

Strategic Evaluation of TB CARE SMS System in Cambodia

by

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Thesis submitted in partial fulfillment of  
the requirements for the degree  
Master of Science in the Duke Global Health Institute  
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ABSTRACT

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# **Abstract**

## **Background**

This retrospective study examined the impact of a USAID-funded and FHI 360-implemented pilot project entitled “TB CARE SMS System” in Cambodia. The primary objective of this study was to compare the “sputum submission to treatment delay” (SSTD) before and after the TB Care SMS System was initiated in December 2011 in the health clinics in Cambodia that correspond to the Kampong Cham Referral Hospital (RH) and Chamkar Leu Referral Hospital. The secondary objective was to capture the impact and limitations of the pilot TB CARE SMS System from the perspective of the healthcare workers and Community Directly Observed Therapy (CDOT) Program workers who use it on a daily basis.

## **Methods**

A time-series regression analysis was used to measure the effect of the pilot project on SSTD. Measuring the secondary objective was conducted with in-person interviews with health center and CDOT workers who have used the SMS system, at 5 health centers (HCs) that use either the Chamkar Leu RH or Kampong Cham RH lab.

## **Results**

With a total of 85 patients used in primary analysis, it appears that the pilot TB Care SMS System did not have the expected impact on the period that the sputum was

sent to the lab for testing until the time the patient started treatment (SSTD).. However, measuring the date from when the sputum labs were sent to when the lab results were received by the HCs, we did not find a statistically significant reduction in delay either, though the trend was in the expected direction, with an apparent reduction of 1.70 days. In the secondary objective, all of both HC staff and CDOT workers believed the new SMS system was better than the original paper-based system.

### **Conclusions**

The results show that the TB CARE SMS System demonstrated no statistically significant impact on SSTD, in the limited 6 month timeframe. However, it is an overall success from the perception of the users.

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## **List of Abbreviations**

CENAT – National TB Hospital (of Cambodia)

CDOT – Community, Directly-Observed Therapy

DST – drug susceptibility test

DR-TB – drug-resistant TB

eHealth – electronic Health

HC – health center

MDR-TB – multi-drug resistant TB

mHealth- Mobile Health

NGO – non-governmental organization

NTP – National TB Program (of Cambodia)

OD – operational district (in Cambodia)

RH – referral hospital

SMS – Short Message Service

SSM – sputum smear microscopy

SSTD – sputum submission to treatment delay

USAID – United States Agency for International Development

TB – tuberculosis

WHO – World Health Organization

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# 1. Introduction

Infesting one-third of the world's population, tuberculosis (TB) is one of the most dangerous infectious diseases in the world. Caused by a bacterium of the genus *Mycobacterium*, TB derives from *M tuberculosis* and *M bovis*. *M tuberculosis* is the form responsible for the human form of the disease, whereas *M bovis* usually infects cows, and as a result humans are infected through their milk (Waldron, 2009). The main transmission route for *M tuberculosis* is from bacteria-containing droplets released into the air when the person with active pulmonary TB coughs or talks. Such droplets can easily remain there for hours. Once these droplets are inhaled by others, what follows depends largely on the individual's unique ability to create an effective cell-mediated immune reaction to the bacteria (Waldron, 2009). Particularly those at risk are the people whose immune systems are already compromised and weakened, like the elderly, malnourished, and those without an adequate protein intake. Historically, this is why TB has been known to be a disease associated with poverty, malnutrition, and overcrowding (Waldron, 2009). In more recent times there has been a resurgence of the disease in patients coinfecting with human immunodeficiency virus (HIV). This combination of TB-HIV is most often a lethal duo, creating a better environment for the bacteria to spread faster and more efficiently throughout the body with little warning.

About 5-10% of the people infected with the TB bacilli will develop active TB at some point in their lives ("Global Tuberculosis Control: WHO Report 2011", 2011). The impact of TB is felt more in select regions of the world. In 2010, there were 8.8 million

newly- diagnosed cases, with the Western Pacific region accounting for 21% of these new cases (“Global Tuberculosis Control: WHO Report 2011”, 2011). This region has one of the world’s highest incidence rates (110 per 100,000 population), with a total (estimated) 1.9 million cases. Four countries (Cambodia, China, the Philippines, and Vietnam) account for 93% of the total estimated incident cases in the region (“Global Tuberculosis Control: WHO Report 2011”, 2011; van Maaren, 2010). In particular, Cambodia has some of the highest TB incidence and prevalence rates in the world. Cambodia has a TB incidence rate of 437 per 100,000 and a prevalence rate of 660 per 100,000, both of which are much higher than its WHO region (“WHO Tuberculosis Profile: Cambodia”, 2010).

## 2. Literature Review

### 2.1 TB Overview

As the world's second largest leading cause of death from infectious disease, tuberculosis (TB) kills and infects millions of people. In 2010 there were 8.8 million newly- diagnosed TB cases, and approximately 1.1 million people died from TB ("Global Tuberculosis Control: WHO Report 2011", 2011). Cambodia ranks among the top 22 countries most burdened by TB, with an alarming mortality rate of 61 deaths per 100,000 people in 2010 alone ("WHO TB Fact Sheet 2010", 2010).

Diagnosis and treatment of TB each have their own set of obstacles and challenges. While the diagnosis of pulmonary TB can be done in a variety of different ways, the cheapest and fastest method is sputum smear microscopy (SSM) ("TB-Diagnosis", n.d.). Once the sputum specimen has been collected and delivered to a qualified laboratory, SSM can be performed in minutes to detect TB through microbiologic examination of a sputum sample. It is used as the front line method for TB diagnosis worldwide despite the fact that it is only about 50% sensitive. The method is not able to distinguish between TB and other mycobacterial infections, In addition to its use for establishing pulmonary TB disease, SSM is also commonly used during treatment to monitor treatment efficacy. SSM is typically only offered in health clinics, where the proper acid-fast staining and microscopy can be performed ("TB-Diagnosis", n.d.). Therefore, diagnosis of pulmonary TB generally requires access to a health care

facility, which can prove to be one of the main barriers to diagnosis in medically-underserved populations.

A new desktop machine called the GeneXpert could be a new potential game-changer in TB diagnosis (Evans 2011). The new GeneXpert makes up for what SSM lacks in two key areas: 1) it is more sensitive than SSM, not prone to so many false-negatives and 2) it can test for drug-resistance (Evans 2011). With the new preferential pricing scheme implemented by the WHO in December 2010, the GeneXpert has become more affordable and accessible to low income countries, like Cambodia (“WHO Monitoring of Xpert MTB/RIF Roll-Out”). Although the new GeneXpert is promising to TB diagnosis, creating rapid TB testing without the necessity of specialized labs and technicians, ultimately the impact of this new technology in resource-limited environments remains untested and relatively scarce (Evans 2011).

Five essential anti-tuberculosis agents are designated as “first line” treatment for standard anti-TB treatment. These include isoniazid (H), rifampin (R), pyrazinamide (Z), ethambutol (E), and streptomycin (S) (“WHO | Pursue High-quality DOTS Expansion and Enhancement”, n.d.). A combination of HRZE is the recommended first-line regimen for the first 2 months, followed by HR for an additional 4 months. If this treatment is not taken for a full six months, there is a significant chance that the person will not be cured, or have a relapse of disease. Because the multi-drug treatment requires such a long course, there is a tendency for patients to stop taking the medicines once they begin to feel better. Such patients who stop treatment early fall into the

category of defaulters or “previously treated cases” (“WHO | Pursue High-quality DOTS Expansion and Enhancement”, p.28, n.d.). Throughout the world, a common strategy for TB treatment has been short-course directly-observed treatment (DOTS). In addition to several other political, diagnostic, supply and evaluation components, DOTS involves direct delivery and observation of medication intake from a healthcare professional for the first few weeks of treatment (“WHO | Pursue High-quality DOTS Expansion and Enhancement”, n.d.).

## **2.2 TB in Cambodia**

Approximately 60% of deaths in Cambodia are due to communicable, maternal, perinatal, and nutritional conditions. Non-communicable diseases account for 30% of all deaths, and injuries for 10% (“WHO Department of Health and Measurement Information”, 2009). Within the communicable diseases category are respiratory infections, diarrheal diseases, TB and HIV/AIDS (“WHO Department of Health and Measurement Information”, 2009). As one of the largest public health problems in Cambodia, TB remains an imminent source of concern. Despite implementation of nationwide DOTS coverage by the National TB Program (NTP) in 1998, Cambodia still has a large smear-positive test rate of 220 per 100,000 people (Sar et al. 2009). Sar et al. (2009) attributes two main reasons to the explosive TB increase: 1) an increase in multi-drug resistant TB (MDR-TB) bacilli from inadequate treatment; and 2) an increase in susceptible individuals due to high AIDS rates.

Drug-resistant TB (DR-TB) is becoming a huge problem worldwide, and Cambodia is no exception. Extremely high levels of DR-TB plague the National TB Program of Cambodia (NTP). In the study by Sar et al. (2009) in Phnom Penh, resistance rates from TB isolates to isoniazid and rifampin were 23.5% and 16.3%, respectively. Overall, isolates from 5.1% of participants were resistant to both isoniazid and rifampin, classifying them as multidrug-resistant tuberculosis (MDR-TB) cases (Sar et al. 2009). This emergence of DR-TB has only further exacerbated the TB prevalence problem. While detection and treatment of DR bacilli is crucial to recovery, routine use of drug susceptibility testing (DST) in Cambodia is lacking. Such low rates of DST handicap DR-TB case detection and treatment (Sar et al. 2009).

Another factor likely contributing to the increased incidence of TB in Cambodia is the high rates of HIV co-infection ("Global Tuberculosis Control 2011", 2011). First detected in the early 1990s, HIV prevalence peaked to 3% in 1997, and have since leveled at 2% (Tamura et al. 2008). As of 2010 Cambodia has the highest HIV/TB co-infection incidence in Asia, with 7% of tested TB patients HIV positive ("WHO Tuberculosis Profile: Cambodia", 2010; Kanara et al., 2008) This percentage does not include non-tested TB or HIV patients, and therefore the actual figure is unknown. TB is the most common cause of death for HIV infected patients (Kanara et al. 2008). As co-morbidity rates continue to escalate in Cambodia, the NTP might be a potential future source for HIV management (Tamura et al. 2008). With high co-infection rates, adherence rates to

both medications (antiretroviral therapy and first-line anti-tuberculosis drugs) would no doubt be even more in jeopardy.

While Cambodia does have nationwide coverage of DOTS, past events hinder delivery of adequate services to combat overwhelming issues relating to TB.

Unfortunately, there was little health system left after the Khmer Rouge defeat in 1979.

Poor infrastructure and high numbers of landmines scattered throughout the countryside made rural healthcare delivery even more difficult. By the end of 1994 the NTP was only active in 10 of the country's 24 provinces (Hill and Tan Eang, 2007).

Making some great strides in conjunction with Cambodia's healthcare coverage plan, the NTP now reports 100% DOTS coverage, 70% smear-positive case detection, 95% success rate of treated TB cases and 85% retreatment success ("WHO TB Profile: Cambodia", 2010). Such strides were made all with donor-based funding (Hill and Tan Eang 2007).

However there is still more progress to be made in successful DOTS program completion, and control of drug-resistant TB cases. Diagnosis becomes even more of an issue for Cambodia with such high rates of DR-TB and co-morbidities, especially HIV/TB. Changing the time until diagnosis and initiation of treatment is fundamental to changing these issues and preventing the further spread of TB.

### **2.2.1 TB Case Detection in Cambodia**

Negative SSM results, extra-pulmonary TB, low access, and low awareness may often lead to delays in TB detection (Storla, Yimer, and Bjune (2008). Pulmonary TB in Cambodia is most commonly diagnosed either with SSM or chest X-ray, when

accessible. SSM is most commonly used in Cambodia, which, like many other low-resources countries, utilizes such testing because of the relative low cost and fast results. As of 2011, the positive rate among smears was 10.1% (Tuberculosis Report 2011). While diagnosis and treatment are free of charge throughout Cambodia, getting people tested is still a major challenge. In addition, the SSM lacks sensitivity in the diagnosis of extra-pulmonary TB (Storla, Yimer, and Bjune 2008). In 2009 there were 15,812 cases of new smear-positive pulmonary TB, 7,686 cases of new smear-negative pulmonary TB, and 14,690 cases of new extra-pulmonary TB in Cambodia (Tuberculosis Report 2011). Although new smear-positive pulmonary TB cases account for the largest number of new cases, the large numbers of smear-negative and extra-pulmonary TB patients illustrates the importance of a chest X-ray in establishing a diagnosis. However, chest X-ray is only available in referral hospitals, usually leaving the health centers (HCs) to test via SSM (Tuberculosis Report 2011).

### **2.2.2 Community DOT (CDOT) Program**

Within the Cambodian NTP, there is a large movement to implement DOTS nation-wide. This is most notably achieved through the new community-DOT program (CDOT), which started in Cambodia in 2002 (Tuberculosis Report 2011). The CDOT program is designed to improve case findings and adherence through community worker intervention, through local volunteers who monitor patient TB drug intake daily for the recommended six-month regimen, and by referring members of the community to local HCs to get tested. The program has been rapidly expanding. As of 2011, the

program covered 857 HCs (Tuberculosis Report 2011). While successful in improving access to information, increasing awareness about TB symptoms, decreasing stigma, and maintaining good compliance levels, challenges remain. These include a limited capacity of HC staff to support CDOT, co-infection with TB/HIV, and seasonal movement of populations (Tuberculosis Report 2011). CDOT workers often serve as a communication link between health centers and patients. The program is also heavily reliant on 13 main non-governmental organization (NGO) supporters responsible for training and implementing the CDOT program. FHI 360 alone implements CDOT in 54 HCs (Tuberculosis Report 2011). Currently, there are monitoring and evaluations being performed in order to further understand the challenges and progress that has been made with CDOT

### **2.2.3 TB in Kampong Cham Province, Cambodia**

The Kampong Cham Province in Cambodia is one of the largest provinces with a total of 10 operational districts (ODs) operating in it. Kampong Cham also has the highest TB infection rates in the country. As of 2011, there were 5,631 new TB cases in the province, more than any other province in Cambodia. Kampong Cham has had a 36% increase in new smear-positive TB cases over that seen in 2010 (Tuberculosis Report 2011). It is unclear whether this is due to a true increase or improvements in case detection. With the fifth worst cure rate out of all provinces (83%) (Tuberculosis Report 2011), treatment and case detection need to be addressed. As a result, FHI 360 created their TB Care SMS Project in Kampong Cham first as a pilot program.

## 2.3 mHealth

The World Health Organization (WHO) has identified five main stages of delay related to TB management: 1. time from admission to suspicion of TB; 2. time from suspicion to ordering SSM test; 3. time from ordering SSM test to getting the specimen to the lab; 4. time from examination of smear to reporting the result; and 5. time from lab return of result to start of treatment (Chen et al., 2011). Therefore, delays in laboratory diagnosis of TB can be extremely impactful to the rest of the cycle. Since infectiousness rapidly diminishes once treatment starts, improvements to the diagnosis stages could potentially cut down on the time that a patient is infectious, reduce patient mortality, as well as time lost from work or home activities due to illness.

As technology expands, so too does the potential healthcare network capabilities. The application of eHealth (electronic health), as it is now commonly referred to, has been substantially growing in the health field. This has been especially notable in the cellular mobile sector (“mHealth: New Horizons for Health through Mobile Technologies”, 2011). Although there is no standard definition to mHealth, it is identified as a component to eHealth as medical and public health practices that are supported by mobile devices (such as mobile phones, patient monitoring devices, PDAs, and other wireless devices ) (“The Role of mHealth in Fight Against Tuberculosis”, 2012). mHealth involves the core functions of a mobile phone, which includes voice capabilities and short messaging service (SMS). More complex applications include packet radio service, 3G and 4G systems, global positioning system (GPS), Bluetooth technology, and

camera utilization (“mHealth: New Horizons for Health through Mobile Technologies”, 2011).

To illustrate the potential of cellular mobile technology in resource-limited environments, there are now over 5 billion wireless subscribers worldwide, and 70% of those users reside in low- and middle-income countries. Wireless signals now also cover about 85% of the world’s population, making mHealth (mobile health) much more common and viable in low resource settings (“mHealth: New Horizons for Health through Mobile Technologies”, 2011). In December 2011, there were 14 million mobile phone subscribers in Cambodia (which is 98% of the country’s 14.3 million population). While these numbers may not only account for Cambodian subscribers, 85% of the country is covered by a mobile phone service (statement by Minister of Telecommunications, So Kuhn (Xinhua, 2011)).

Multiple mHealth initiatives are being conducted worldwide, especially in resource- limited settings, where mobile use is prevalent and potentially more beneficial. In the second global survey conducted on eHealth by the WHO in 2009, several countries reported up to six mHealth programs per country. These ranged from health call centers to decision support systems (“mHealth: New Horizons for Health through Mobile Technologies”, 2011). However, evaluation of mHealth activities by WHO member states is extremely low (12%) and needs to be incorporated more into mHealth project management (“mHealth: New Horizons for Health through Mobile Technologies”, 2011).

### **2.3.1 mHealth and TB**

Despite the spread of mobile technology across the globe, mHealth applications for TB remain relatively unexplored, and evaluations of these programs to an even lesser extent. According to the WHO's Stop TB program, there are five main areas that need to be explored further in regards to mHealth and TB: 1. treatment adherence, monitoring; 2. TB diagnosis and treatment; 3. mobile diagnosis; 4. disease surveillance, and 5. health and awareness dissemination ("The Role of mHealth in Fight Against Tuberculosis", 2012).

Monitoring of TB diagnosis and treatment can be especially problematic in high burden areas where technical and human resources are limited. Most countries still use paper-based methods to request and record diagnostic support and results, substantially prolonging the time from test collection to diagnosis and the subsequent start of treatment ("The Role of mHealth in Fight Against Tuberculosis", 2012). There may be many benefits to a mHealth-based system of initiating and monitoring TB diagnosis and treatment. One such advantage would be the warning capacity that many of the current mobile-based data collection software have in case of missing or faulty data. Another potential benefit would be the streamlining of data reporting systems from laboratories to health clinics and patients ("The Role of mHealth in Fight Against Tuberculosis", 2012). Other potential benefits to the application of mHealth and TB should be explored and further evaluated.

## 2.4 Pilot TB Care SMS System

In the Kampong Cham province of Cambodia, paper patient records are traditionally maintained using a “Sputum Collection and Specimen Sending Book”. The sputum is sent to the lab for testing and the results of the SSM are kept in the “TB Patient Book” if a patients tests positive for TB (either through SSM, chest X-ray, or both). Treatment is started on doctor’s orders, typically after positive test results come back or empirically if signs and symptoms are consistent with TB prior to availability of confirmatory testing.

Started in December 2011, the TB Care SMS System was created by FHI 360’s Cambodia office with funding from USAID. The objectives of the program were focused on decreasing the turnaround time from sputum collection to diagnosis notification. By decreasing the turnaround time, the program would ideally facilitate early diagnosis, initiation of treatment, and minimize TB transmission within each community. Another objective of the program is to help track TB test results for monitoring and further follow up action. The pilot TB Care SMS Program currently covers a total of 4 labs with 15 corresponding health centers over 2 operational districts of Kampong Cham and Chamkar Leu (ODs) in the Kampong Cham province of Cambodia. It works within the existing framework for TB SSM test collection to the corresponding labs. Results are returned to the health clinic, from which patient notification can begin.

Through development of the pilot program, the framework for TB diagnosis and treatment was identified. Five main steps were identified:

1. The health center staff collects sputum for SSM from TB suspects.
2. The sputum smears are delivered from the health centers (HCs) to the TB lab.
3. The lab tests the sputum smears and puts the results in a result box.
4. After about one or two weeks, the results are collected and delivered back to the HC.
5. After the HC receives the result, it makes a call to the CDOT (community-based directly observed therapy) worker, who in turn notifies the patient to come back to HC for further treatment and diagnosis.

When the SMS program was implemented, the five steps were modified as follows;

1. The health center staff collects sputum for SSM from TB suspects.
2. The sputum smears are delivered from the health centers (HCs) to the TB lab.
  - **A SMS text with the sputum smear details of each patient and date is sent from the HC to the laboratory's electronic system confirming that the HC sent the sputum samples via regular courier.**
3. The lab tests the sputum smears and instead of putting the results in a result box:
  - **Sends an SMS text message to the CDOT and the HC only if the test is smear positive for TB. The CDOT worker contacts the patient telling them to return to the HC to receive further diagnosis or treatment.**
4. As a quality check, the paper results are still delivered back to the HC after about one or two weeks (refer to Figure 6 in Appendix A).

Prior to the SMS pilot intervention, the average turnaround time between the time the HC sent the test to the lab (sputum submission) and when the lab sent back the results (diagnosis) was about 10 days (“Introduce ICT to TB Care SMS System”, 2011). FHI 360 has done an internal evaluation of the turnaround time for the TB Care SMS Program. With the new SMS system, the new average time from sputum submission to when HC and CDOT notification is reported is about 6 days (based on results from February 2012) (“Introduce ICT to TB Care SMS System”, 2011). This is based on the date the HC sends the test sample to the date when the HC receives the results. However, time from when the sputum specimen samples are sent in to when the patient is brought in by the CDOT worker in order to initiate treatment has not been measured.

The role of the HC staff and CDOT worker is very important within the new SMS system. The HC staff helps to facilitate the SMS program by sending in sputum samples for testing to one of the 4 labs in the pilot program. After receiving the results back from their corresponding lab via SMS, these results are recorded in the TB Patient Register so that when the patient comes to the HC, the results are recorded and treatment can be initiated. Once the patient is brought in, it is their role to start the patient on adequate treatment. CDOT workers are notified as soon as they are assigned a patient who tests positive for TB from the SSM lab results. The workers are notified of the patient’s name and information, and they are responsible for bringing the positive patient in for treatment and (possibly) further testing.

Although the program seems to have been fairly successful so far, there are a few reported challenges. One is the frequent change of phone number by users, as often times in Cambodia people change their mobile numbers because of new discounts or better rates. Another difficulty seems to be the lack of understanding English texts for native Khmer speakers at both the labs and HCs. The pending TB diagnosis results still remain a problem, as the system still has to wait for the lab to conduct the tests on the SSM. Finally local use of web based systems for monitoring and follow up remain a challenge.

## **2.5 Impressions of the Literature**

Although many of the mHealth projects have been deemed “successful”, objective evaluations are lacking. In fact monitoring and evaluation of these mhealth programs only accounts for 12% of the research being done of their intervention techniques (“mHealth: New Horizons for Health through Mobile Technologies”, 2011). Many, including the WHO (ref) are calling for further monitoring and evaluation of these mhealth technology projects, so that future practices are grounded in evidence.

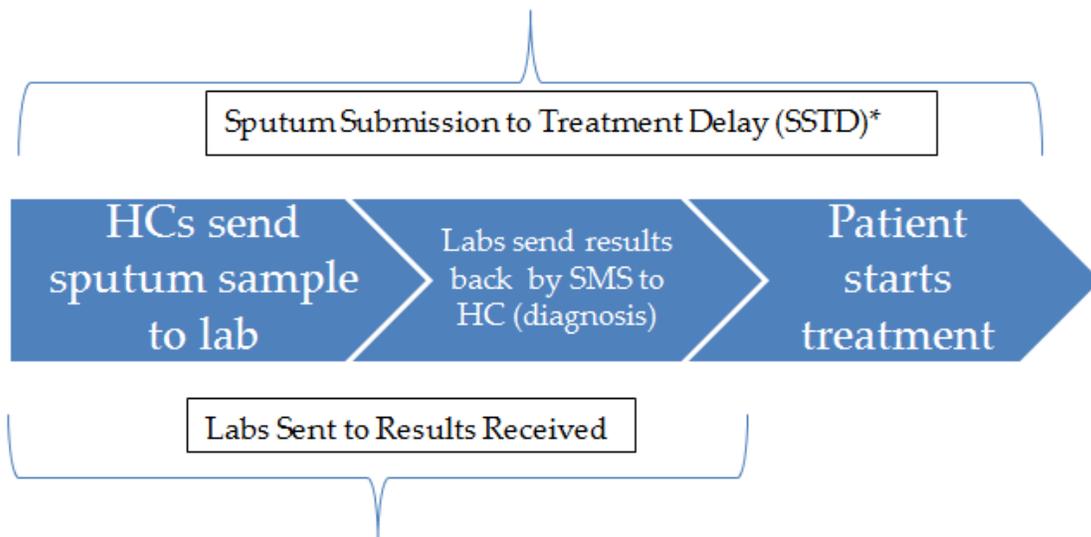
While Cambodia is one of the top countries in the world most burdened by TB, new programs (like the TB Care SMS Project) are taking advantage of the prominent mobile technology systems to benefit people throughout the country. Making use of the rapidly expanding market for mobile phones, FHI 360’s project creates a possible innovative solution to reduce the delay from TB diagnosis to treatment.

### 3. Methods

#### 3.1 Hypotheses

**Hypothesis:** Time from sputum submission to treatment (SSTD) will be shortened among Cambodian patients cared for in health centers that have implemented the TB Care SMS System and which do not have an adjacent or attached diagnostic laboratory

**Null Hypothesis:** The implementation of the TB Care SMS System will have no impact on the time from sputum submission to treatment (SSTD) among patients cared for at implementation health centers without adjacent or attached laboratories.



\*Denotes the Primary Outcome

**Figure 1: Time Points being Measured in the Analyses**

## **3.2 Objectives**

The primary objective of this retrospective cohort study was to compare the time from sputum submission to treatment (termed “sputum submission to treatment delay”, SSTD) before and after the TB Care SMS System was initiated in the health clinics in Kampong Cham Province, Cambodia. The secondary objective of this study was to explore healthcare worker and community DOT worker perceptions of the advantages and disadvantages of the TB Care SMS System compared to the previous paper-based system.

## **3.3 Outcome Measures**

The primary outcome measure is the SSTD defined as the interval of time from the date when the specimen was submitted to the lab for testing until the date when the first dose of TB treatment is given. The secondary objective was measured by both quantitative and qualitative themes around usefulness of the new SMS system using a mixed method approach.

## **3.4 Study Design**

### **3.4.1 Primary Objective**

The study is designed as a retrospective analysis comparing SSTD among sputum smear-positive TB patients at selected HC in Kampong Cham Province, Cambodia, before and after implementation of an SMS intervention. SMS has been implemented in 15 health centers in the province. Of these 15, 5 have attached lab

facilities and 10 do not. We assumed that HCs with lab facilities available on site may not have benefited from the impact of the pilot SMS program as much as HCs without lab facilities. Thus we targeted our assessment on those without lab facilities.

In Kampong Cham Province there are two main referral labs. One located at the Kampong Cham Referral Hospital (RH), and the other at the Chamkar Leu RH. Data collected comprised a convenience sample taken from 2 out of 7 health centers that use the Kampong Cham Referral Hospital (RH) lab for diagnosis [Krala HC and Moha Khoung HC] and 3 of 5 HCs that used the Chamkar Leu RH's lab [Speu HC, Sopheas HC, and Chamkar Andoung- Chamkar Kausou HC] for diagnosis (Figure 2, Appendix A). Of the 10 health centers without attached or adjacent labs, the 5 that were sampled were chosen because a) they were known to have a higher patient load of TB than other health centers based on reported TB cases from 2011 and b) they were within reasonable car-driving distance from the town of Kampong Cham, reflecting time and budget constraints in getting to each location.

The inception cohort for our retrospective study includes all patients who tested positive for TB with sputum smear microscopy and were started on their first dose of TB treatment at the 5 HCs during the inclusion dates. Inclusion dates for the pre-SMS program sample were those diagnosed and started on treatment between January 2011 and November 2011, and for the post-SMS program sample, diagnosed and started on treatment between December 2012 and June 2012.

### **3.4.1.1 Subject Selection:**

For the primary objective, each HC's "Sputum Sending book" and "TB Register book" were reviewed to find eligible subjects based on dates of diagnosis (the former) and treatment initiation (latter), and the following inclusion criteria:

#### **Inclusion Criteria:**

- Diagnosis and treatment initiation occurred within the defined pre-SMS or post-SMS time periods (January 1, 2011-November 30, 2011 for pre-SMS and December 1, 2011-June 30, 2012 for post-SMS)
- A patient at one of the 5 selected HCs (see Figure 2)
- Pulmonary TB defined as a positive SSM
- Started on TB treatment

#### **Exclusion Criteria:**

- Patient outside the selected HCs
- Only extra-pulmonary TB
- Pulmonary TB but negative SSM
- Diagnosis and treatment occurred outside the defined time periods
- Tested positive for TB with another test, besides SSM

### **3.4.2 Secondary Objective**

To explore healthcare worker and community DOT (CDOT) worker perceptions of the advantages and disadvantages of the TB Care SMS System compared to the previous paper-based system, a mixed method approach was taken. Surveys with both quantitative, closed-ended questions and open-ended, qualitative questions were administered to the HC workers from each clinic. A convenience sample method was used from a list of CDOT workers and HC staff who were trained and familiar with the SMS pilot program. Survey subjects included 1-3 participants from each of the 5 clinics, as well as CDOT workers, who have used the pilot SMS System. These surveys were

administered orally in Khmer by an interviewer/translator, their responses recorded, and later translated into English by the same interviewer. The interviews were done one at a time, and each survey lasted approximately 30 minutes. The CDOT workers were likewise interviewed with a different survey (maximum 15 minutes), and selected based on their familiarity with the program (if they had used it before) and willingness to participate. These CDOT workers were asked to come to their corresponding health center on the scheduled day of the interview and were compensated for time and travel.

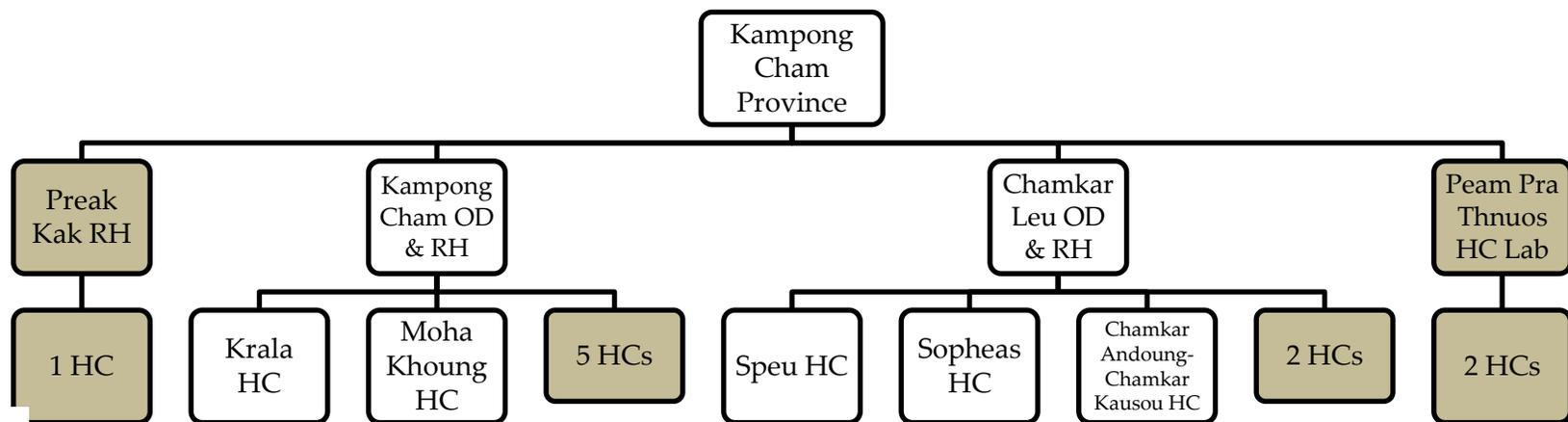
#### **3.4.2.1 Subject Selection:**

##### **Inclusion Criteria:**

- Healthcare worker or CDOT worker at either one of the 5 HCs chosen (See description in Figure 2)
- Experience with pilot TB Care SMS System
- Willing and consented participant

##### **Exclusion Criteria**

- Does not work at any of the 5 HCs and is not a CDOT worker, nor HC staff connected with these facilities
- No experience and unfamiliar with the pilot TB Care SMS System
- Unwilling and non-consented participants



22

\*Shading denotes HC sites that were not sampled

**Figure 2: Health Center Organization and Hierarchy of Sites Using Pilot SMS System in the Kampong Cham Province, Cambodia**

### **3.5 Data Collection Methods**

Data was collected in July 2012 with an in-person visit to each of the 5 HCs, and working out of the FHI 360 country office in Phnom Penh, Cambodia. The pre-SMS data, including SSTD, was measured for the year before the TB Care SMS System was implemented, from January 2011 to November 2011. The post-SMS data were collected 6 months after the program had been implemented, from December 2011 to June 2012. This information was collected from the local TB Register books and Sputum Sending books from each HC, which contained patient information, test results, and treatment start date.

To collect data on the primary objective, the PI, accompanied by an interviewer/translator, traveled to each of the 5 HCs. Since photocopy was unavailable at the HC locations pictures were taken in order to copy the local TB Register book and Sputum Sending book from 2011 and 2012. This local TB Register book and Sputum Sending books have records indicating age, sex, test date, results of the test, if and when they were treated, and outcome of treatment. The records are in spreadsheet format for each patient, and once the patients tests positive they are recorded in a separate section of the book (TB Register book), where detail about treatment dates and methods are recorded. Each patient that met the inclusion criteria was assigned a unique study number. Names were covered in the transcription/photograph process, so that no patient names were collected. Records recorded in Khmer were translated into English by the same

interviewer/translator. This information was then transferred to a password-protected Microsoft Access (Microsoft Office®, 2010) database in and later analyzed in STATA 12 (SmallStata12®).

For the secondary objective, surveys were administered in person, verbally in Khmer with each HC worker and CDOT worker, and the answers were written on a paper form. After the answers were transcribed onto paper each day, they were then translated into English (the day of the interview), transferred onto a password-protected Microsoft Excel (Microsoft Office®, 2010) spreadsheet, and saved to a portable USB drive. Data was also collected from the local TB Register book and Sputum Sending book from each HC, recorded for the appropriate timeframe, and saved onto USB drive as well. Only gender, age, test date, test results, and treatment start date was recorded. The paper copies, laptop, and USB drive were all kept in safe, locked facilities accessible by only the research team in order to ensure confidentiality and safety of information.

### **3.6 Statistical Analysis**

Variables for analysis were collected directly from the handwritten record books into Microsoft Excel, the spreadsheet was then converted into STATA format. The data available in the clinic records showed the date of first patient encounter, date the specimen was sent, date results received and a separate record showed date treatment started. Because delays can occur at multiple time points, analyses included time from each pre-treatment point to the date of treatment initiation. Unfortunately, only the date when specimens were sent for diagnosis was recorded, without the precision of a time

stamp. Thus, the date the specimen was sent was considered day 0. If the “result date” was recorded as being the same day as the day it was sent, it was presumed that the specimen results were received the same day as being sent, and that time period was recorded as “0” days. Further, if the date for treatment initiation was also the same day as results received, it was recorded as “0” days. If treatment initiation was before the date the lab was sent or received, it was assigned a negative number, reference to the date the specimen was sent, assuming the doctor started treatment on an empirical basis. Records in which the lab results appear to have been received before being sent were excluded under the assumption that these were clerical errors (n=4). This assumption was based on looking at electronic records available for 2011 in the CENAT database (see Section 6.1.1 for further discussion).

Subjects were characterized by age and sex using medians and means. Each p-value was set using 95% CIs. To compare the primary outcome of interest across pre- and post-SMS time periods, we used a simple interrupted time series in order to model the effect of the pilot SMS program as a form of intervention. We decided to use this approach because the data contains many different observations over time, and the exact point of the pilot SMS Program is known (Sadish, Cook and Campbell 2002). An interrupted time series model helps to determine the relationship between an intervention (SMS) and the outcome (time to treatment initiation). A simple interrupted times series model shows the time lapse between diagnosis and treatment and can help account for any possible confounders or variations between HCs. STATA 12 for

Windows was used for statistical analysis. Statistical significance was determined using the criteria level of 0.05 for all p-values.

Another assumption is that all 15 HCs in fact started the pilot SMS program in December 2011, when they should have, and that by January 2012 all 5 HCs sampled were using the program. This assumption is tested using the online SMS reporting system that the lab facilities use to transmit the SMS.

## 4. Ethics

The protocol was reviewed and approved by Duke's Institutional Review Board (IRB), Protocol A0982. It was also reviewed by Cambodia's Director of the National TB Program, Dr. Mao Tan Eang, who determined that in their context the planned data collection and analysis was consistent with program evaluation and did not require further local IRB review.

To ensure patient confidentiality, information was recorded directly onto the PI's password-protected laptop from the Sputum Sending Book and the TB Register.

Photographs of these records were used as a backup copy to authenticate the original data inputs into Microsoft Excel, and the names on these records were edited out.

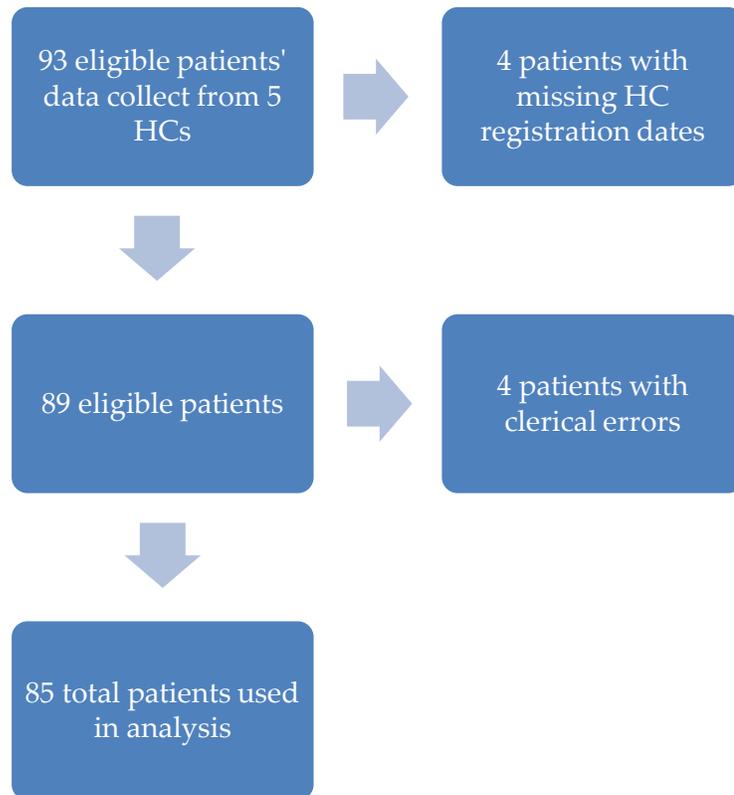
During data collection patients were assigned patient identification numbers, and names were never recorded. Only sex and age were recorded on each patient. No identifiable information was collected that could be traced back to specific patients. Data was kept on a password protected computer with encrypted software.

In data collection for the secondary objective, each HC worker and CDOT worker was verbally consented and informed about the study in Khmer. Signed consent forms were not collected because no HC worker or CDOT worker names were collected, and instead they were assigned individual number. No identifiable information was collected on any of the HC workers or CDOT workers during the verbal interviews.

## 5. Results

### 5.1 Primary Objective Results

There are seasonable variations in the epidemiology of reported TB cases. Therefore, although nearly a year of pre-SMS data were collected, only data from months corresponding to post -SMS data (January-June) were included in the analysis. In addition, among the 93 eligible subjects enrolled from the 5 HCs, patients were excluded because of missing dates (n=4), and clerical errors (n=4) (see Figure 3). Therefore 85 total patients were used in the primary analysis.



**Figure 3: Patient Enrollment Process from SMS Pilot Program Evaluation in Kampong Cham, Cambodia from Main Analysis**

General characteristics for the pre- and post-groups are shown in Table 1 using a t-test method. In the pre-program cohort there were a total of 51 patients and 34 in the post-group. There were notable differences in the number of subjects enrolled across the HCs. Specifically, the Chamkar Andong-Chamkar Kaosu HC had many more patients in the pre-group (n=15) than in the post-group (n = 3). Speu HC had significantly more patients in both groups (p = 0.011 (CI 0.09, 0.63), especially compared with the other 4 sites. Thus, Speu HC comprises a significantly greater representation in the overall post-SMS sample.

**Table 1: Subject Characteristics in Kampong Cham, Cambodia**

	<b>Pre-Program</b>	<b>Post-Program</b>	<b>P- Value</b>
<b>Variable</b>	(n = 51)	(n = 34)	
<b>Patient Characteristics:</b>			
Female, No. (% of total)	16 (31.37)	15 (44.12)	0.098
Age, median (SD), years	50 (17.52)	50.5 (18.74)	0.951
<b>Health Centers:</b>			
Chamkar Andong- Chamkar Kaosu HC, No. (% of total)	15 (29.4)	3 (8.82)	0.147
Krala HC, No. (% of total)	3 (5.88)	1 (2.94)	0.756
Moha Khnong HC, No. (% of total)	10 (19.61)	6 (17.65)	0.213
Sopheas HC, No. (% of total)	4 (7.84)	3 (8.82)	0.227
Speu HC, No. (% of total)	19 (37.25)	21 (61.76)	<b>0.011</b>

\*Bold denotes statistical significance

\*\*SD, standard deviation

Using the interrupted time series analysis (Table 2), we were not able to demonstrate that the SSTD decreased significantly in the post-SMS program time frame, from January 2011 to June 2012. Measuring the date from when the sputum labs were sent to when the lab results were received by the HCs, we did not find a statistically

significant reduction in delay either, though the trend was in the expected direction, with an apparent reduction of 1.70 days.

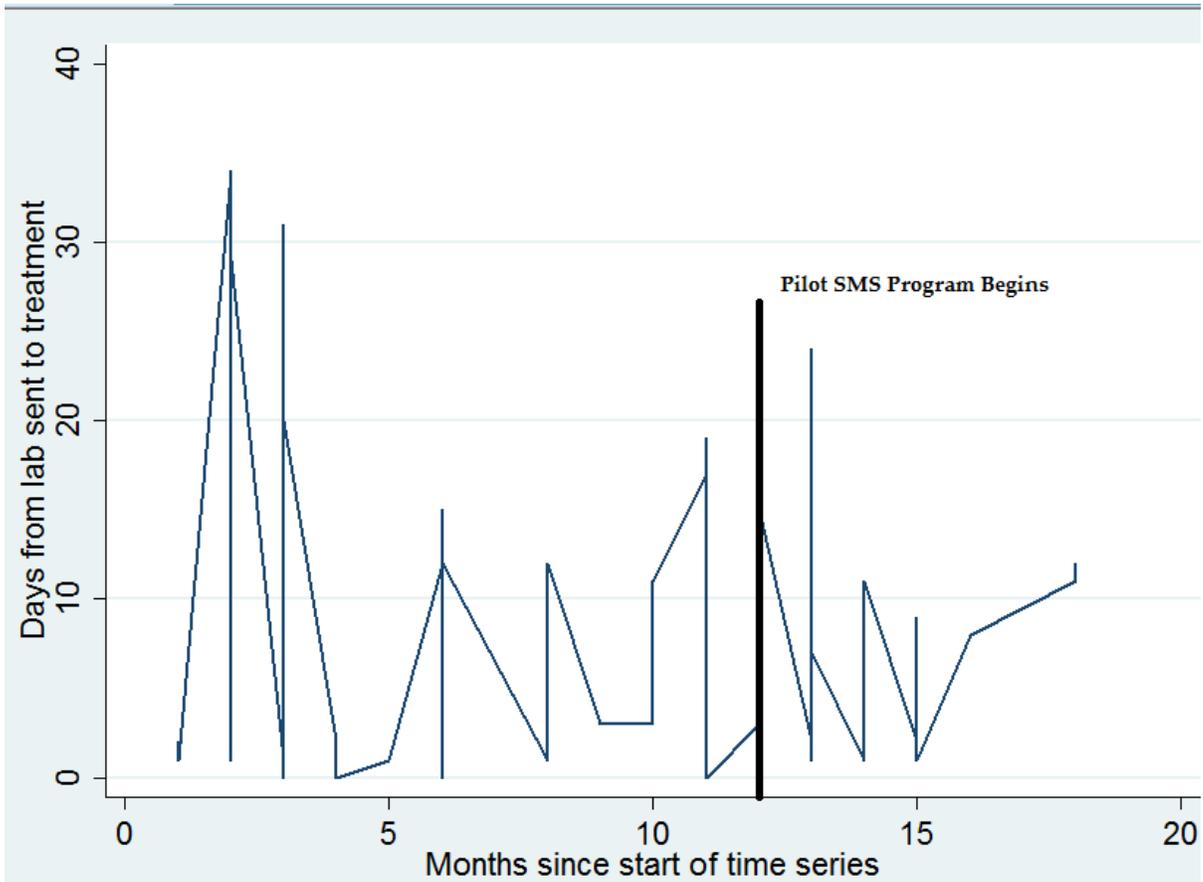
**Table 2: Change in SSTD on Pilot SMS Program in Kampong Cham, Cambodia**

	<b>Change in Duration After SMS</b>	<b>P-Value</b>	<b>95% CI</b>
<b>Variable Outcomes:</b>			
SSTD*	0.066 more days	0.883	(-8.28, 9.60)
Labs Sent to Results Received	1.70 less days	0.310	(-5.01, 1.61)

\* Primary Outcome

\*\*Bold denotes statistical significance

Looking at an interrupted time series graph, like Figure 3, may help bring some clarity to the effect of the pilot SMS intervention. In Figure 3 there seems to be a decrease in SSTD in the month of December 2011 following the implementation of the SMS program. The decrease in December is then followed by a sharp increase in SSTD. This may be due to the seasonal variation of TB cases around January, since January 2011 appears to have had a major increase in TB cases as well. The drastic increase around January 2012 is followed by several other decreases in SSTD, after the SMS program is implemented. It is clear, however that the increases in SSTD after the pilot program are relatively small compared with the increases in SSTD before the program. There may also be a delayed reaction after the program was implemented for the effects to fully be captured. These results were surprising based on previous analysis by FHI 360 on the date from when labs were sent to when results received, but FHI 360's calculations had more accuracy in measurement, since the outcomes were based on all 15 HCs, and not just a sampling of 5.

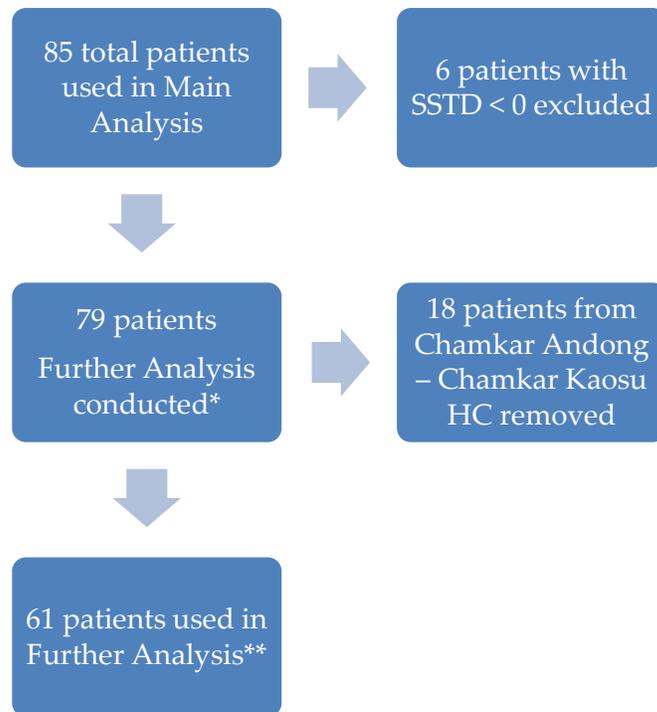


**Figure 4: Interrupted Time Series Graph of SSTD Before and After the Pilot SMS Program is Implemented in Kampong Cham, Cambodia**

### 5.1.1 Exploratory Analysis

As previously noted (Section 3.6.1) there were some time values for SSTD that were  $< 0$  days, which we assume indicates that the patient started treatment before the sputum was sent to the labs to be tested. We performed additional exploratory analyses through further data exclusion by looking at the impact of the following: 1) SSTD  $> 0$  and 2) the effects of individual HCs on the outcomes (see Figure 5). First negative durations of the date the sputum labs were sent to when results were received were

removed from analysis (n = 79). These observations (n=6) were removed because the patients began treatment before the sputum was sent the pilot SMS program was not able to have an effect on this population. After analyzing the primary outcomes excluding negative SSTD values, we explored the effect of the SMS Pilot Program on the 4 HCs which were similarly represented in both pre- and post-sampling, excluding the Chamkar Andong – Chamkar Kaosu HC, which itself had previously (see Table 1) had a much larger sample size in pre-group (n=15) than in post-group (n=3). Without Chamkar Andong – Chamkar Kaosu HC analysis will be done on only 61 patients.



\*First analysis conducted (Table 3)

\*\* Second analysis conducted (Table 4)

**Figure 5: Data Exclusion Process from SMS Pilot Program Evaluation in Kampong Cham, Cambodia from Further Analysis**

In the exploratory analysis where we excluded patients who appeared to have been started on therapy before labs were sent (durations SSTD < 0, n = 79), we do not see a significant change, but we do see a trend in the expected direction (p= 0.701, CI -11.34, 7.67). With the intervention of the SMS Pilot Program there are 1.80 less days from the date sputum labs are sent to when the patient initiates treatment (Table 3). The duration from when labs are sent to when results are received is 3.41 less days after the program, and the p-value approached but did not obtain statistical significance at 0.055 (-6.90, 0.08).

**Table 3: Interrupted Time Series Further Analysis without Durations < 0 on Pilot SMS Program in Kampong Cham, Cambodia**

	<b>Change in Duration After SMS</b>	<b>P-Value</b>	<b>95% CI</b>
<b>Variable Outcomes:</b>			
SSTD*	1.84 less days	0.701	(-11.34, 7.67)
Labs Sent to Results Received	3.41 less days	0.055	(-6.90, 0.08)

\* Primary Outcome

\*\*Bold denotes statistical significance

We also performed a second exploratory analysis after noting that one HC (Chamkar Andong – Chamkar Kaosu) had substantially more observations in the pre-group (n=15) than in the post-group (n=3) (Table 1). Excluding Chamkar Andong – Chamkar Kaosu HC would make the pre-/post-program groups more similar. Without patients from Chamkar Andong – Chamkar Kaosu HC, the population is reduced substantially (n = 61). Without the observations from the Chamkar Andong – Chamkar Kaosu HC, the p-value of SSTD after the program intervention is approaching statistical significance at 0.057 (CI -11.63, 0.18) showing 5.72 less days from date sputum sent to patient initiation (Table 4). The duration from lab to results also approaches statistical significance at 0.073 (CI -7.56, 0.35) with a reduction of 0.15 days.

**Table 4: Interrupted Time Series Further Analysis without Durations < 0 and Chamkar Andong – Chamkar Kaosu HC Observations on Pilot SMS Program in Kampong Cham, Cambodia**

	<b>Change in Duration After SMS</b>	<b>P-Value</b>	<b>95% CI</b>
<b>Variable Outcomes:</b>			
SSTD*	5.72 less days	0.057	(-11.63, 0.18)
Labs Sent to Results Received	3.61 less days	0.073	(-7.56, 0.35)

Eliminating observations of SSTD < 0 and observations from Chamkar Andong – Chamkar Kaosu HC, severely limits the population (n = 61), so strong and accurate conclusions cannot be drawn. It is interesting to note, however, that the impact of Chamkar Andong – Chamkar Kaosu HC ultimately has some kind of negative effect on the overall impact of the pilot SMS program on SSTD.

### **5.1.2 Test for Autocorrelation**

After exploratory analysis, an autocorrelation regression was run to test whether or not the error terms that were previously removed (durations of SSTD < 0) are correlated. The scatterplot used to test for autocorrelation did not have a set pattern therefore there was no need to correct for it in Section 5.1.1. Likewise, an autocorrelation regression was run to test for patterns within the Chamkar Andong – Chamkar Kaosu HC, and there appeared to be none present.

## **5.2 Secondary Objective Results**

The total number of CDOT workers interviewed was 14 (n=14), and total number of HC workers interviewed was 7 (n=7). Stratified by HC, all five HCs had 3 CDOT workers interviewed; except Krala HC, which had 2 CDOT workers available for interview. Since there were both quantitative and qualitative questions on each interview, the results were analyzed differently. The quantitative questions were analyzed using STATA 12 and qualitative questions were analyzed using comparative techniques.

### 5.2.1 CDOT Worker Quantitative Results

Table 5 describes the overall demographics of the CDOT workers. Most of the CDOT workers were male. All of the CDOT workers were above the age of 35 years old, most were between 45 and 55 years. A majority of the CDOT workers had at least a lower secondary education.

**Table 5: CDOT Worker General Characteristics and Understanding of Pilot SMS Program in Kampong Cham, Cambodia**

	<b>CDOT Workers Interviewed</b>
<b>Variable</b>	n = 14
<b>Patient Characteristics:</b>	
Female, No. (% of total)	4 (28.57)
Age, median, years	45 - 55
Education, median, level	Lower Secondary
<b>Understanding of SMS Program</b>	
Understand SMS, No. (% of total)	14 (100)
Like SMS, No. (% of total)	14 (100)
Believe SMS Should Replace Paper, No. (% of total)	14 (100)
Would Recommend SMS, No. (% of total)	14 (100)

Since all 14 CDOT workers answered that they would recommend the SMS Project over the old diagnosis system, linear regression modeling was not possible. It is however, important to note some of the other answers in the survey about how CDOT workers would evaluate the SMS Project. In the interview, CDOT workers were asked about their perception of the SMS Project, usefulness, and whether or not they would recommend this program be used in the future over the old, paper-based system. All 14

of the CDOT workers reported that they all understood the SMS Project, how it works, and all of them said that they liked the new SMS program, compared to the old paper-based system. They unanimously also said that they would permanently replace the paper based system in favor of the SMS one and that they would recommend this SMS Project to other co-workers in HCs across the country.

### **5.2.2 CDOT Worker Descriptive Results**

The CDOT workers were asked several qualitative questions about the procedure they followed after they received the SMS from the lab reporting the positive TB test result of the patient, how long it took for the patient to come into the HC, and what they thought some of the advantages, and disadvantages of the SMS Project were. All CDOT workers were trained in December 2011 to follow the same protocol to tell the patient that they have TB, and then they (the CDOT workers) are responsible for bringing in the patient for treatment to the HC. These questions were intended to capture if each CDOT worker follows protocol and what some of the problems are that they may encounter.

The first qualitative question was about the procedure that each CDOT worker followed after they had received the SMS from the lab reporting the patient who had tested positive. Most of the responses followed the same pattern. First they would tell the patient about the positive TB diagnosis. Then they would tell the patient to go to the HC, either with them or on their own when they were available to go, to get the

medication. Finally they would remind the patient that they were responsible for monitoring their daily medication intake.

The next question was about how long it usually took the CDOT workers to report to the patient to tell them of their diagnosis. Nearly all said that it took one day or less to tell the patient, though one mentioned that it could take them one week or more to find and communicate results with the patient, and there was discussion about how it depended on where the patient lived and what time of day it was when they received the SMS.

The next question was about what problems may arise in notifying the patient of their TB diagnosis. The answers varied to some extent but many CDOT workers stated that educating patients was a large component of what they had to do. From learning that TB was curable with proper treatment to how TB spreads; the CDOT workers responded that they had to inform their patients about many different aspects of TB. All of them mentioned that they had to inform their patients about how to cover their mouths when coughing with either a mask or krama (cotton scarf). Spitting seemed to be another issue that many of the CDOT workers discussed with their patients, and how patients should not spit in public anymore. One of the other most common concerns was discussion with patients how the CDOT workers had to watch them take their medication daily. Another problem some of the workers encountered was embarrassment, and how a patient being too embarrassed to come into the HC was a

problem. Stressing self-care, in regards to resting and taking medicine, was another common response.

Regarding the question about how long it typically took the patient to come into the HC after they found out about their diagnosis, all participants mentioned that it would usually only take a patient one day at most to come in to the HC for treatment. Some responders even mentioned that it could take as little as one hour. Some CDOT workers also mentioned that it depended again on the time of day and how far away the patient lived from the HC for them to come in.

CDOT workers were also asked about what they perceived to be some of the strengths of the SMS Program. Most mentioned that the program saved both time and money. Most also mentioned that they received the test results quicker with the new program, and that the patients could in turn take action on treating their TB faster. A few responders also mentioned improved safety in regards to reduced spreading of TB infection to people in the community and how the program helped cut down on the infectious period for several patients. Two responders did not list any advantages at all.

Although most CDOT workers remarked that there were no disadvantages to the program for them, a few mentioned disadvantages including not having the SMS in the Khmer language, stating that they preferred the SMS was in Khmer instead of English. One responder mentioned that needing more training in the SMS system, and another mentioned how they did not understand some of the SMS codes sent from the lab. Two

also mentioned that the lab phone numbers changed frequently, so it was difficult to keep track of the lab phone numbers.

### 5.2.3 HC Worker Quantitative Results

Similarly to the CDOT worker responses, since all 7 of the HC workers interviewed answered that they would recommend the SMS Project over the old diagnosis system, linear regression modeling was not possible. However, overall demographics and responses can be analyzed in percentage format in order to see specifically their perceptions and responses to the SMS Project were.

**Table 6** describes the overall demographics of the HC workers that were interviewed. Most were male and were between 15 and 65 years old. Except for one of the 7 HC workers, who had lower secondary education, all the rest had had upper secondary education.

**Table 6: HC Worker General Characteristics and Perception of Pilot SMS Program in Kampong Cham, Cambodia**

	<b>HC Workers Interviewed</b>
<b>Variable</b>	n = 7
<b>Patient Characteristics:</b>	
Female, No.	1
Age, median category, years	45 - 55
Education, median category, level	Upper Secondary
<b>Knowledge of SMS Program</b>	
Trained on SMS, No.	7

Understand SMS, No.	7
SMS Easier, No.	7
<b>Recommendation of SMS Program</b>	
Like SMS, No.	7
Should Replace Paper, No.	7
Recommend to Other HC Workers, No.	7
<b>Perception on SMS Program (1- Excellent to 4-Needs Improvement)</b>	
Objectives Met, mean	1.29
Expectations Met, mean	2
Usefulness , mean	1.43
Rate Format, mean	1.14

**Table 6** describes the knowledge the HC workers had on the SMS Project and how to use it. All of the HC workers stated that they had been trained on how to use the SMS Project, and likewise all of them said that they understood how to use the new SMS system. Also all of the HC workers said that the new SMS system was easier to operate than the old paper based diagnosis system.

**Table 6** is meant to capture the evaluation that the HC workers gave towards the SMS system. One hundred percent of the HC workers said that they liked the new SMS system. Five out of 7 stated that the objectives of the SMS Project were met completely, while 2 workers said the objectives were only somewhat met. In regards to whether or not the HC workers' expectations were met, 4 out of 7 said excellent, 1 out of 7 said it was very good, and 2 workers stated that the SMS system needed improvement. In rating usefulness of the program, 4 out of 7 said it was excellent, and 3 workers said it

was very good. For rating the format of the project, most 6 HC staff said it was excellent, and 14% said it was very good. Finally in whether or not the HC workers would recommend the new SMS project to their colleagues in other HCs across Cambodia, 100% of them stated they would recommend using it.

#### **5.2.4 HC Worker Descriptive Results**

In addition to quantitative survey questions, HC workers were also asked open-ended questions to explore what they thought were some of the advantages and disadvantages of the SMS Program. These qualitative results strongly confirmed the quantitative findings

The HC workers described several advantages of the program. There was unanimous agreement that the program helped save time and save money and most HC workers reported that the SMS Program helped obtain the TB test results faster in order to take quicker action (in diagnosing TB). A majority also mentioned that the program helped safety in that it reduced spreading of TB to other people, especially the patients' children and other vulnerable family members. Several also mentioned the fact that the program kept the patient information secret by labeling them with patient ID numbers instead of names.

Most of the HC workers did not report any disadvantages to the program. A few, however, listed some disadvantages. One responder mentioned that the TB test results and lab code were not sent together in text messages. He suggested that it may be quicker if these two important pieces of information were sent together in a single text to

cut down on confusion regarding identification of the patient for whom the result was being reported. Another responder mentioned that the lab often changes their phone number without texting in advance, and it would be nice to know when the labs change their phone numbers. The same responder also stated that they get charged for texting across networks, and suggested that it would be better if the lab and HC used the same networks. The third responder mentioned that a disadvantage is that the lab results are sent in English, and suggested getting the results texted in Khmer would be nicer to have.

## **6. Discussion**

### **6.1 Discussion on Primary Objective Analysis**

It is expected that an SMS system such as the one in place in Kampong Cham Province will reduce turnaround time for laboratory reporting of TB results. However, unless these reductions in laboratory delay translate into actual patient benefit, they are of limited value. Thus, our intent was to evaluate whether the new SMS system also impacts an important patient outcome – SSTD. In our main analysis, based on a very limited sampling of Kampong Cham health centers, we were unable to show a significant improvement in delays to treatment during the first 6 months of the new SMS program. However, when refining the analysis to only include patients who had not started therapy before sputum submission and accounting for differences in HC contribution in the pre- and post-phases, we found nearly a 6-day decrease in delay in treatment, nearly reaching statistical significance. While we were disappointed that we were not able to show that the pilot SMS program had an impact on either time from when labs were sent until lab results were received or SSTD, we believe this is a result of our limited sampling scheme, small sample size, and early implementation of the program, and should not be viewed as a reflection on the ultimate success of the program. Our findings indicate the important role of the CDOT worker, and that their getting rapid text messaging and bringing in the patient for treatment is of critical

importance. Since the CDOT worker is part of the pilot SMS program, their reaction time to the test message from the lab is essential. Because the CDOT workers all unanimously agreed in the descriptive section that they understood and would recommend the pilot SMS program. However, when asked about what some of the problems may be in bringing in the patient there seemed to be quite a few, this could be the explanation for the decrease in time to results, but no time until treatment.

A time-series analysis was used to approach the data from the pre-/post-program. As previously mentioned in Section 3.6, this method was chosen because there are several different observations over a given period of time and the time-series method allows us to capture any variation in SSTD after the program. Later in Section 6.3.4 we will discuss the limitations to this approach, but using Figure 4 it appears there is a delayed impact on SSTD after the program was implemented in December 2011. Since Figure 4 clearly displays a positive impact in SSTD after the program, and there are observations that do not allow the program to have an impact, an exploratory analysis was performed.

First in the secondary analysis, negative SSTD durations (Table 3) in which a patient started treatment before the sputum was sent to the lab are removed. As previously mentioned, these observations are removed because these patients already started treatment, the pilot program is not impacting the results, or cutting down on time to treatment at all.. Taking out durations of  $SSTD < 0$  decreases the time to treatment initiation and the time from when sputum results are sent to be tested to when

the results are received. The primary outcome measure, SSTD shows a trend in the expected direction, with a decrease of 1.84 less days to treatment ( $p=0.701$ , CI -11.34, 7.67). The secondary outcome measures approaches statistical significance without these observations of SSTD  $< 0$ , ( $p=0.055$  -6.90, 0.08) and demonstrates a decrease in time when results are received by 3.41 less days.

After even further analysis excluding both negative durations and results from Chamkar Andong – Chamkar Kaosu HC made both outcomes even more statistically significant. Observations from Chamkar Andong – Chamkar Kaosu HC were excluded in this analysis because the substantial differences in patients in the pre-/post-program groups. In eliminating the observations from Chamkar Andong – Chamkar Kaosu, there were no individual effects from the HCs, which may have caused some confounding in the main analysis. Excluding the observations from Chamkar Andong – Chamkar Kaosu HC, increased the impact of the pilot SMS program and decreased both outcomes, cutting down on time to treatment by 5.72 less days ( $p=0.057$  CI -11.63, 0.18) and time results were received by 3.61 less days ( $p=0.073$  CI -7.56, 0.35) .

Theoretically a decrease in any duration during the time that a patient is infective could be beneficial; however this depends on the setting and interaction with other people. A further analysis of cost-benefit would help answer whether or not this impact is effective enough to justify the program. If, as the descriptive analysis suggests, the SMS-system is easier to use and less expensive than the paper-based system than perhaps this decrease in time to results received would be deemed cost-effective.

In the exploratory section, after SSTD > 0 and Chamkar Andong- Chamkar Kaosu are removed, the decrease in time until treatment is approaches significance at a decrease of 5.72 days (CI -11.63, 0.18). This is very exciting, although the sample size is limited, cutting down on when the patient initiates treatment may justify the program. A bigger study, involving all 15 HCs and a larger timeframe needs to be researched further to see if these numbers are valid.

## **6.2 Discussion on Secondary Objective Analysis**

In general it appeared that both HC and CDOT workers would recommend the TB Care SMS System in the future over the old, paper-based system. This opinion was unanimous in the quantitative results and vast majority of HC and CDOT workers like the SMS program overall. Both qualitative and quantitative data backed up these opinions and overall consensus that the program had done a good job in meeting its objectives on cutting down the time it took to start treatment.

As far as demographics, most CDOT workers were males in between the ages of 45 and 55 years old, and most had at least lower secondary education. The majority of the HC workers were male as well, between the ages of 45 and 55, and all, except one had upper secondary education. 100% of these HC and CDOT workers stated that they were trained on the SMS, understood it, and believed it to be a better system than the old program.

It is very important to note both the CDOT and HC worker perceptions of the SMS program because ultimately they are the ones who are using the system on a daily

basis. Most reactions were extremely positive, and not very many responders had anything negative to say about the program, besides suggestions for improvements. It might be interesting to measure in the future what the lab users' perception of the SMS program is, and if they find it compatible. For now it seems that the current users of the SMS program are extremely content with it and think that it significantly impacts the time to diagnosis. The ultimate compliment for them is to recommend it to their colleagues in other HCs, and all have responded that they would recommend the TB Care SMS System in the future.

### **6.3 Study Limitations**

The main study limitation is that the analysis was a retrospective collection of data collected for public health programmatic activities, not data collected for research purposes. In addition, our overall sample size is small, and we had few numbers of HC's sampled and uneven contribution of data from HCs in the pre- and post-SMS periods.

#### **6.3.1 Design Limitations**

The TB Care SMS System was implemented starting in December 2011 and data were collected for analysis starting only 6 months' into the program, allowing only limited amount of data to be collected for a pre/post-program evaluation. In order for the pre-program period to be comparable, the collection was also limited to 6 months of data before the program in the same months, between January and June 2011. And although all HCs involved in the pilot SMS System were supposed to start in December,

they were given until January in the data to correct for the initiation of program implementation. This short time frame of pre-/post-program period of only 6 months overall severely limited the data that could be used.

Another limitation was that we only had data from 5 HCs. These HCs were chosen through a convenience sampling based on proximity and ability to coordinate interviews with CDOT workers and HC staff. Likewise, HC staff and CDOT workers who were interviewed were also chosen from a convenience sampling based on familiarity with the pilot SMS program and availability on the day of HC visits. This has an inherent bias in sample selection, but was based on ability to coordinate the program and where the TB Care SMS System has actually been implemented so far, which is only in the Chamkar Leu OD so far.

### **6.3.2 Collection Limitations**

Interviews are always prone to some source of bias, whether from the interviewer or interviewee, so response bias could have been a factor in the answers for the HC worker and CDOT worker survey. The PI of this evaluation is non-FHI 360 affiliated but could have been mistaken for a FHI 360 employee, and therefore could have prompted a certain response bias. Recall bias may have also influenced several answers, as many HC and CDOT workers could not think of many disadvantages to the program, whether because there were none or none could be thought of at that point is unknown.

There may have also been some interviewer bias and translations errors. There was one interviewer and translator who both conducted interviews and translated them from English to Khmer and the responses back again. This may have prompted translation errors either into Khmer or back into English. And although the interviewer/translator was also not affiliated with FHI 360, he could have been mistaken as an employee by the respondents.

Although both the Sputum Sending book and the local TB Register book are supposed to be standardized across all HCs in Cambodia, there may have been some discrepancies in category definitions and understandings. The evidence of this could have been in the SSTD < 0 sums that were encountered. Unfortunately the true reason behind these numbers might never be known or understood.

### **6.3.3 Data Limitations**

Records are prone to human error and upkeep, especially since the data collected is mostly paper-based from the Sputum Sending book and TB Register. This is why 4 observations were removed from primary analysis. These were believed to be the results of clerical errors because the date the labs were sent was chronologically before when the results were received.

In total there were not a lot of observations that could be modeled, especially after specific data exclusions were made (n = 61). Again this could be quite the contentious point for why strong conclusion cannot be drawn from this evaluation, but remains an important point for reflection as to why there were so many values of SSTD <

0. These conclusions will be discussed in the following sections, but an important point of strong validity might not be able to be made due this strong limitation in the data records.

#### **6.3.4 Data Analysis Limitations**

Although the interrupted time series analysis was the best method of analysis to fit the data, it comes with a few validity concerns. This regression method estimates linear trends over time, if the trend is not linear, as it may not be in this case, than there are larger standard errors. It also assumes that the pilot SMS program had an immediate effect, which in fact it may not have, and the true effects of the program may not be seen until several months later. Since data was collect in early July 2012, then it is possible that the post-evaluation period was not long enough to truly identify the full impact of the program on SSTD or time from labs sent to results received.

## 7. Conclusions and Recommendations

Since the number of actual observations was small, our confidence in the conclusions is limited, but overall it appears that the pilot TB Care SMS System did not have the expected impact on the period that the sputum was sent to the lab for testing until the time the patient started treatment. After removing the negative durations and observations from the Chamkar Andong- Chamkar Kaosu HC, the pilot SMS program had even more of an impact on time from labs sent to results received as well. After removing these observations which did not have opportunity to be effected by the pilot SMS program, the impact of 5.72 less days until treatment after the pilot SMS program is important. These implications could have an important impact on designing and evaluating future mhealth programs in the future. The evaluation stage of designing a program is very critical to its success and needs to be regularly enforced for a program to maintain its true potential and continuously adapt to the needs of the patients. Defining the success of a program is not always defined by statistical significance either, but also the users' perception of the program.

Although this project encountered several data discrepancies it is important that these mhealth evaluations are carried out regularly. In the future it would be better to scale up the size of the evaluation and wait at least a year until after the program is implemented to carry out any kind of evaluation. Having a years' worth of data and

scaling up to more HCs would have been more appropriate for a proper evaluation, especially since the sample size would be bigger and more representative of all 15 HCs currently enrolled in the pilot SMS System. These HCs however were chosen based on the impact of the program would have on HCs without labs attached to their HCs. So therefore the results can only be representative of HCs without labs.

Since there appears to have been severe differences between HCs, and especially in this project with the Chamkar Andong – Chamkar Kaosu HC, these differences should be explored more in-depth. Since an interesting finding was that sex also influenced the impact of the SMS program, researching more about the impact of sex on the outcome of the SMS program should be explored as well. It is a point worth investigating to see if this program affects women more than men in TB treatment outcomes.

Another recommendation for future evaluations of the TB Care SMS System would be to incorporate qualitative data about lab user perceptions. Capturing the lab procedure and opinions firsthand would be a strong component into what exactly is done at the labs. These lab technicians also use the SMS System on a daily basis and therefore would have important insight into problems or success of the program would be.

Having a cost-effectiveness evaluation done on the TB Care SMS System in the future would be important to see if the mhealth impact is truly money saving as many HC and CDOT workers suggested it was. This could have strong implications if this

program is seen to be much more cost-effective than the paper-based system, and could make a better argument for more money allocated to the project in the future.

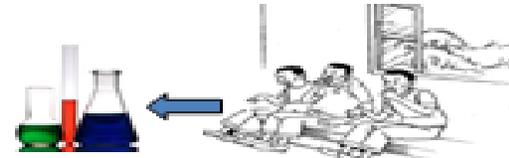
It is also important to note the suggested improvements that the HC and CDOT workers recommended themselves. Having the SMS changed to be in Khmer instead of English might allow for less confusion and allow more Cambodians to use the SMS System if the program is to scale-up. Using mobile phones within the same network could also cut down on cross network communication and cost.

Even though this evaluation study may have had problems in drawing strong conclusions about impact on time to treatment, all of the users interviewed approved of and would recommend this program in the future. User perception is very important in implementing programs, and the fact that all of the CDOT and HC workers unanimously approved of this program are an essential success because they are the ones who use the SMS program on a daily basis. So although the data may not have proved that the TB Care SMS System is having an impact on the time patients are starting treatment, the user-perception is that the program is overall successful.

## Appendix A: Figures

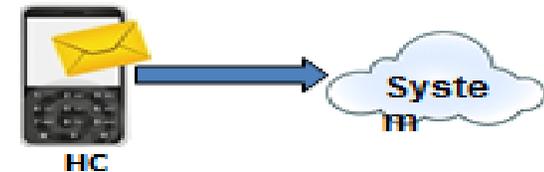
### TB diagnosis process Black: existing, blue: via SMS system

1. Health Center Staff collect sputum from TB suspects and prepare smears



2. Sputum smear delivery

- *Text the sputum smear details and send it via SMS to the system*
- Deliver sputum smears to Lab as usual



TB CARE I

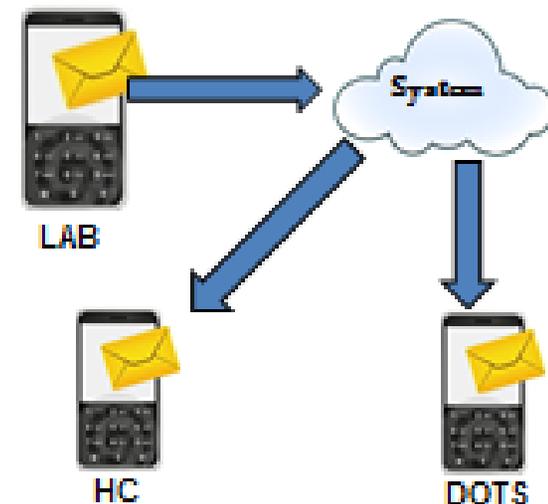
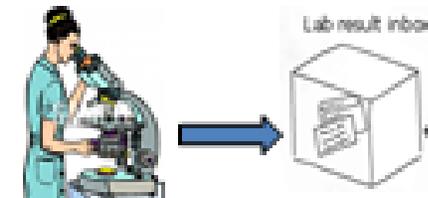


## TB diagnosis process

Black: existing, blue: via SMS system

3. After the smear examination,

- Place the result in the lab result box
- *Text the TB result and send it via SMS to the System*
- *The system immediately distributes the TB result via SMS to HC and C-DOTS volunteer*



TB CARE I



## The TB diagnosis System via SMS system (Con't)

4. The TB result collection takes place as usual

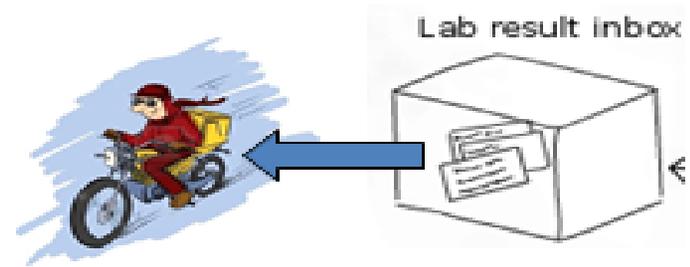


Figure 6: Diagram of Pilot SMS Program in Kampong Cham, Cambodia (Tonsing 2011)

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