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Development Innovations Venture
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Second Quarter Milestone Update
May 15, 2011

“Proteinuria Self-Test For Early Detection of Pre-Eclampsia”

Over the past few months, Jhpiego has been working both with JHU-CBID engineers and the USAID/Nepal Mission and MCHIP to prepare for the pilot studies in Nepal, and optimize the prototype for those studies. Below is a summary of both activities.

I. Pilot Study Design for Proteinuria Self-Test at Community Level

Jhpiego is currently working with Nepal Family Health Project and USAID/Nepal and MCHIP to address remaining questions and prepare for field-based testing, which is planned to first take place at a busy ANC clinic (Koshi Zonal Hospital) with pregnant women and trained health care workers. Originally planned for early 2011, this is now likely to take place in June or July, but the research protocols and IRB submissions have been approved, and this has allowed us to make a significant improvement to the prototype design itself, and ensure that the Koshi Zonal Hospital has implemented the utilization of the standard proteinuria POC diagnostic, so that our pilot has an appropriate basis for comparison.

The community-based pilot study, the subsequent step to the ANC clinic, and “Objective 2” under this DIV grant, has been preliminarily designed but not yet finalized nor have we submitted the protocol for ethical approval (Johns Hopkins University IRB and Nepal Health Research Council), as we anticipate the results and implementation of this precursor study (ANC clinic) to yield important information which may have implications on the final protocol for the community-based pilot study. Furthermore, if there are yet additional revisions to the prototype, those changes may also have slight modifications for the study design at the community level. **We expect to submit the final design for ethical approval by 31 August, and that this will not affect our overall timeline for this award.**

The current design for the community-based pilot study will take place in two VDCs in a terai district, where PE/E prevalence is higher. Following ethical approval from NHRC and the JHU IRB, Jhpiego will supply the Female Community Health Volunteers (FCHVs) with the proteinuria self-test so they can educate pregnant women in their ward in their second and third trimesters and support them to use the test. Specifically Jhpiego and its partners in country (Nepal Family Health Project and MCHIP) seek to determine FCHVs’ and pregnant womens’ ability to use the new test and correctly identify the color change in the

presence of elevated proteinuria. Healthcare providers will also educate pregnant women using BCC materials during ANC visits and have access to the standard POC proteinuria test to improve the quality of ANC, as well as be prepared to receive and manage referrals for positive test results from the community. During the study period MCHIP will strengthen the referral system and quality of case management of the referred cases. This small pilot is designed to initially explore the community-based issues around distribution, education, test use and referral to help shape subsequent effectiveness studies and demonstration projects, if and when the technology gets registered.

Specifically, the pilot study design includes the following critical steps which still need to be completed:

- Ongoing engagement of local stakeholders and partners in study design, protocol, and implementation
- Finalize protocol with objectives, study procedures, consent forms, and data collection tools
- Submit and receive ethical and research approval from Johns Hopkins IRB, Nepal Health Research Council, and USAID
- Produce enough field-ready prototypes for pilot study
- Develop IEC (Information, Education, Communication) materials for FCHVs
- Conduct orientation for district health team, healthcare providers, and FCHVs
- Implement and Monitor Pilot study
- Analyze and finalize report for results dissemination

II. Prototype Development

The Jhpiego/JHU-CBID engineering team has been conducting rigorous laboratory assessments and improvements to the current technology, resulting in some modifications to the platform to deliver the reagent, and a minor adjustment to the reagent itself. The platform has shifted from a felt tip marker form to a “roller pen” modeled after a white-out pen, in which the user can squeeze the pen to release the reagent. This a) prevents the problem of the felt tip drying out and b) improves the consistency of reagent reaching the paper. Other robustness/resilience studies of the reagent and platform have been very promising, and we feel confident in this prototype generation as being “field-ready.”

We also made a change to the reagent so that it changes color, with a more “obvious” color change, at a lower threshold, now at 0.3g/l. As a screening test, this threshold is indicative of elevated protein in the urine, and will be a basis of referral for additional and confirmatory tests for PE/E.

Proteinuria Self-Test For Early Detection of Pre-Eclampsia
Milestone 3: Final Report
June 4, 2012

Introduction

To reduce maternal mortality related to pre-eclampsia/eclampsia, a simple, low cost, non-invasive diagnostic test is needed to be widely available in low resource and often rural settings of developing countries. In these settings, many women are often not tested during pregnancy for elevated proteinuria, because they are not able to make it to a health facility. Our new screening test for proteinuria was designed to be prepared by the existing community health agent or volunteer; the health volunteer handles the pen and prepares the test paper and distributes the test paper to the pregnant woman, who then uses the self-test at home.

Over the past year, with support from USAID, Jhpiego has been able to complete proteinuria self-test pen prototypes and initial pilot testing of the device in southern Nepal. The Jhpiego Innovations unit has worked with JHU-CBID engineers, the USAID/Nepal Mission and MCHIP to optimize the prototype for the proteinuria self-test pen and to prepare for and conduct the pilot studies in Nepal. Both objectives of the DIV award were met and a brief summary is provided below. Attached please find the Final Report on the pilot test which details the results.

Results

Objective 1: Utilize data from the laboratory-based validation study and the ANC clinic study in Nepal to make improvements to the proteinuria self-test reagent and to the marker pen design for refined prototype that is appropriate and practical for a low-resource setting
Status: completed

As reported previously, the Jhpiego/CBID engineering team made improvements to the proteinuria self-test pen design, including both the reagent and the delivery system. The platform was used for the field test that was conducted in Nepal in November 2011 where unexpected results with the delivery system were noted. Based on these results and further bench testing completed in Baltimore in January 2012, additional changes to the reagent and the delivery system have been made to conclude in further improvements. The team is expecting to move forward with production of a small number of pens using funds donated by a private foundation.

Objective 2: Conduct a small scale pilot study in a rural district in Southern Nepal to assess acceptability and feasibility of utilizing this proteinuria self-test at the community level
Status: completed

A field study was conducted in November 2011 and was stopped early due to unexpected results. During the field investigations, a high rate of positives on the screening test was

observed. One factor was the interpretation of a partial color change (in the form of crescent-moon edge or spots) as positive. While field investigations confirmed that the screening self-test is over-screening, as compared to dipstick test results at the Mangalbare Primary Health Facility, it was also confirmed that Female Community Health Volunteers (FCHVs) and pregnant women (PW) are interpreting correctly as per instructions as measured by observer who concurred with PW and FCHV interpretations. Additionally, storage is being done as instructed. However, yellow with green crescent-moon edge is noticed on previously prepared strips but not freshly prepared ones; the oral instructions were that any color other than yellow was to be considered positive. The visual flash cards used for training and education showed uniform colors but crescent-moons or spots in the circle of reagent had not been observed in the prior phase of the study. Finally, it was confirmed that strips do not change color with increasing time duration, and PW read the result within 3 minutes.

Following the end of the study, we conducted visits to pregnant women/participants enrolled in order to inform all participants of study change and retrieve previously-distributed strips. We encouraged women to attend regular, routine antenatal care. Appropriate actions regarding notification to partners and IRBs were also conducted and reported to USAID.

Though numerous indicators based on qualitative interviews with pregnant women and FCHVs were not able to be collected due to the early cessation of the field study, invaluable information was still gained and a large percent of the indicators were collected. Please see Table 1 on page 4 for full list of indicators and results by objective.

Key lessons learned

The following points are key lessons learned from the team as a result of the prototype development and the field tests.

1. When acquiring specifications from a manufacturer for an off the shelf part, be sure to always validate those specifications with another method other than direct communication (i.e. either spec sheets and/or material testing).
2. Training and education is critical to successfully administering the test. Verification needs to be done to make sure that after the initial training, users still use the technology as originally communicated and intended.
3. Understanding user interpretation is critical to the success of our threshold determination. The instructions for use surrounding how to interpret the color change is very important in its wording. It's very easy for the instruction to cause a completely different interpretation result.
4. There will be differences between a clinic-based study facilitated by prepared study staff and a community-based study with much less control. Try to minimize this as much as possible through training and preparation.
5. Using pictorial tools for *data recording (M&E)* requires iterative pre-testing to ensure the people filling out the pictorial forms understand the questions and how to record responses.

6. Verification and validation testing needs to be done to confirm that the reagent does not undergo adverse reactions with respect to all complimentary parts and materials in the kit.
7. The results from step 3 showed that there is a clear acceptance in our focus group study with regards to the concept of using a pen to make a strip and women's willingness to use the test. All the other positive feedback that was found in step 3 fundamentally assures and confirms that we are pursuing a very usable and likable method to screen for these conditions.

Conclusion

The experience afforded by the Development Innovations Venture award grant is extremely important in the process of moving forward with the proteinuria self-test pen platform. Thanks to new knowledge gained and lessons learned from the prototypes developed and the field test supported with this award, the team is now rapidly moving forward with the next generation prototype and working with commercial partners to make a small number of prototypes while also moving forward with preparing for the next round of field testing.

Table 1. Indicators and results by objective

Indicators	Result
<i>1. Utilize data from the laboratory-based validation study and the ANC clinic study in Nepal to make improvements to the proteinuria self-test reagent and to the marker pen design for refined prototype that is appropriate and practical for a low-resource setting</i>	
Engineering recommendations for reagent composition and marker pen design	completed
Calculations for number of tests per pen, number of tests to be assembled at screening site and estimates of test effectiveness in environmental conditions	completed
Prototype of proteinuria test exist, incorporating recommendations from lab study	completed
Number of prototypes of proteinuria tests manufactured and ready for use in field-based pilot	40 pens were manufactured in-house
<i>2. Conduct a small scale pilot study in a rural district in Southern Nepal to assess acceptability and feasibility of utilizing this proteinuria self-test at the community level</i>	
Number of stakeholders who are engaged and encourage women to use the self-test	40 (HF staff)
Number and type of behavior change materials and radio spots developed and used	2 sets (one for FCHVs and one for PW)
Number and type of FCHVs who are trained in use of the self-test	27
Existence of referral guidelines and cards for women with positive self-test	completed
Number and percent of PW who performed the self-test and have their results recorded by a FCHV	388
Number and percent of PW with a positive self-test	262 (68%)
Number and percent of PW with a positive self-test who are referred to a health clinic	262 (100%)
Number and percent of PW with a positive self-test who are referred who arrive at the clinic	152 (58%)
Number of FGD and interviews held with PW or FCHVs	Not completed due to the unexpected results.
Number and percent of PW who would use the test again	
Number and percent of PW understood how to use the test	
Number and percent of PW with positive tests who correctly interpreted the test result	
Number and percent of FCHVs who believe they can correctly instruct and support women to use the self-test	
Qualitative summary of issues distributing the test and issues with referrals	
Qualitative summary of social, religious and cultural norms	
Qualitative summary of influences that would facilitate women's use of the self-test	
Number and percent of women who prefer to be reminded to use the self-test	
Number and percent of PW who perceive barriers to test use	
Number and percent of PW who perceive benefits to test use	
Number and percent of PW who believe any pregnant woman is susceptible to PE/E	
Number and percent of PW who like aspects of the test, by aspect	
Number and percent of PW who dislike aspects of the test, by aspect	
Number and percent of PW who recommend changes, by type of change	