



HIV/STI Surveillance Research Center, and
WHO Collaborating Center for HIV Surveillance

مرکز تحقیقات مراقبت اچ آی وی و عفونت های آمیزشی،
مرکز همکار سازمان جهانی بهداشت



Minimal standard format of NIH and NIMAD proposals

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Some slides borrowed from Dr. Ali Mirzazadeh presentation with permission.

تاریخچه مؤسسه

- در حقیقت احیای «مرکز ملی تحقیقات علوم پزشکی کشور» مصوب ۱۶ اسفند سال ۱۳۷۱ در شورای گسترش دانشگاه‌های علوم پزشکی کشور
- راه‌اندازی مرکز در سال ۱۳۷۷ بعد از تصویب اساسنامه آن در شورای گسترش دانشگاه‌های علوم پزشکی کشور رسید
- فعالیت جدی از سال ۱۳۷۸ با ردیف بودجه مستقل با مدیریت پروژه‌های استراتژیک، ملی و جامع در حوزه‌های گوناگون بهداشت و درمان کشور
- تعطیلی مرکز پس از ۲۰۶۹ روز فعالیت در ۲۳ آبان‌ماه سال ۱۳۸۳ با تصمیم شورای عالی اداری مبنی بر اصلاح ساختاری وزارت بهداشت (ادغام در معاونت تحقیقات و فناوری وزارت بهداشت)

کمیته‌های پژوهشی

کمیته‌های تخصصی سال ۱۴۰۰ الی ۱۴۰۳

- ۱- درمانهای نوین، فناوری و نوآوری‌های علوم پزشکی
- ۲- دارو، تجهیزات پزشکی، سلامت و امنیت غذایی
- ۳- بیماری‌های غیرواگیر، صعب‌العلاج و مزمن
- ۴- بیماری‌های نوظهور، بازپدید و واگیر
- ۵- سیاست‌گذاری و اقتصاد سلامت
- ۶- سلامت روانی و آسیب‌های اجتماعی
- ۷- سلامت الکترونیک و هوش مصنوعی
- ۸- حوادث سوانح، بلایای طبیعی و سلامت محیط‌زیست
- ۹- جوانی جمعیت، خانواده و سبک زندگی

کمیته‌های تخصصی امروز

- ۱- آسیب‌شناسی، ژنتیک و سلول‌های بنیادی (پژوهش‌های ترجمانی)
- ۲- بیماری‌های غیرواگیر
- ۳- بیماری‌های واگیر و اختلالات ایمنی
- ۴- خونشناسی و سرطان
- ۵- فناوری و نوآوری‌های علوم پزشکی
- ۶- کشف و ارزیابی داروها (غذا و دارو)
- ۷- علوم اعصاب و سلامت روان
- ۸- جوانی جمعیت و سلامت باروری

حمایت مالی از پژوهش در

مؤسسه ملی توسعه تحقیقات علوم پزشکی ایران (NIMAD)

گرنٲ اصلی (Main Grant)

گرنٲ محقق جوان (Young Researcher Grant)

گرنٲ با اعتبار محدود (Small Grant)

گرنٲ مقاله برتر (Top Paper Grant)

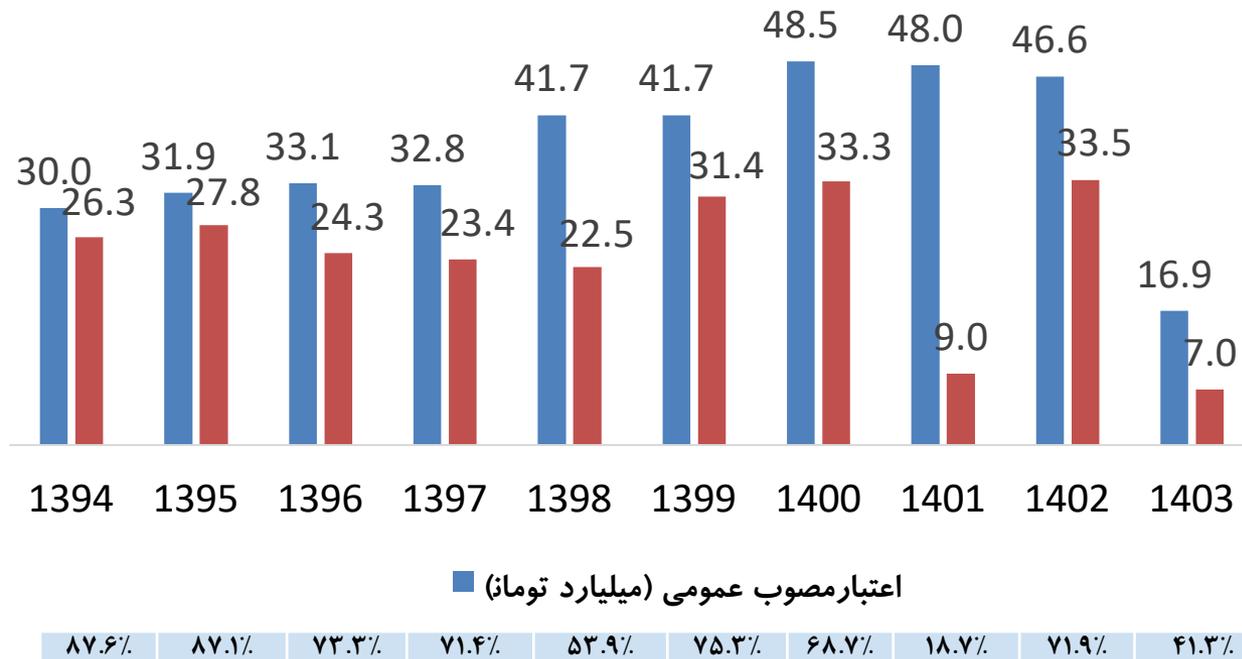
گرنٲ پژوهشگر فرهیخته (Elite Grant)

گرنٲ‌های بین‌المللی (International Grant)

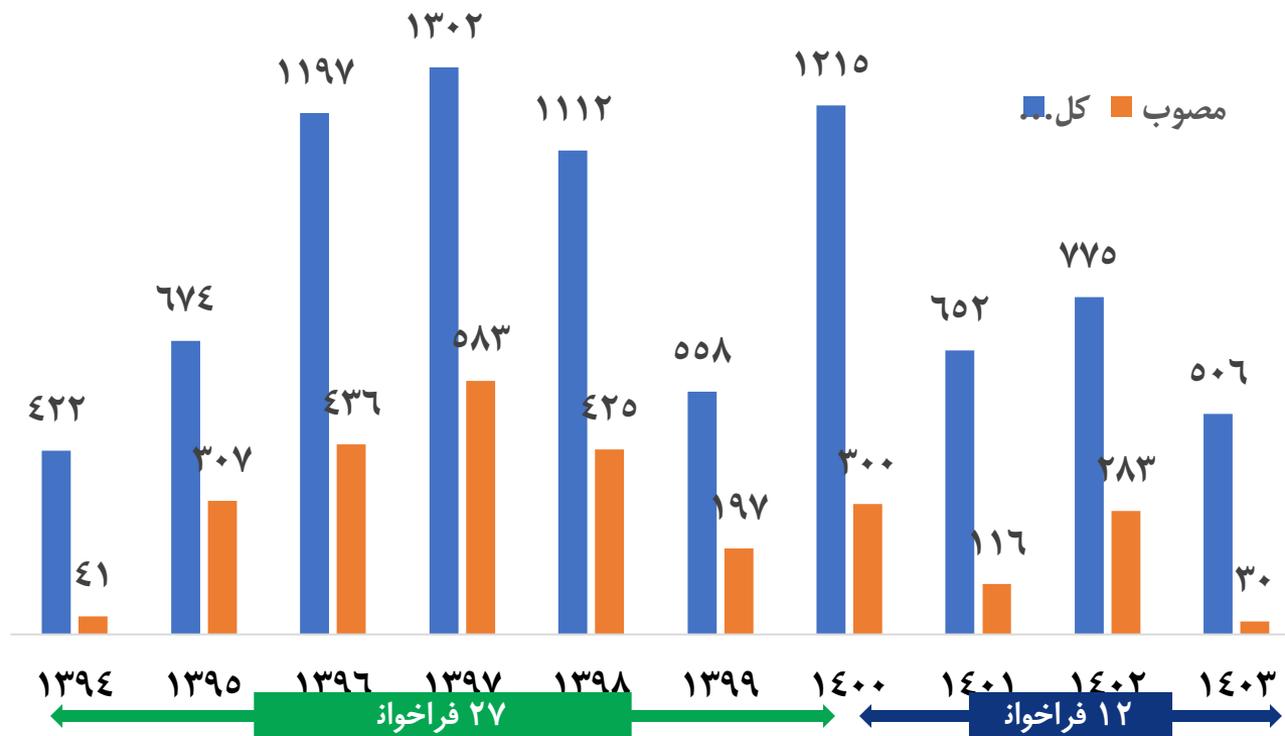
گرنٲ‌های مبتنی بر RFP

گرنٲ‌های مشترک با نهادهای مشابه (مثل بنیاد ملی علم ایران)

اعتبارات عمومی مندرج در قانون و تخصیص آذبه مؤسسه در هر سال

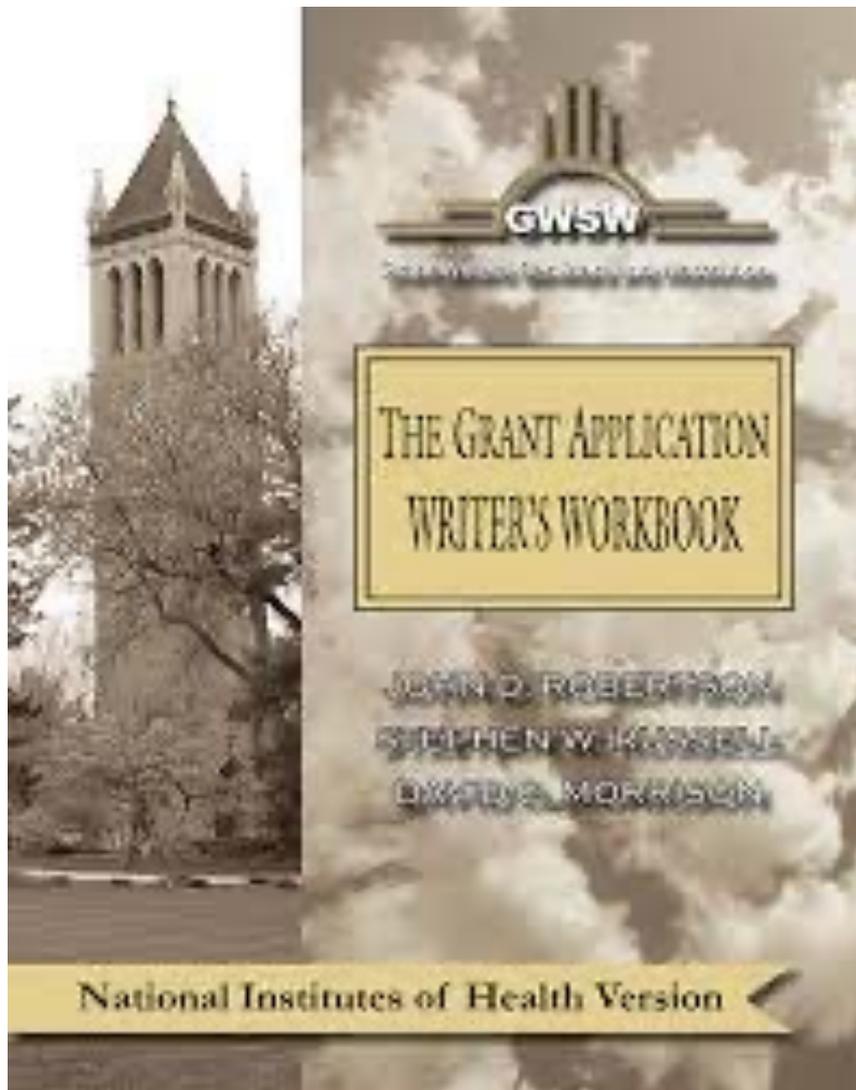


الگوی طرح‌های دریافتی و مصوب مؤسسه



Minimal standard format of NIH and NIMAD proposals

<http://nimad.ac.ir>



GREAT WORKS FOR STUDENTS AND FACULTY

THE GRANT APPLICATION
WRITER'S WORKBOOK

JOHN D. ROBERTSON
STEPHEN W. KOSSELL
DUSTY C. MORRISON

National Institutes of Health Version

BASIC ELEMENTS OF GRANT WRITING

- Define your project. ...
- Identify the right funding sources. ...
- Contact the funders. ...
- Acquire **proposal** guidelines. ...
- Know the submission deadline. ...
- Determine personnel needs. ...
- Update your timeline. ...
- **Writing your proposal**

How to find a powerful Idea for
your Application

1. Identify **a relatively under-explored niche** within the area of your broad research interest.
2. Develop a **long-term research goal** in the niche area and conceive a continuum of research that will be needed to reach that goal.
3. Conduct **a comprehensive, critical review** of the related literature.
4. List **key words** that characterize the subject you have chosen and the names of investigators who have been active in the area during the last ten years.
5. Develop **a preliminary idea** for your proposal.
6. Search **databases of already funded grants** and use what you learn to refine and improve your idea.
7. Seek **constructive criticism** of the idea from knowledgeable colleagues, further refine your idea, if necessary.
 - You can accept or reject the ideas of the experts.
 - You should be confident that the final idea is doable and completely sound and make a difference in your field when acted upon.
8. Identify **alternative/additional granting agencies** to target with your application.

NIH Grant Components Checklist

- Appendices
- Biosketches
- Budget
- Budget justification
- Cover Letter
- Equipment (if applicable)
- Enrollment Form
- Facilities and Other Resources
- Human Subjects
- Inclusion of Children
- Inclusion of Women, Minorities
- Letters of Support
- List of Appendices
- Project Narrative
- Project Summary
- Research plan (Specific Aims + Research Strategy)**
- Resource Sharing Plan
- Special Agents, Vertebrate
- Title

Research Plan

- SPECIFIC AIMS (1 PAGE)
- RESEARCH STRATEGY (6 or 12 pages)
 - Significance (4-5 pages)
 - Scientific Premise
 - Significance of the Expected Research Contributions
 - Innovation (1/2 page)
 - Approach
 - Each specific aim (same format)
 - Introductory Paragraph
 - Technical Preliminary Studies
 - Research Design
 - Expected outcomes
 - Potential problems & Alternative approaches
 - Timeline
 - Future directions (optional)

SPECIFIC AIMS Section

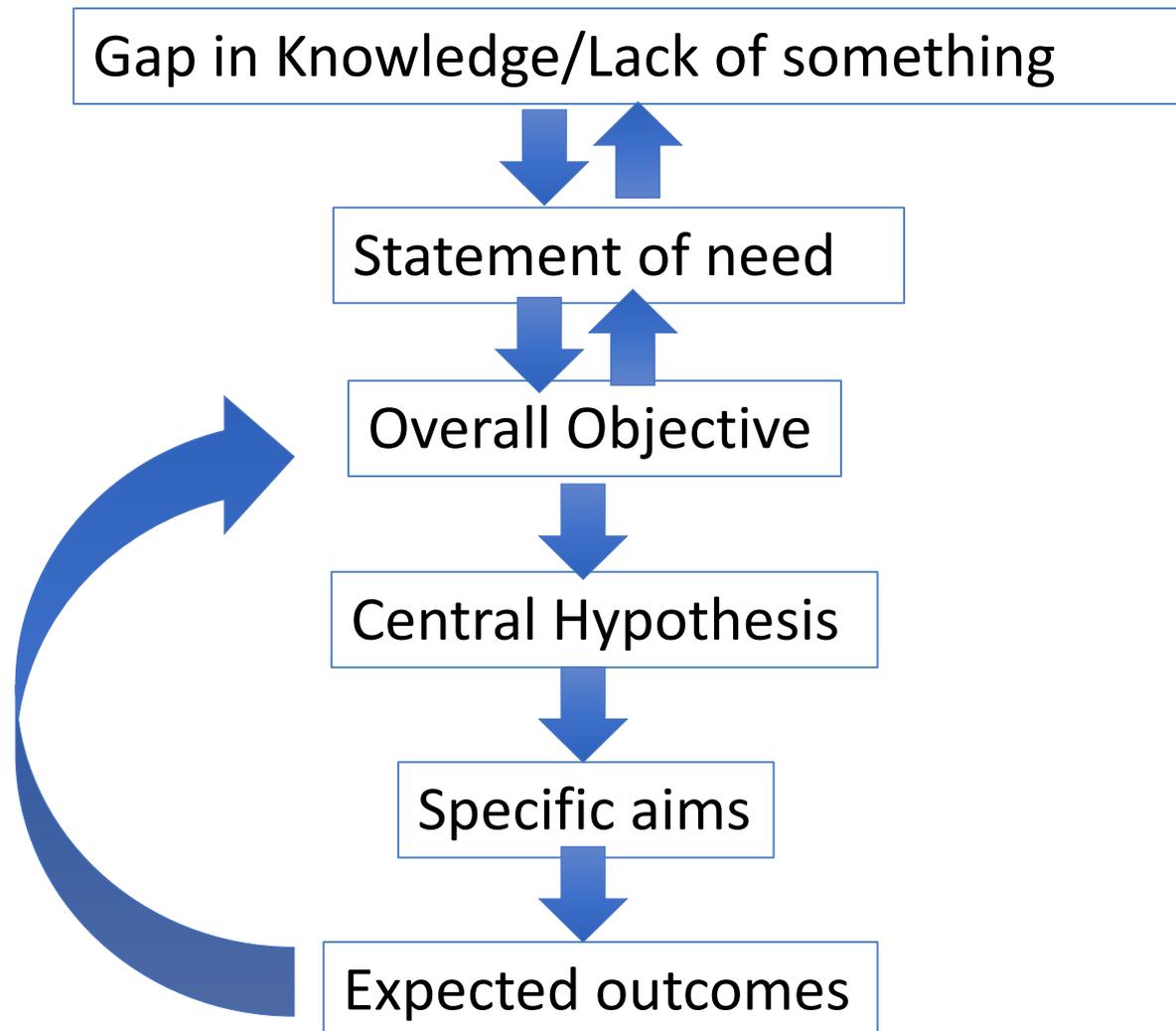
- “State concisely the **goals** of the proposed research and summarize the **expected outcome(s)**, including the **impact** that the results of the proposed research will point on the research field(s) included. List succinctly the specific objectives of the research proposed.
- e.g. to test a stated hypothesis, create a novel design, solve a specific problem, challenge an exciting paradigm or clinical practice, address a clinical barrier to progress in the field, or develop new technology. “
- you are limited to **one page**.

SPECIFIC AIMS Section

Paragraph 1	Current Knowledge Gap in Knowledge/Lack of something Statement of need and consequence of not meeting the need
Paragraph 2	Long-term Goal Overall Objective Central Hypothesis and How Formulated Rationale
Paragraph 3	<ul style="list-style-type: none">• Specific aim / working hypothesis 1• Specific aim / working hypothesis 2• Specific aim / working hypothesis 3
Paragraph 4	Expected outcomes Positive Impact

**NIH: Only ONE page
NIMAD: TWO pages**

Links and flow of Specific Aims Section



SPECIFIC AIMS Section

By the end of the first paragraph, the reviewers must **completely convinced there is a gap/lack** that is hampering progress in an NIH-relevant, or NIMAD field.

By the end of the second paragraph, the reviewers should understand 1) what **continuum of research** is that you will be following long term 2) What is the **next step** along that continuum 3) what is your **best bet** regarding how to take that next step and 4) **why** you want to do so

By the end of the third paragraph (aims), the reviewers should understand how you **objectively test** your central hypothesis by pursuing specific aims/working hypothesis

By the end of the fourth paragraph, payoff paragraph, the reviewers should understand the **expected outcomes** and the veridical advancement that your proposal would bring to your field and **positive impact** that such progress would have.

SPECIFIC AIMS Example

Title:

Peer-driven HIV self-testing for Iranian female sex workers, their clients, and partners

SPECIFIC AIMS Example

Iran has the highest burden of HIV in the Middle East (1). However, only 7.9% of HIV-infected Iranians are on lifesaving antiretroviral therapy (ART) (2). The largest gap in the continuum of HIV care is diagnosis. Of the 75,700 people in Iran estimated to be living with HIV (3), only one-third know their status (3). Sexual transmission now accounts for 42% of new diagnoses following a decade-long increasing trend (3). Female sex workers (FSW) are increasingly recognized as a key population at high risk for acquiring and transmitting infection, with prevalence as high as 8.6% in some cities (4, 5). Our prior studies found that one-third of FSW seen at facilities and two-thirds at street venues had not tested for HIV in the past year (6).

To increase HIV testing among FSW, expansion outside facilities and outreach programs is required. Self-testing offers an appealing option for highly vulnerable populations to know their HIV serostatus (7). How to most effectively reach Iranian FSW, their clients, and their other partners with self-testing remain to be tested. We propose to assess the feasibility and acceptability of “primary” distribution of oral and blood HIV self-test kits by trained FSW leaders to peers and “secondary” or onward distribution by FSW to other peers, their clients, and partners. The success of self-testing for individual and public health benefits also depends on the ability to link newly diagnosed persons to care. We therefore evaluate whether a small cash incentive (i.e., conditional cash transfer) can improve the uptake of testing, onward referral through the social network, with completion through confirmatory testing and linkage to HIV care. We have two specific aims:

SPECIFIC AIMS Example – continued

Aim 1: To develop a feasible and acceptable *primary and secondary HIV self-testing distribution program to female sex workers, their clients, and other partners*

We propose a mixed-methods study to develop a program for the distribution of HIV self-test kits, instructions on their use, and means to link persons testing positive to care. Perspectives will be gathered from an expert panel of program directors and health officials followed by focus group discussions and key informant interviews with FSW in Tehran and Isfahan. *We will assess motivations and concerns for self-testing, ways to invite peers, sexual partners, and clients to self-test, and means to ensure linkage to HIV care for those who self-test positive. The effort will produce standard guidebooks for oral fluid- and blood- based HIV self-testing and a community-friendly online instructional video for use and referrals. To pilot the approach, FSW informants will be invited to do the rapid self-test (oral and blood) following the self-test guidebooks, watching the videos, and being supervised by an HIV testing counselor. FSW feedback and counselor observations will refine the self-test guidebooks. FSW informants then will be trained and given three oral and three blood self-test kits to introduce to their peers, partners, and clients. They will be asked to encourage their peers, partners, and clients to report what they liked or did not like about the self-test, ways they have been approached, and suggestions to improve the distribution of self-tests. FSW informants also attend a post-test qualitative interview to describe the positive and negative experiences they had with peers, partners, and clients when distributing self-tests. These data will be used to refine the secondary distribution plan.*

SPECIFIC AIMS Example – continued

Aim 2: To test the uptake of HIV self-testing and linkage to care among female sex workers, their clients, and other partners recruited via social media with and without low monetary incentives

Through respondent-driven sampling approach, we will recruit and train FSW leaders (seeds) to refer 280 FSW peers in Tehran and 140 FSW in Isfahan. After verifying eligibility and providing consent, FSW will be randomly assigned 1:1 to two private groups within the local Telegram social networking application. In one arm, peer leaders will post the self-testing guides and videos for 12 weeks and offer participants four free HIV self-testing kits (choice of oral or blood) for their own use or to give to other clients, partners, or peers. The program includes avenues for reporting results, and linkage to HIV care if positive. The offer will be repeated every two weeks until accepted or declined. The second arm will additionally receive low-value monetary incentives to assess the marginal effects on reporting of results, presenting to HIV care if positive, and the uptake of peer, client, and partner use of self-tests. We will continuously monitor HIV stigma in Telegram group conversations, the uptake of HIV self-testing, self-test results disclosure, behavioral change, linkage to care, suggestions to improve distribution, and adverse events. Our null hypotheses are 1) the low value incentives will not increase self-testing uptake, onward distribution, and linkage to care; and 2) HIV self-testing uptake in both groups will be similar to the ~30% HIV testing uptake historically seen through outreach. Our study is powered to detect 15% differences from these baselines.

This exploratory R21 application builds on our community partners' access to FSW and unique, productive collaborations between academic and governmental colleagues in the USA and Iran.

Research Plan

- **SPECIFIC AIMS (1 PAGE)**
- RESEARCH STRATEGY (6 OR 12 PAGES)
 - Significance (4-5 pages)
 - Scientific Premise
 - Significance of the Expected Research Contributions
 - Innovation (1/2 page)
 - Approach
 - Each specific aim (same format)
 - Introductory Paragraph
 - Technical Preliminary Studies
 - Research Design
 - Expected outcomes
 - Potential problems & Alternative approaches
- Timeline
- Future directions (optional)

Approach

- Are the overall strategy, methodology, and analyses well-reasoned and **appropriate** to accomplish the specific aims of the project?
- Have the investigators presented strategies to ensure a **robust and unbiased approach**, as appropriate for the work proposed?
- Are **potential problems, alternative strategies**, and benchmarks for success presented?
- If the project is in the early stages of development, will the strategy **establish feasibility** and will particularly risky aspects be managed?
- Have the investigators presented adequate plans to address relevant biological variables, such as **sex**, for studies in **vertebrate animals or human subjects**?
- If the project involves clinical research, are the plans for
 - 1) **protection of human subjects** from research risks
 - 2) **inclusion of minorities** and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

Approach

- Approach
 - ✓ Each aim
 - Introduction
 - Research Design
 - Expected outcome
 - Potential problems & Alternative Strategies
 - ✓ Timeline and Benchmarks for Success
 - ✓ Future direction

Approach example 1

Table 1 - Overview of proposed research methods by aim

	Aim 1	Aim 2
Primary aim	Develop a feasible and acceptable primary and secondary HIV self-testing distribution program to female sex workers, their clients, and other partners	Test the uptake of HIV self-testing and linkage to care among female sex workers, their clients, and other partners recruited via social media with and without low monetary incentives
Data collection method	<ul style="list-style-type: none"> - Desk review, expert panel discussion - Qualitative focus group discussion - Key informant feedback - In-depth interview 	<ul style="list-style-type: none"> - Online baseline survey - Review of HIV self-testing kits pin numbers - Review of consultation records at HIV counseling and care/treatment sites - Online follow-up surveys for self-test acceptance, rejection and refusal - Exporting and review of private Telegram group conversations
Sampling methods	Maximum variation through purposive inclusion of stakeholders and policy-makers; combined street, facility, service and peer-referral recruitment of FSW	<ul style="list-style-type: none"> - RDS-based peer referrals for FSW participants - FSW participants will invite their peers, partners and clients to self-testing and completed the online follow-up forms
Study sample	To saturation	<ul style="list-style-type: none"> - FSW from Tehran and Isfahan, age 18 years and older, who had sex for money in the previous month, have an active Telegram account, and HIV-negative or unknown HIV status. - Peers, partners and clients of FSW participants
Design	Qualitative	<ul style="list-style-type: none"> - Single-blind parallel randomized controlled trial - Qualitative and quantitative
Intervention	None	<p>Group 1: Peer-leaders to post HIV-related content and invite to self-testing</p> <p>Group 2: Peer-leaders to post HIV-related content and invite to self-testing + monetary incentives for successful testing and returning results, or inviting clients, partners or peers for HIV testing.</p>
Sample size	12-20 (FSW), 10 (FSW) and 60 (peer, partners, and clients) in Tehran and 12-20 (FSW), 10 (FSW) and 60 (peer, partners, and clients) in Isfahan	<p>Group 1: 210 FSW (140 in Tehran and 70 in Isfahan)</p> <p>Group 2: 210 FSW (140 in Tehran and 70 in Isfahan)</p>
Outcomes / outputs	<ul style="list-style-type: none"> - Refined adopted guidebook for oral fluid-based and blood-based HIV self-testing + educational videos - Refined protocol to successfully approach and invite FSW to self-testing in the next phase of study 	<p>Primary: HIV self-testing uptake, returning of results, test positivity rate, linkage to care</p> <p>Secondary: a) Same outcomes among FSWs' partners, clients and peers, b) stigma on HIV prevention and testing c) reasons for rejection and refusal, d) positive and negative events after self-test offer to peers, partners or clients, e) suggestions to improve self-testing program</p>
Independent measures	----	<p>Main predictor: group assignment</p> <p>Other predictors (baseline data): Demographics, socio-economic status, sex and drug related risk behaviors, recruitment type</p>
Analysis	<ul style="list-style-type: none"> - Theme analysis on motivators and concerns for doing an oral fluid-based and blood-based HIV self-test and best ways to approach and invite other FSW to self-testing 	<ul style="list-style-type: none"> - Intent to treat analysis to assess the effect on primary and secondary outcomes - Theme analysis on HIV prevention and testing stigma - Poisson regression to assess correlates of self-testing

Approach example 1 – continued

Overall approach

We propose an exploratory study to develop, pilot test, and evaluate the distribution of HIV self-tests to FSW and their partners in two cities of Iran. We seek the optimal combination of using peer leaders, social networks, social media, and incentives to provide HIV testing to FSW with potential ways to reach their clients and partners. The approach will also monitor stigma, new HIV case detection, and linkage to care. Mixed methods are proposed, including qualitative, quantitative programmatic evaluation, and a controlled intervention.

Research team

Our team draws on decades of complementary, collective experiences with FSW and methods for intervention development and evaluation. Please note that all investigators based in Iran will be supported by Iranian funds through NIMAD. **Dr. Ali Mirzazadeh, MD, MPH, PhD (Principal Investigator)** is an assistant professor of Epidemiology and Biostatistics at the University of California in San Francisco (UCSF) and Senior Investigator at the HIV/STI Surveillance Research Center in Kerman (HIVHUB), Iran. *Dr. Mirzazadeh has a joint appointment with the HIVHUB; the HIVHUB letter secures their commitment in resources and contributed personnel.* Dr. Mirzazadeh has been on the forefront of HIV research among FSW in Iran with multiple relevant publications, many with the proposed investigators. **[REDACTED], PhD (International Project Director)** is a research specialist at UCSF who has led the implementation of projects with FSW and other key populations in Iran, and served as primary analyst for data from complex designs. **[REDACTED] (Post-doctoral Fellow)** is a physician and PhD (graduated in Aug. 2017) in Clinical Trials & Translational Research at Mount Sinai, NY. He has unique experience in designing and monitoring trials as well as causal inference analysis in infectious disease epidemiology. **[REDACTED] (PI of the Tehran site)** is a professor at Tehran University of Medical Sciences and director of the Iranian Research Center for HIV and AIDS (IRCHA), the referral center for HIV patients in Iran and the host for the largest HIV-positive support clubs including FSW groups. **[REDACTED] (Tehran Project Director)** will lead recruitment and data collection at IRCHA. **[REDACTED] (Qualitative Co-Investigator)** is an assistant professor of psychiatry with years of experience in qualitative and mixed methods on health research in marginalized groups including FSW. **[REDACTED] (PI of the Isfahan site)** is the director of the Infectious Diseases Research Center (IDRC) and an associate professor of infectious diseases at Isfahan University of Medical Sciences. **[REDACTED] (Isfahan Project Director)** is an epidemiologist with unique experience in sexual health and STI research in Iran and among FSW. She will lead recruitment and data collection at IDRC. **[REDACTED] (Co-Investigator)** is the Director of the Center for Public Health Research in the San Francisco Department of Public Health. His unit coordinates epidemiological and evaluative data on the city's "Getting to Zero" campaign – a multi-sector effort to increase testing, linkage to care, ART use, viral suppression, and PrEP uptake to achieve 0 new HIV infections by 2020. The team has collaborated in numerous formative assessments, qualitative studies, behavioral surveys, and HIV testing programs among FSW in 13 cities in Iran, including Tehran and Isfahan (5, 6, 9, 21-23) and internationally (24), [(25). We have enlisted two advisors: **[REDACTED]** from the Iranian CDC to provide technical oversight and ensure results will be used for policy change if successful, and **[REDACTED]**, *associate professor and associate director of center for Health Incentives and Behavioral Economics at the University of Pennsylvania, to apply experience in the development of HIV self-testing interventions among FSW and their partners and clients (19, 26).*

Approach example 1 - continued

Study sites and target population

The study will be done in two cities, Tehran and Isfahan, *to include geographic and cultural variation*. Based on surveys of HIV prevalence and multiple population size estimation methods, we estimate there are 6,700 (2,100 - 34,000) eligible FSW in Tehran, and 2,300 (1,150 - 5,850) eligible FSW in Isfahan (3, 10, 12).

Approach to Aim 1: To develop a feasible and acceptable primary and secondary HIV self-testing distribution program to female sex workers, their clients, and other partners

Summary. Aim 1 entails the development and pilot testing of self-testing materials and methods of self-test kit distribution. Input will be from existing guidelines and instructions, local expert input, and FSW pilot testing and feedback. Details of the steps follow.

1.1. Developing standard written guidebook. Using WHO guidelines on HIV self-testing and partner notification (27), a UNAIDS technical guide (28), and instructions for the Oraquick In-Home HIV Test (29), we will develop two FSW-oriented, user-friendly guidebooks in Farsi, one for oral fluid-based and one for blood-based HIV self-testing. *We will also develop a self-test distribution guidebook on best strategies to approach clients, partners, and peers to introduce self-testing, disclose results, access referrals to care, and mitigate conflict and harms.*

1.2. Expert panel discussion. To validate the content and assess the face-validity of drafted self-test guidebooks and *secondary-distribution guidebook*, we will present the materials to an expert panel of public health professionals, clinicians, HIV counselors, laboratorians, and representatives from FSW communities and the general population (civil society bodies enlisted to guide HIV prevention and care programs). The panel will be hosted and led by our advisory team from the HIV national program at the Ministry of Health. Using the final approved self-test guidebooks, we will develop short educational videos to show how to use the oral- and blood-based HIV self-testing kit and correctly read the result. As an example, our group produced short educational videos for use through our telegrem.me/HIVSTI group (**Fig. 2**).

1.3. Formative assessment. We will conduct a qualitative study using focus group discussions (FGD) to identify FSW motivations and concerns for doing an oral fluid- or blood- based HIV rapid self-test, the best ways to approach and invite other FSW, *partners, and clients to self-testing, and refinements to the self-test and secondary-distribution guidebooks and educational videos.*

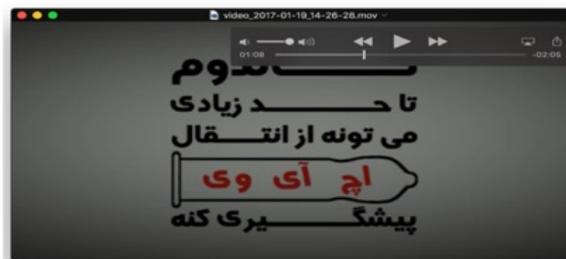


Figure 2. Short Educational video for HIV/STI risk, prevention and testing (source: telegrem.me/HIVSTI)

Approach example 1 – continued

1.3. Formative assessment. We will conduct a qualitative study using focus group discussions (FGD) to identify FSW motivations and concerns for doing an oral fluid- or blood- based HIV rapid self-test, the best ways to approach and invite other FSW, *partners, and clients to self-testing, and refinements to the self-test and secondary-distribution guidebooks and educational videos.*

Sampling. A maximum variation sampling approach will be used to recruit diverse FSW by age, *neighborhood income level where they work or live*, and their means for seeking clients (*e.g., social media apps, on streets, word of mouth and peers*). Eligible FSW from facilities, street locations, and social networks will be invited to participate in two FGD in Tehran and two in Isfahan consisting of 6-10 each (total 12-20).

Eligibility. FSW are eligible if they a) are *18 years and older*, b) sold sex for money in the past month, c) *and have a Telegram account*. We will not exclude FSW who already know they are HIV positive as they would contribute insights through experience with testing, diagnosis, and referral to care.

Procedures. Each focus group will last a maximum of 1.5 hour, be facilitated by a female research team member (*Dr. Vameghi*), and have a female note taker. After collecting basic demographic and background information, the leader will explain the study aims, risks, and benefits of participating, and conduct verbal informed consent. Questions will solicit concerns and motivators for HIV self-testing and the best strategies to approach and invite other FSW to self-testing. The leader will use an FGD guide, the HIV self-testing and self-test distribution guidebooks, and the educational videos. The FGD will be audio recorded and the leader will remind participants not to use names or identifying information. FSW participants who are a popular opinion leaders or capable of being leaders in their community, interested in educating others about HIV prevention and testing through online social networks, and experienced using Telegram will be invited as peer leaders (*also as RDS initial seeds*) for next phase of study. Participants will be reimbursed for travel, provided a meal, and given a monetary incentive (\$10).

FGD data analysis. After each FGD, the note taker and facilitator will meet to document contextual observations that may inform data analysis. Audio files will be transcribed in one week after the FGD. *All transcript texts will be analyzed using Atlas.ti version 8 (30). Dr. Vameghi will analyze the data using the codebook for the deductive codes or new codes that corresponds closely to the topic discussed in each FGD related to logistics (addressing*

concerns and understanding best ways to approach and invite other FSW, partners and clients to self-testing), self-test guidebooks and educational videos. Data will be used to fully develop study procedures to successfully recruit and retain eligible FSW for the next phase of the project (Aim 2).

Approach example 1 – continued

1.4. Piloting of survey instruments. After finalizing instructional materials, the procedures for self-testing and data collection will be pilot tested with a different set of 10 FSW (same eligibility criteria *excluding FSW who already know they are HIV positive*) at each site. FSW will be invited to do both oral and blood HIV self-tests using the written guidebooks and educational videos, individually and under the supervision of an HIV testing counselor. Participants will be asked about the clarity of guidebooks and videos and ways to improve unclear items. They will review and complete the online baseline data collection form and provide feedback for improvement on content and face-validity of these instruments. The next step will entail training for the self-test distribution to peers, clients, and partners. Pilot participants will be given three oral and three blood self-test kits to introduce to their peers, partners, and clients. FSW will be asked to invite their peers, partners, and clients (whether they accept a self-test or not) to complete an anonymous short online survey soliciting what they liked or did not like about the self-test, ways they have been approached, and suggestions to improve the distribution of self-tests. FSW themselves will be also asked to complete a post-test form and attend a post-test qualitative interview to describe the positive and negative experiences they had with peers, partners, and clients when distributing self-tests. These data will be used to refine the distribution self-test guidebook and plans. Pilot FSW participants will be provided \$10 (as mobile/data eGift or cash) for doing the oral and blood self-tests and giving feedback, \$5 for every peer or partners or clients who completed post self-test form and \$15 for completing the post self-test form for themselves and attending in the post self-test qualitative interview (lead by a trained female research team member). Data and observations from this phase will be used to improve the guidebooks and instruments (Appendix A listed the data elements for data collection Form A to E) through an iterative process and via structured discussions between co-investigators led by the PI.

Approach example 1 – continued

Approach to Aim 2: To test the uptake of HIV self-testing and linkage to care among female sex workers, their clients, and other partners recruited via social media with and without low monetary incentives

Summary. In a randomized controlled trial with concealed allocation, 280 eligible FSW in Tehran and 140 eligible FSW in Isfahan (N=420) recruited by RDS, will complete an online baseline data collection form. After a run-in period, they will be randomly assigned to two private groups on Telegram. In both groups, trained peer leaders will communicate with their assigned participants on Telegram by sending 2-3 messages, chats, posts, and educational videos on HIV risk and prevention each week for 12 weeks. Every two weeks, participants will be informed by Telegram group discussion and individual secret chat about the importance of HIV testing and that they can receive a free HIV self-testing kits for themselves and three for their partners, clients, and peers (4 total) of the modality (oral or blood) of their choice. In one randomly assigned arm, participants will additionally receive monetary incentives for successful testing and returning their results, linkage to an HIV care site, and inviting their clients, partners or peers for HIV testing. We will continuously monitor HIV stigma in the social network group conversations, the rate of HIV self-testing, client/partner/peer testing acceptance rates, frequency and reasons for self-test refusals, the preferred delivery mode of self-tests, return of results, linkage to care within 12 weeks from a positive result, and retesting within 12 weeks from a negative result.

We propose the use of Telegram because it is free, popular among Iranians (11) and FSW (31), requires only basic internet, is not censored/filtered in Iran, and does not require a name or phone number. Additional advantages are verification of receipt and reading messages, private Telegram supergroups for online FGD chat rooms, self-destructing device-to-device encrypted secret chats (i.e., not saved to a server or cloud), and the ability to send a photo of test results through secure online communication (32).

2.1. Peer leader recruitment, eligibility and training. We will recruit 34 FSW peer leaders (20 in Tehran, 14 in Isfahan) drawing from FGD and key informants, referrals from providers, facilities, street locations, and social networks. In addition to being current or former FSW, peer leaders will also be active on Telegram, popular opinion leaders or capable of being leaders in their community, and interested in educating others about HIV prevention and testing through online social networks. Leaders may be openly HIV-positive and serve as role models for positive living. Peer leaders will be trained and evaluated for inviting peers (i.e., other FSW) to the study, comfort in using Telegram, HIV counseling and testing, ability to train others on self-testing, HIV knowledge, and the procedures of the study to receive certification as test counselor and peer leader.

2.2. Trial participant recruitment. In Tehran and Isfahan, 10 peer leaders with high numbers of peers in their social network and agreeing to recruit will be selected as seeds. They will be instructed to initiate peer recruitment by inviting 3 FSW peers to participate in the self-test study. Those interested will be linked via Telegram using

e-coupons to an offline or a secure encrypted online screening form with general demographic questions and questions regarding eligibility. Each eligible consenting FSW will complete the online baseline survey and in turn be given three e-coupons to recruit other FSW peers. Both seeds and FSW participants will be incentivized \$3 (as mobile/data eGift or cash) for each successful recruit.

Approach example 1 – continued

2.3. Eligibility. FSW are eligible if they a) are age *18 years and older*, b) had sex for money in the previous month, c) have an active account in Telegram, and d) are HIV-negative or unknown status.

2.4. Screening and consenting. One coordinator at IRCHA and one at IDRC will review submitted screening forms and profiles in the Telegram accounts to ensure eligibility. *The coordinator will send a follow-up request to make sure the account is active. If doubts about eligibility remain, the coordinator may pose additional questions. After agreeing to participate, the coordinator will collect consent through an online form. We will also present the option for FSW to talk directly to coordinators by phone for consent and for additional information.*

2.5. Baseline data collection and run-in period. After consent and Telegram account verification, participants receive a thank-you message and invitation to the online baseline survey (Appendix A, Form A). Participants will be paid \$5 (*as mobile/data eGift or cash*) after completing the survey. They will then be told that we will contact them once the study is ready to begin (i.e., after the run-in period) and they will be paid another \$5 after joining their assigned private Telegram group. The run-in provides enough time to recruit at least *70 FSW in each city per wave (see below)*, to ensure that FSW use the social network, and to assess retention.

2.6. Study waves and random allocation. To avoid long waiting periods, the study will be conducted in 4 waves in Tehran and 2 in Isfahan. Each wave will consist of 70 FSW, with randomization to the private Telegram groups when RDS-recruitment of 70 FSW is complete. Randomization sequences will be generated for the Tehran and Isfahan study sites separately using a web-based free software, MinimRan (33). Peer leaders and persons who analyze the data will not be aware of group assignments.

2.7. Group activities. *Trained peer leaders* will join their groups and communicate with assigned participants on Telegram, sending 2-3 messages, chats, posts, or educational videos on HIV prevention each week for 12 weeks. Participants can connect with other group participants and peer leaders by expressing thoughts, experiences, or friendly conversations. *Every two weeks, participants are informed in Telegram group discussions and individual secret chats about the importance of HIV testing and that they can receive a free HIV self-testing kit for themselves and another three free kits for their partners, clients, and peers. We will document reasons for refusal of self-testing by FSW (Appendix A, Form C) and by their peers/partners/clients (Appendix A, Form D). We will measure participants' attention and retention using Telegram's marks (✓ and ✓✓) as proof of receipt and reading messages during the 12-week intervention period and 12-week follow-up. We will continuously monitor stigma on HIV and testing in groups conversations, responses, and reactions. Participants in the low monetary incentive arm will receive \$2 for returning their test results, and \$2 for every successful invitation of clients, partners, and peers, and \$2 for successful linkage to care. Incentives will be provided as mobile/data eGift or cash. Persons who test positive will be presented with several options for linkage to care by the study coordinators. Counseling and referral to care and other support services will be provided according to national guidelines, which include linkage and retention navigators.*

Approach example 1 – continued

2.8. Strategies to improve retention. At enrollment, preferred methods, sequence, and number of phone or email reminders will be configured with the participant at the baseline survey. To maximize retention, we will use the following: 1) obtaining and updating contact information at baseline and when groups begin, 2) providing two incentives (one at baseline and one at the beginning of the groups) and another two incentives for the arm incentivized to return result, client/partner/peer testing, and linkage to care, 3) using a Telegram platform where participants are friended by the study profile and join a private group to receive updates and provide new contact information, 4) obtaining user ID on at least two applications other than Telegram (e.g., Instagram, What's app, Viber, Badoo, Facebook), 5) making the study wait short by running four waves, 6) having one peer leader per each six participants for individual follow-up, 7) obtaining the Telegram or other social networking application ID of up to three peers for each participants upon their agreement, and 8) making “check-in” contacts with participants for special events and expressing thanks for their participation.

2.9. Study outcomes. Four primary outcomes will be assessed among the RDS-recruited FSW to determine the success of the self-test distribution programs: 1) HIV testing uptake, 2) return of results, 3) yield of new HIV diagnoses, and 4) linkage of new diagnoses to care (by self-report and by review of records at HIV counseling and care sites). *Secondary outcomes include the above for FSW partners, clients, and non-recruited peers and changes in stigma on HIV and testing in groups conversations, responses, and reactions. HIV results will be*

collected by self-report (Appendix A, Form B) or by sending a photo of the self-test kit result window through secret Telegram chat. We will also collect reasons for rejecting an offer to self-test (Appendix A, Form D), reasons for not wishing to distribute self-tests (Appendix A, Form E), suggestions to improve the program (Appendix A, Form A), and data concerning clients, partners, and non-recruited peers (Appendix A, Form C).

2.10. Data management. We will use encrypted Qualtrics Web Survey tools as our data entry system. At the baseline survey, FSW will login into the system with their unique Telegram account code. Our data manager will export de-identified coded Qualtrics data into STATA weekly for data quality control, including internal consistency checks, missing values, and errors. We will have paper-based surveys available as backup.

Approach example 1 – continued

2.11. Sample size and data analysis plan

Sample size calculation. A sample size of 420 FSW participants is based on measuring the overall proportion of HIV self-testing uptake. Assuming that the acceptance rate in one group is 30% (9), and could be increased by 15% with monetary incentive, with $\alpha=5%$ ($z=1.96$), and 80% chance to detect such a difference ($\beta=20%$), we need 180 FSW for each group. Although self-test trial of FSW in Kenya had high retention (>95%) (19), *we increase the sample size to 420 to account for 15% lost to follow-up and non-response (31). Based on FSW population sizes (10, 13), 2/3 will be from Tehran and 1/3 from Isfahan. Although not part of the sample size calculation, we expect to collect data on acceptability of self-tests in partners and clients as FSW participants will be encourage or incentivized to approach and distribute three self-tests to these groups.*

Data Analysis. Drs. Mirzazadeh and Navadeh, experienced in statistical analysis of complex behavioral data, will lead quantitative analyses. Analysis will be done in R [35] and STATA (Statacorp, TX). RDS weights (Gile's Sequential Sampler estimator) will be calculated using the RDS package in R (35) and applied to adjust point estimates, confidence intervals, and hypothesis testing within the peer referral data. Comparison of the study arms in Aim 2 will be intent-to-treat, testing the null hypothesis that the monetary incentive does not increase the uptake up testing in FSW. Analysis will also test the null hypotheses that testing will be similar to the uptake measured in outreach surveys. RDS-weighted Poisson regression models will characterize correlates of testing uptake by baseline characteristics (Appendix A, Form A). Dr. Vameghi will lead the content analysis on the qualitative analysis, using the exported Telegram group conversions and posts. She will identify themes related to HIV prevention, barriers and facilitators to testing, HIV knowledge, sex work, social norms, FSW culture, and stigma; monitor changes in themes over time; and relate themes to outcomes of the distribution programs.

2.12. Potential problems and alternative strategies considered. To avoid failing to achieve recruitment goals we will closely monitor recruitment, hold frequent meetings to discuss recruitment strategies, and adapt recruitment strategies if we fall >20% off milestones by study midpoint. For example, we can re-engage formative phase participants for referrals, add more seeds, increase incentives, enroll FSW at hotspots, and include clients of vulnerable women centers. We include multiple strategies to minimize drop-out such as collecting multiple contact information and the use of social media to maintain contact with participants.

Research Plan

- **SPECIFIC AIMS (1 PAGE)**
- RESEARCH STRATEGY (6 OR 12 PAGES)
 - Significance (4-5 pages)
 - Scientific Premise
 - Significance of the Expected Research Contributions
 - Innovation (1/2 page)
 - Approach
 - Each specific aim (same format)
 - Introductory Paragraph
 - Technical Preliminary Studies
 - Research Design
 - Expected outcomes
 - Potential problems & Alternative approaches
 - Timeline
 - Future directions (optional)

Significance and Innovation

- **Significance:** the impact something will have on some other things.
- **Innovation:** a new and substantively different way of considering/addressing something, which opens new horizons.

Significance

- Does the project address an **important problem** or a **critical barrier** to progress in the field?
- Is there a **strong scientific premise** for the project?
- If the aims of the project are achieved, how will **scientific knowledge, technical capability, and/or clinical practice be improved?**
- How will successful completion of the aims **change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?**

Significance section components

- Scientific Premise
 - Overall scientific premise
 - Scientific premise for Aim 1
 - Scientific premise for Aim 2
 - Scientific premise for Aim 3
- Significance of the Expected Research Contribution

4-5 Pages

Significance section formulation

- Overall and for each aim:
 - Discuss strength and weaknesses of relevant literature
 - Use preliminary data to support of the scientific premise
- Significance of the Expected Research Contribution
 - Clearly state the research contribution that you expect to make / positive impact on advancing knowledge or improving practice

4-5 Pages

Significance example 1

There is a high undiagnosed burden of HIV in Iran. As of 2015, 28,663 cases of HIV had been reported in Iran (3). UNAIDS models suggest there are 75,700 people living with HIV (PLHIV) (3), with an increasing proportion among women (2). A continuum of care analysis estimated only 7.9% of HIV-infected Iranians are on antiretroviral therapy (ART) (2, 8) (**Fig. 1**). The primary loss in the continuum is the first step: 70% of Iranian PLHIV are not aware of their HIV status. Massive scale-up of HIV testing for persons at risk for HIV is urgently needed.

There is a low level of HIV testing among female sex workers (FSW) in Iran. FSW are an underserved population at high risk for HIV in Iran, the Middle East, and worldwide. In 2010, we surveyed 1,005 FSW at vulnerable women facilities and outreach sites in 14 cities of Iran. HIV prevalence was 4.5% (4) and only 27.5% of FSW had tested for HIV in the previous year and received their results (9). To increase serostatus awareness, HIV rapid testing was introduced at facilities for vulnerable women and clinics used by FSW in 2012. By 2015, there was an improvement to 75.1% of FSW testing in the last year if they were clients of these facilities. However, among FSW recruited outside of facilities (i.e., by outreach), only 34.0% had tested in the previous year (6). Meanwhile, there are no data on HIV prevalence and testing among the clients and other sexual partners of FSW in Iran. Innovative HIV testing approaches are needed to reach these populations.

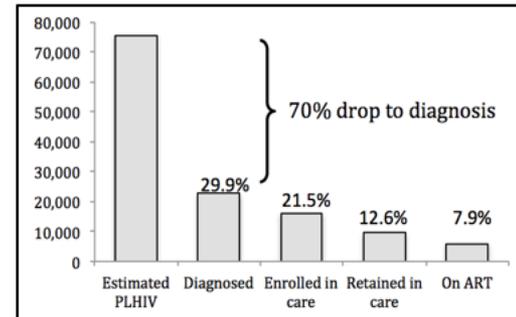


Figure 1. The continuum of HIV care and treatment in Iran, 2015

Current HIV testing programs do not reach the majority of FSW due to the stigmatized and illegal nature of sex outside of marriage in Iran. The Iranian HIV program provides testing to FSW via non-governmental community-based organizations (CBO). To the present, 39 CBO have reached ~9,000 FSW with on-site or peer outreach HIV/STI services (unpublished, CDC-Iran). Our estimate of the number of FSW in Iran is 228,700 (153,500 - 294,300) indicating the vast majority is not reached (10). Meanwhile, clients are increasingly seeking FSW through mobile social apps such as Telegram (the most popular free, uncensored/filtered messaging app used by ~20 million Iranians (11)). FSW are therefore becoming less accessible on streets through outreach (12). The current Iranian testing guidelines also require going to an HIV testing clinic, even when first encountered through outreach. This policy presents a substantial structural barrier for groups engaging in stigmatized and illegal behaviors. Given the status of sex outside of marriage in our society, this barrier may be greater for FSW than for drug users in Iran (13). Stigma carries over to the clients and other sexual partners of FSW. This scenario is particularly worrisome as HIV surveillance data in Iran indicate a shift in the epidemic away from injection drug use and towards unsafe sex in heterosexual populations, particularly women (3).

Significance example 1 – continued

HIV self-testing presents a promising avenue for FSW and their partners to know their serostatus in highly stigmatized contexts. Self-testing has high potential but unproven success in increasing case detection and linkage to care for HIV-positive persons in marginalized populations. For example, the uptake of self-testing was 51.1% among FSW in China (14); however, data on linkage to care after self-testing are scarce. “Intent to link” ranged from 81.6% to 100%, and two studies were able to demonstrate four of four new infections were linked to care within two months (15). Different dissemination modes for self-testing have been studied (16), including through CBOs, clinics, pharmacies, peer outreach, peer-leaders, mail, or vending machines. One study on preferences of MSM in Los Angeles found 67% requested self-test kits via mail, 30% by online voucher redeemed at pharmacies, and 3% by vending machine (17). Peers may have particular appeal for distributing self-test kits among FSW and to their clients, potentially exponentially expanding the number of persons tested and increasing the HIV case detection yield (18). *A study in Kenya including 102 FSW from antenatal and post-partum care, found 75% and 80%, respectively, successfully gave self-tests to partners and clients (19).* However, to our knowledge, no study has developed and evaluated a peer-based self-testing program for FSW in highly sensitive settings such as Iran.

Expected research contributions. If the aims of the project are achieved, we will have gained practical knowledge on how to disseminate self-testing kits as means to increase HIV status awareness among members of the most highly stigmatized populations. Results provide implementation science evidence on how to add self-testing to the available HIV epidemic control armaments. As our aims address the primary hurdle in the HIV care continuum for Iran and many countries, our study stands to greatly increase ART use, benefitting PLHIV and preventing onward transmission through viral suppression (20).

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Innovation

- Does the application **challenge and seek to shift** current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions?
- Are the concepts, approaches or methodologies, instrumentation, or interventions **novel to one field** of research or **novel in a broad sense**?
- Is a **refinement, improvement, or new application** of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Innovation formulation

- Use literature to diplomatically frame the **status quo**
- **Why** what you propose represents – in your opinion - a substantive departure from the status quo.
- Describe **how** what you are promising will break down barriers that have prevented others from reaching the new horizons that you envision.

1/2 Pages

Innovation example 1

Our exploratory R21 application addresses the most necessary next steps in bringing the marginalized, at-risk networks of FSW into HIV prevention and care. We seek the best ways to combine social networks, social media applications, self-testing technology, RDS peer referral, and incentives to reach previously untested populations. Moreover, few efforts have been able to recruit the clients and partners of FSW. If successful, the program can be quickly brought to scale and substantially improve HIV case finding in a concentrated epidemic in a region of the world with severe barriers to prevention and care for women and other marginalized populations. The approach can also serve as a platform for the delivery of other HIV prevention interventions with proven efficacy. For example, the combination of social media, peer-referral, and self-testing can also recruit high-risk HIV-negative persons into pre-exposure prophylaxis (PrEP) programs.

Create an informative title

- The importance of title (should be eye catching).
- Appreciate that you have up to 200 characters (including punctuation) and space for your title (NIMAD proposals 100 characters)
- Appreciate that your title should emphasize the payoff from proposed research
- Steps to select a suitable title:
 - ✓ Title should include the payoff of the research not the process you will yield that product.
 - ✓ Use the overall objective from the specific aims section and the “contribution” sentence from the first part of the significance subsection of the research strategy section to inform writing of your title.
 - ✓ Make a list of words and standard abbreviations that are candidates for use in your title.
 - ✓ Create a large number of titles, using combinations and permutations of the words and abbreviations you have selected. Select what you think are the top 10 from the list.
 - ✓ Ask colleagues and layperson to select the most informative, interesting title.
 - ✓ Refine the final candidate(s) until it is possible to settle on one of them as your title.

Review Criteria and Impact Assessment

NIH Grants – Evaluation Criteria

- Review of applications based on NIH standard review criteria
 - Significance
 - Innovation
 - Approach
 - Investigators
 - Environment

NIH Grants Evaluation Criteria

- **Significance:** Does the study address an important problem? How will scientific knowledge and practice be advanced?
- **Innovation:** Are there novel concepts or approaches? Are the aims original and innovative?
- **Approach:** Are design and methods well-developed and appropriate? Are problem areas addressed?
- **Investigator:** Is the investigator appropriately trained?
- **Environment:** Does the scientific environment contribute to the probability of success? Are there unique features of the scientific environment?

Overall Impact score

- Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a **sustained, powerful influence on the research field(s)** involved, in consideration of the review criteria, and additional review criteria (as applicable for the project proposed).

What Determines Which Grants Are Funded?

- Impact Score—Scientific merit
- Program considerations
- Availability of funds

The ABCs of Hepatitis

Did you know there are different kinds of hepatitis? Learn about the similarities and differences among Hepatitis A through E.

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