorrhea will receive free treatment according to WHO guidelines.

In the standard strategy/arm, MSM who enter the clinic will be provided with a free gonorrhea test alongside handwritten postcards from other MSM in the local community. Our previous RCT has already created standard operating procedures, survey instruments, and educational materials for this intervention. The postcards will be generated through an open call for suggestions about tailored, hand-written messages that are clinic specific and locally appropriate. We will use standardized methods developed by the World Health Organization to design the open call. Briefly, this will involve creating a steering committee, promoting the open call, judging submissions, recognizing excellent submissions, and implementing selected ideas.

In contrast, the community-engaged strategy/arm will include all elements of the standard strategy, in addition to the following key components: gift recipients will be invited to submit handwritten postcards of their own, print images from instant cameras, or create videos promoting gonorrhea testing (to be viewed at the same clinic); men who agree to participate will be invited to a pay-it-forward event where they will meet other people who have donated, and will also be invited to related participatory activities organized by the local clinic to promote gonorrhea testing.

In the control arm, MSM will be informed about the importance of gonorrhea testing but will not receive handwritten postcards or other community engagement activities. Among men who choose to receive gonorrhea testing, they will have access to the same diagnostics, treatment, and follow-up provided in the other two arms. Donations in the two pay-it-forward arms will be organized using WeChat, a hybrid between Twitter and Facebook that allows micro-payments.

We will use intervention mapping[27], a method used in public health to design these

components in a way that is tailored to the local context and facilitates their implementation. We will be guided by several behavior change taxonomies that have been developed by implementation scientists to assist in the development of implementation interventions[2 3] Briefly, examples include categories of behavioral change techniques that focus on changes to increase knowledge, changes to awareness and risk perception, and changes to social influence.

Formative testing, finalization of interventions, and development of instruments

Formative Digital Qualitative (n=50)

To further develop and fine-tune our implementation strategies in preparation for the RCT, we will conduct a series of digital qualitative research activities. These activities will explore the perceptions of men who have sex with men (MSM) in Guangzhou, Shenzhen, Zhuhai, Jiangmen, Foshan, and Dongguan on HIV and other STI testing, with a focus on barriers and facilitators to testing for HIV and other STI (especially Gonorrhea and Chlamydia), perceptions of public STI clinics, perceptions of MSM-led clinics, as well as perceptions of community-engagement in the MSM community. First, we will recruit up to 50 people to participate in an online chat-based focus group discussion (FGD) on WeChat. The SESH team will disseminate a call for participation over social media. Participants who are interested to participate will provided with a link to the participant information sheet and consent form, and following their consent, will be directed to an enrollment survey. Personal identifiers will never be shared with anyone outside of the research team.

There will be no more than eight participants per FGD. In order to participate in this focus group discussion (FGD), individuals must meet the following criteria: Age 18 years or older (Age of majority in China); Sex assigned male at birth; Have had anal sex with a man at least once; Speaks Mandarin Chinese or Cantonese; and currently living in Guangzhou, Shenzhen, Zhuhai, Jiangmen, Foshan, and Dongguan. Second, we may follow up with no more than 25 participants for further in-depth interviews conducted over voice call on WeChat. Third, we will conduct digital ethnographic activities on digital spaces and sites mentioned by participants throughout the course of the study, to articulate stakeholders associated with such spaces, and describe how community identities, interactions, and engagement occur in these spaces.

Formative Quantitative (n = 350)

We will field test our two implementation strategies at several MSM-led clinics and public clinic in Guangzhou, China. We will recruit a total of 350 participants. The eligibility criteria include at least 18 years old and mentally capable to provide informed consent to test for gonorrhea; men who have had anal sex with another man over the past year; have not been tested for gonorrhea in the past year; reside in the city in the past three months; speak Mandarin Chinese or Cantonese; and owning a mobile phone. This will allow us to improve the strategies using learning evaluation methods[30] that involve iterative Plan-Do-Study-Act cycles based on user feedback. We will also develop and fine-tune our process evaluation instruments for fidelity assessment[31], gratitude assessment[32, 34], and organizational readiness[35] at this stage of research.

Formative Qualitative (n = 50)

We have developed an interview guide as part of formative testing. Main topics in the interview guide will include the following: (1) reasons for getting tested; (2) understanding and perception of the pay-it-forward concept; (3) specific questions about emotions of gratitude after receiving a test that is supported by another community member; and (4) self-identity in the MSM community and level of integration within a community; (5) intention and motivation to initiating and mediating helping behaviors within the community. We will obtain a recorded verbal informed consent from all interviewees before the commencement of the interview. Interviews will last about one hour and will take place either in person or over the phone based on participant preference.

Interviews will be audio-recorded and personal information will not be recorded. Unintentional recording of personal information will otherwise be redacted before transcription. Each participant will receive a small monetary incentive of ¥50 (7.50 USD) for their participation. All recorded interviews will be transcribed, and transcripts will be checked by one research staff member. Summaries of interviews will be written up for preliminary data analysis. In addition, we will collect anonymized text from handwritten postcards and other community engagement activities.

Pragmatic Programmatic cluster RCT

Sample size and power considerations

We used a binary outcome cluster RCT design for sample size calculation where the unit of randomization is the clinic. In order to achieve a 90% power and allow for 0.05 type-I error, 12 overall clusters (4 in each arm) are needed. Thus, the sample size includes a total of 12 clusters and 1200 participants (100 per cluster), based on cluster randomized trial sample size calculation principles. We expect this study will have 85% power to detect a 10% difference in azithromycin resistance between intervention arms and routine gonorrhea antibiotic surveillance data from other cities in the same province. Nevertheless, further calculations will be made following formative research endeavors that will estimate the prevalence of these outcomes. The calculation would be performed using the software PASS (version 15) with the formulas developed by Hussey and colleagues.[36]

Randomization

Figure 2 shows the cluster RCT design flowchart. We will assign clinics to study arms on a 1:1:1 basis using covariate constrained randomization. We will use covariate constrained randomization to decrease potential bias associated with unbalanced study arms. We will balance the number of MSM-led and public clinics in each arm because these are unique implementation structures. All men recruited via one clinic will be assigned to one arm. We will recruit and screen men until we meet our sample size of 1200 men.

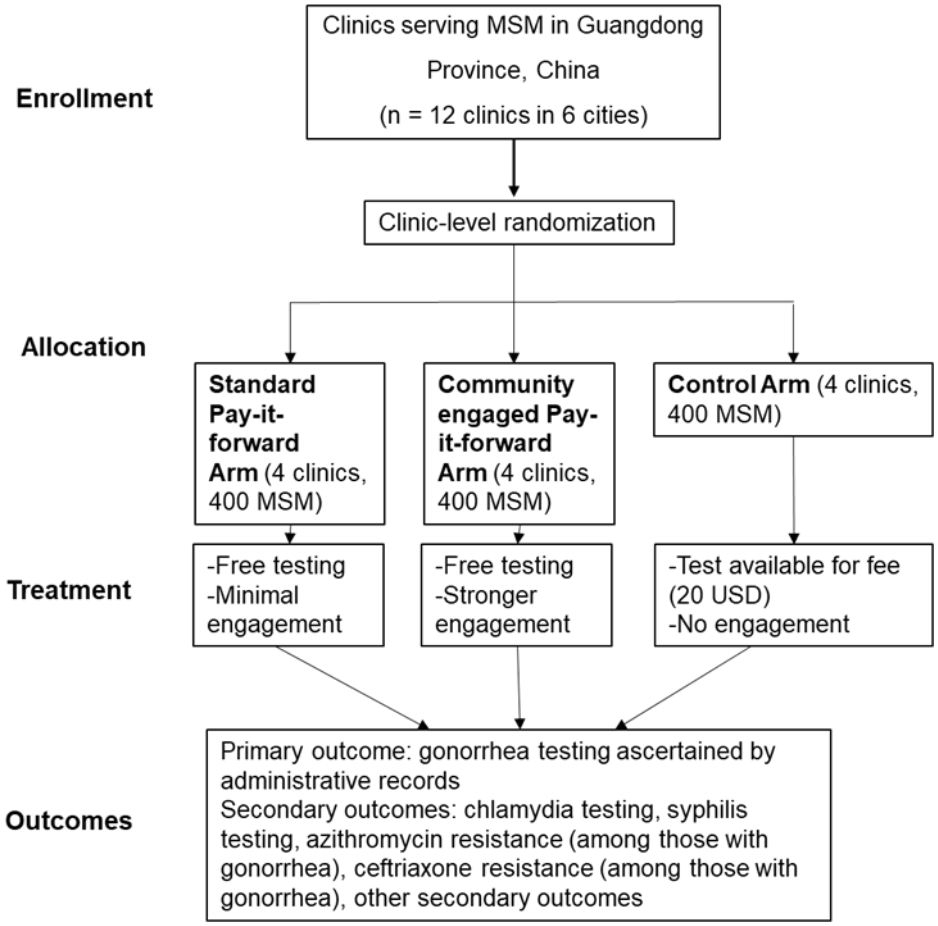

Figure 2. Pragmatic RCT flowchart. Each city will have one MSM-led clinic and one public clinic participating.

Intervention delivery strategies

The duration of the intervention is one year at each clinic, with the potential to continue based on local commitments. All clinics will have dual gonorrhea/chlamydia point-of-care molecular tests on-site. This diagnostic is approved by the US FDA and the Chinese national regulatory authority. Men who agree to be tested will have specimens collected from pharyngeal, rectal, and urethral sites. Specimens will be pooled based on excellent sensitivity and specificity. Turnaround time for test results will depend on the local clinic. Surveys will be done online in order to facilitate implementation. All participants diagnosed with gonorrhea will receive ceftriaxone and azithromycin in accordance with WHO recommendations for first-line gonorrhea therapy.

Outcome measures

The primary outcome of the RCT will be gonorrhea test uptake ascertained by administrative review from participating clinics. We used this same primary outcome in previous quasi-experimental and RCT trials evaluating pay-it-forward. Secondary outcomes will include syphilis testing, amount donated towards pay-it-forward, antimicrobial resistance measures, positive tests for gonorrhea and chlamydia, measures of gratitude and community solidarity,

and per unit costs associated with the intervention (Table 2) .

Table 2. Secondary outcomes of the cluster RCT

Outcome	*Time Frame*	*Ascertainment*
Syphilis testing	During enrollment visit	Administrative data
Amount donated	During enrollment visit	Administrative data
Azithromycin resistance based on culture and molecular methods	During enrollment visit	Laboratory result
Ceftriaxone resistance based on culture and molecular methods	During enrollment visit	Laboratory result
The number of participants who tested positive for Gonorrhea	During enrollment visit	Laboratory result
The number of participants tested positive for chlamydia	During enrollment visit	Laboratory result
Cost per test[1]	During enrollment visit	Costing data collection
Adapted gratitude scale	During enrollment visit	Self-report
Community solidarity scale[4]	During enrollment visit	Self-report[2]

[1]Cost per test is defined as the cost associated with respective interventions (development, start-up, implementation, intervention) per individual who reported testing for gonorrhea and chlamydia following the intervention; economic test and financial cost are reported separately.
[2]Community solidarity involves engagement, social network support, and a sense of belonging. These items were used in our previous pay-it-forward research study.[4]

Data analysis

The primary outcome will be gonorrhea test uptake among MSM. Generalized mixed effects models will be used to examine two main hypotheses: one comparing the superiority of the community- engaged strategy compared to the standard pay-it-forward strategy; and another comparing the superiority of the standard pay-it-forward strategy to the control arm. The estimated intervention effects will be reported with 95% CIs and p values. Descriptive analysis will be used to summarize the characteristics and behaviors of the participants in each arm.

We will include participants diagnosed with gonorrhea whose isolates can be cultured and calculate the minimum inhibitory concentrations (MICs) for specific antibiotics. MICs will be described as geometric means, and the distributions among gonorrhea strains in the intervention arm will be compared to surveillance data using a Mann-Whitney test. We will use the midpoint between the specific value and the next higher or lower dilution value to calculate the mean for MICs above or below the pre-specified thresholds. We will calculate the prevalence rates and 95% confidence intervals of gonorrhea resistance and decreased susceptibility to pre-specified antibiotics. Bivariate analyses and multinomial logistic regression will be used to determine the variables associated with infection with resistant or decreased susceptible strains of antibiotics. We will compare the frequency of resistant strains in the three arms using a chi-squared test for trend.

Oxytocin sub-study

One community-engaged MSM-led clinic and one control MSM-led clinic will be selected to conduct a pilot quasi-experimental study to assess the impact of the community-engaged intervention on measures of salivary oxytocin. We aim to recruit 100 participants from each

site (n=200) for this sub-study. This sub-study aims to investigate the use of oxytocin as an objective biomarker to reflect feelings of warm glow. Oxytocin is a hormone produced in the hypothalamus and associated with trust and altruism measures.[37-39] Studies have also administered intranasal oxytocin to study its effect on gratitude and pro-social actions.[39] We aim to measure salivary oxytocin before and after the intervention to ascertain if such changes may be attributable to the intervention. Changes in oxytocin levels will also be measured against changes in levels of warm glow and other baseline characteristics to ascertain the relationship between these factors. Collected saliva samples will be stored at -40 degree Celsius for a minimum of 6 months after collection and disposed of following the standard laboratory protocol per study site.

Implementation evaluation

The RE-AIM framework has been extensively used in implementation research to evaluate the implementation of evidence-based interventions. At this stage, we will evaluate the other dimensions of the implementation of the standard pay-it- forward and the community-engaged pay-it-forward arms with a view to understand both the factors that influence men to get tested and those that motivate men to donate. Given the novelty of pay-it-forward to raise fund, its sustainability partly depends on men willing to donate. Understanding the drivers of financial sustainability across individuals and clinics may help inform policy makers and interested researchers in resource-limited settings about the potential of using the strategy to promote underfunded public health services.

We will use a sequential explanatory mixed methods design.93 In this design, quantitative data is followed up with qualitative methods to expand or explain the quantitative results. The quantitative component of our design will measure reach, implementation, adoption and maintenance by adapting validated implementation research instruments to assess acceptability and appropriateness at the individual level (related to adoption) and fidelity and organizational readiness at the clinic level (related to implementation). We will also administer a gratitude questionnaire that has already been validated in China to test upstream reciprocity (related to maintenance). Details of these instruments are provided in Table 3 below. The qualitative data will use in-depth interviews grounded in upstream and social reciprocity theories to explore the processes and mechanisms that affect the results, and how these differ by individual (geography and socioeconomics) and organizational (geography and readiness) characteristics. Our mixed methods study will be conducted during and after the RCT.

Quantitative surveys

Surveys with clinics, project implementers and participants will be conducted. We will administer an organizational readiness survey in all clinics in the standard and community-engaged arms. All clinic staff involved in the implementation of the pay-it-forward intervention will be encouraged to take the survey which will assess the motivation and capabilities of their clinic. Every month, in each clinic in the standard and community-engaged arms, a convenience sample of 10 men will be selected and a member of the Guangdong Provincial STD Control Center staff will assess the extent to which pay-it-

forward is implemented in accordance with the protocol. All recruited participants in the study in all clinics in the standard and community-engaged arms will be asked to take a brief survey assessing their perceptions of acceptability and appropriateness of pay-it-forward and the relevant implementation strategy. They will also complete a pay-it-forward-specific adapted version of the Gratitude Questionnaire-6 (GQ-6).

Qualitative interviews

MSM and pay-it-forward organizers will be recruited for in-depth interviews. We will recruit MSM in the clinic, immediately following participation in the RCT. Purposive sampling strategies will be used to recruit MSM who are involved in each implementation strategy arm, those who participate and those who do not, and those who provide a higher donation and lower donation. Among organizers, we will recruit them by sending a text message to a purposive sampling of organizers. This will include those at MSM-led clinics and public clinics, organizers who identify as gay and those who do not, and other key characteristics. We will develop a topic guide to guide the MSM interviews based on the literature review, fieldnotes and reflections during the implementation of RCT.

Main topics will include the following: (1) reasons for getting tested; (2) understanding and perception of the pay-it-forward concept; (3) specific questions about emotions of gratitude after receiving a test that is supported by another community member; and (4) self-identity in the MSM community and level of integration within a community; (5) intention and motivation to initiating and mediating helping behaviors within the community. We will obtain a recorded verbal informed consent from all interviewees before the commencement of the interview. Interviews will last about one hour and will take place either in person or over the phone based on participant preference.

Interviews will be audio-recorded and personal information will not be recorded. Unintentional recording of personal information will otherwise be redacted before transcription. Each participant will receive a small monetary incentive of ¥50 (7.50 USD) for their participation. All recorded interviews will be transcribed, and transcripts will be checked by one research staff member. Summaries of interviews will be written up for preliminary data analysis. In addition, we will collect anonymized text from handwritten postcards and other community engagement activities.

Sample size and power considerations

A total of 25 MSM participants and 25 pay-it-forward organizers will be recruited for individual interviews. Enrollment will cease when no new themes and sub-themes emerge, inferring data saturation. All eight participating clinics that are implementing the pay-it-forward intervention (both standard strategy and community-engaged strategy) will be invited to respond to questions related to implementing the intervention (see Table 3). All participating clinics will be invited to answer questions related to organizational implementation and maintenance. Operational definitions and example measures of the five dimensions of RE-AIM adapted for the study are shown in Table 3.

Outcome measures

The outcomes will include (1) primary RE-AIM data comparing differences between the community-engaged pay-it-forward strategy and the standard pay-it-forward strategy; (2) qualitative data describing mechanisms related to test uptake and donation decisions, respectively.

Data analysis

Thematic analysis will be used to analyze qualitative data. A codebook will be developed by a senior qualitative researcher. Two research assistants will then code the transcripts based on the codebook. NVivo version 12 (Nvivo, Columbus, OH) will be used for qualitative data analysis. Descriptive data analyses, independent sample t tests and chi-square tests will be used to compare differences in RE-AIM measures between pay-it-forward and standard-of-care arms. We will generate a global implementation score and scores of separate dimensions and convert to a z-score. Correlates of global implementation and implementation dimensions will be examined using general linear mixed models (GLMM). In addition, qualitative data on social networks will be applied to disentangle the connection between an individual's gratitude and position within a network comprised of helping relationships (both direct and indirect relationships). Finally, we will use linguistic inquiry word count to analyze textual information gathered as part of community engagement activities.

Safety management plan

Criteria for withdrawal: if participants want to quit the study for any reasons; Data and safety monitoring will be done by project implementers.

Data management information

For the surveys and demographic questionnaires, all data are directly entered into computers at UNC Project China office as participants complete the surveys. Programs to ensure accuracy, completeness, and internal consistency are automated. Data can be readily downloaded and converted to the format of commercially available statistical software. During collection of the online portion of the study, all data will be transmitted securely using SSL (TLS) 128-bit encryption across the Internet (HTTP). SSL provides users with the assurance of access to a valid, "non-spoofed" site, and prevents data interception or tampering with sensitive information. The SSL certificate that will be used for this project will use 128-bit encryption, the preferred security level of government and financial institutions. 128-bit encryption offers protection that is virtually unbreakable. For example, if a hacker could crack a standard 40-bit SSL session in a day, it is estimated that it would take well beyond a trillion years to accomplish the same thing against a 128-bit SSL session. A dedicated server, which eliminates security issues involved with shared hosting environments where hundreds of websites and users reside on one shared web server as well as ensuring both physical and network security, will be used to house the data. Data will then be stored in a secured server at Dermatology Hospital, Southern Medical University. The server will be configured with redundant hard drive array to ensure reliability. Access to the data will be password protected within the server's firewall. Only the PI and a designated senior staff member will have the password to access to the "key" that links the non-descript identifier to personally identifiable information. IP addresses of participant's computers will not be

collected at any time. Cookies will not be used in any way to track participant activity. A quick link will exist on each survey page to provide participants a rapid way to switch to an innocuous website if their privacy is interrupted while completing the survey.

For participants' urine testing results and clinical outcomes, the data will be recorded directly input into Health Information System (HIS) at Dermatology Hospital, Southern Medical University. Data will be downloaded and stored the same way as the survey data.

Table 3. Dimensions of RE-AIM in implementation research adapted for pay-it-forward.28

Dimensions	Level	Operational definitions	Measurement method
Reach	Individual	• Proportion of MSM who enter the clinic who are screened for eligibility • Percent of MSMs who visit the clinic compared to the MSM in the catchment area	Administrative data will be collected on the demographics, socioeconomics and geographic location (zip code or equivalent level) of those enrolled in pay-it-forward to test if there are differences in the characteristics of those who get tested and those who do not. Population of MSMs will be collected from public data to assess the potential reach of the pay-it-forward intervention within the overall MSM population in the area.
Effectiveness	Individual	• How effective are the two implementation strategies in promoting gonorrhea test uptake? • Does pay-it-forward influence secondary outcomes (chlamydia testing, treatment and prevention outcomes)?	The primary outcome is gonorrhea test uptake from the RCT which will be measured using administrative data from participating clinics. Other secondary indicators are test uptake, treatment rate among those infected, azithromycin resistance, ceftriaxone resistance, and 100% condom use.
Adoption	Individual	• Do the participants find pay-it-forward acceptable and appropriate? • Is there a relationship between acceptability and appropriateness and testing outcomes? • What are the demographic, socioeconomic and geographic differences between those who found pay-it-forward acceptable and appropriate and those who did not?	Quantitative data will be collected using an adapted version of the Acceptability of Intervention Measure (AIM) and the Intervention Appropriateness Measure (IAM). Qualitative data will be collected from interviews to gain additional insights about the results from these instruments.
	Organizational	• How do feelings of gratefulness contribute to test adoption and donation behaviors?	The $R=MC^2$ instrument will be adapted for use in clinics.

Implementation	Organizational	• What is the extent to which local staff implement the pay-it-forward according to the SOP, and the extent to which legitimate adaptations are needed?	Fidelity checklists (as specified by Carroll et al.) will be used to measure adherence to protocol related to content and dose. Interviews with clinic staff will be used to determine reasons for deviation from protocol and to track and document legitimate adaptation.
Maintenance	Individual	• What is the average donation per participant in each arm? • Is there a relationship between testing and donations? • What are the facilitators and barriers of donation? • What are the demographic, socioeconomic and geographic differences between those who got tested after receiving the gift relative to those who were not?	Tracking donations stratified by testing status, socioeconomics and demographics. Interviews with participants will examine the individual context of donating.
	Organizational	• What is the average donation per clinic in each arm? • Is organizational readiness associated with higher donation rates? • What are resource commitments from the public health sector, MSM organizations, and others to sustain pay-it-forward?	Administrative data will be used to track donations at the clinic level. Interviews with organizers who are able to continue the program after the 12-month RCT phase will examine facilitators and barriers of maintaining the intervention.

*Maintenance data will be collected for an additional 12 months (following the RCT) at selected clinics.

Discussion

Pay-it-forward is a novel behavioral and financial model. Our previous studies showed that it is cost-effective but the study findings have limited representativeness due to the primary involvement of MSM-led clinics but an exclusion of public clinics are a major provider for STD testing in the Chinese setting. There is also a lack of understanding the implementation process and a missed opportunity of optimizing the implementation strategy. By enhancing the community engagement components of the strategy, our trial aim to test the effectiveness of an enhanced pay-it-forward implementation strategy in comparison to the standard pay-it-forward approach and a control arm. We propose a programmatic cluster RCT to document high-quality evidence on the effectiveness of different pay-it-forward implementation strategies and to better understand the real-world practices. The proposed study will provide an evidence base on whether community-engaged pay-it-forward implementation can strengthen effectiveness and to inform future expansion of pay-it-forward intervention strategies to improve gonorrhea testing and treatment for MSM in diverse clinic settings in China.

This study has important implications for evidence-based practices for delivering important but underfunded public health services in a novel and efficient way. Hybrid implementation study designs focus not only on effectiveness but also assessing implementation outcomes. Generating evidence on the implementation itself will inform evidence-based practices and enable us to tap into the potential of normalizing or integrating the pay-it-forward interventions into existing programs to promote gonorrhea testing among a key community. Our hybrid implementation-effectiveness design has a primary focus on testing two pay-it-forward implementation strategies as well as evaluating other domains including reach, adoption, implementation, and maintenance. These will help inform what is possible in routine practices, translate researching findings into practices and scale up the strategy in gonorrhea testing service delivery and beyond.

Our trial will also have added value to the current body of literature on altruism and generosity research in changing behaviors. Our implementation evaluation will underscore the individual and organizational-level mechanisms affecting test uptake and donating behaviors in the pay-it-forward arms. We will test against the upstream reciprocity theory and measure whether generosity is associated with uptake and donating behaviors. This evidence will be relevant to interested health researchers, program implementers and public health authorities to leverage human kindness and warm glow to promote healthy behaviors, engage key stakeholders.

We anticipate that this novel financing model may also have policy implications for transitioning fee-based to subsidized health services in China and beyond. Pay-it-forward is effective in pooling small funds for essential services to support other service users in the community. Such pro-social behaviors could potentially be contagious when managed well. In addition, if proven practically more cost-effective, it is also possible to use pay-it-forward strategies to mobilize

microdonations from economically better off areas to cover essential health services in places that are underdeveloped.

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