Minding the Gap
An Approach to Determine Critical Drivers in the Development of Point-of-Care Diagnostics

Joany Jackman, PhD,* Manny Uy, PhD,* Yu-Hsiang Hsieh, PhD,† Anne Rompalo, MD,‡
Terry Hogan, MPH,† Jill Huppert, MD, MPH,§ Mary Jett-Goheen, BS,†
and Charlotte Gaydos, MS, MPH, DrPH†

Abstract: A point-of-care test (POCT) for Chlamydia trachomatis detection is an urgent public health need. Technological advances in diagnostics have made solutions possible. Yet no reliable POCT exists. Our goal was to address the gap between Chlamydia POCT needs and successful POCT development by determining which characteristics of POCTs are most critical and if any flexibility in the attributes assigned those characteristics exists between technology developer and end user.

Methods: We used a process known as warfare analysis laboratory exercise (WALEX) in combination with design of experiment methodology using discrete choice experiments to describe the attributes of the most realistic rather than the most ideal POCT. The WALEX was conducted as an interactive oral and simultaneous electronic discussion among experts with differing expertise but linked by a common interest in the development of a Chlamydia POCT.

Results: Our studies demonstrated which features of the ideal Chlamydia POCT were considered critical to test acceptance by users and which were open to negotiation. In particular, end users were more lenient on the requirement for the fastest ideal test and the lowest 1-time instrument costs, if the requirement for higher throughput, lowest cost, and vaginal sample source collection was preserved. Design of experiment methods used in forced choice question design provided confirmation of opinions derived from oral and electronic WALEX comments.

Conclusions: The WALEX in combination with discrete choice experiment helped us achieve our goal in identifying the gaps in the Chlamydia POCT and in determining the most realistic solutions to bridge those gaps.

Key Words: point-of-care test, sexually transmitted infection, Chlamydia trachomatis, design of experiments, discrete choice experiment

(Point of Care 2012;11: 130–139)

Despite many years of effort and many valid attempts to develop point-of-care tests (POCTs), there are very few marketed POCTs for sexually transmitted infections (STIs) available today. This begs the question why there is still no POCT available for many of our common STIs especially when there are such technological advances in other fields of medicine? Why do tests developed for bacterial infections such as streptococcal pharyngitis and viruses such as human immunodeficiency virus fail to translate to other STIs? What prevents these rapid tests performed in the clinical laboratory from moving to the personal test market, that is, patients waiting at clinics or home testing? Identifying the key gaps in technology, which are preventing the acceptance or development of tests for the personal POCT market for STIs, was the focus of our investigations. In particular, we wanted to address the apparent gap between the tests being developed by industry and the user’s expectations of a valid POCT for STIs.

Our decision to focus on POCT needs for chlamydia diagnostics was based on the input from our large-scale focus group study and large survey of experts in POCT. Physicians and clinical staff from public and private clinical sites ranked “onsite/within-visit” chlamydia testing as the most pressing need for current clinical diagnostic POCT. Although the current nucleic acid amplification tests (NAATs) meet the requirements for sensitivity and specificity for chlamydia diagnostic assays, current NAATs, which are the clinically accepted assays for chlamydia diagnosis, they are too complicated, too-labor intensive, or not appropriately time sensitive to meet the needs for an in-clinic POCT. In our online survey, which invited STI experts and clinicians to “build their own test,” the characteristics selected were high sensitivity and low cost; however, within a fairly narrow range of time (5–25 minutes), there was no clear preference, suggesting that time was a factor that could be granted some leeway to develop assays to meet the clinical need.

To investigate this aspect further, we used a tool originally developed to bring together experts with a variety of viewpoints to address a common problem known as a warfare analysis laboratory exercise (WALEX). As part of the WALEX, anonymous on-site surveys using discrete choice experiments (DCEs) were used. The goal of these combined processes, WALEX combined with DCE, was to identify the ranges of attributes, which would promote test acceptance and identify the interdependency between them rather than present desirable attributes as discrete independent single values, which developers need to design with rigid adherence. We wished to define the path to the best achievable design today rather than the best theoretical design for the perfect test.

METHODS

WALEX Description

The WALEX process involves facility design, analytical planning, and software to enhance group interaction. As shown in Figure 1, infrastructure, hardware, software, and people are part of the design. The challenge of this process is to capture all...
of the diverse viewpoints and assemble them into supporting documentation. The electronic seminar support system is a suite of software tools that supports collaboration by networking participants through laptop computers. The physical configuration of warfare analysis laboratory (WAL) includes the main seminar area, electronic support of collaborative discussions, easy availability of technical and analytic data, integrated audio and visual infrastructure, and advanced modeling and simulation capabilities. During briefings and moderated discussions, participants can enter comments that can be viewed by all other participants using computer groupware. If necessary, they can enter their comments anonymously. With a large group of participants in this type of setting, the oral debate can range across issues unevenly, leaving some incompletely examined. Some participants dominate discussions by virtue of their authority or personality. Often, sidebar conversations take place between certain participants, distracting from the main issue. The electronic seminar support can overcome these weaknesses of a large group discussion by promoting the exchange of opinions and assessments, with a candor uninfluenced by rank or organizational hierarchy through anonymous comments. The electronic discussion (e-discussion) promotes candid audience input regardless of the participant’s position, personality, or verbal communication skills. It also permits electronic surveying and voting of the audience and provides sophisticated decision analysis tools designed to quantify subjective assessments from the participants.

The WALEX process addressing Chlamydia POCT development was initiated by establishing the parameters of the problem to be addressed related to POCT for STIs. The experts from the Center for POCT STI were interviewed by the WALEX team members with regard to the current standards of STI POCT development. Current standards were discussed, and specific gaps were identified in the design or in the attributes of specific tests. In addition, information from focus groups organized by the center was used to identify areas in which there are perceived gaps in the current need. These issues were used to design the overall problem by asking participants to identify the most critical characteristics in each of the areas for a successful STI POCT. On the basis of the needs assessments, from the focus groups, chlamydia had been selected as the most important STI to target for development of an STI POCT and was used as the subject of the WALEX.

**Participants and Instructions**

Participant recruitment for the WALEX was by-invitation only, and names of 30 participants were recommended by members of the Center for POCT STD, including clinicians, laboratory professionals, and regulatory officials, who had sufficient expertise in STIs; and experts in engineering sensor designs, or personnel, who interacted with the US Food and Drug Administration (FDA). One company currently developing POCT for chlamydia was also invited to the WALEX to provide an

---

**FIGURE 1.** Overview of WALEX process. Schematic of WALEX design (top right) and facility design (lower right). Flowchart of WALEX components interactions and steps (left). Reproduced with permission from John Nolan.®
additional perspective from a commercial developer’s viewpoint. Before the WALEX, all participants were sent a reading list with publications grouped into 4 subject areas: the WALEX process, STI characteristics and needs assessments, POCT design needs, and POCT diagnostic technology.

The WALEX was initiated with a short instructional briefing and overview of the issues and problems, which needed to be addressed during the 4-hour session. A moderator presented the following primary topic areas: Characteristics of POCT/technical design, Manufacturing transition, Risk, and Market acceptance. Each area was supported by a list of questions for group discussion. All discussions and e-discussions were recorded for review and subsequent summation.

WALEX Survey Design and Analysis
Before the WALEX, the survey questions were prepared based on interviews with the center staff and results of the focus group discussions. These inputs were used to design a parameter list and the ranges at which a POCT should operate. Regulatory guidelines for test approval were reviewed and used to determine which parameters were not optional and had minimal federal standards for test approval. This information was used to design a scenario for the choice experiments. Because federal regulations require that the specificity and sensitivity of a new test for STI are not defined by end users or developers, these 2 parameters were fixed in the scenario and not open to choice by the participants as they would be in actual practice. The assumption was that any test FDA cleared and marketed would have to meet these minimal standards and, therefore, was not a matter of choice for this WALEX.

Design of Experiments and DCEs
The design of experiment (DOE) method was used to develop the extremes of each node (parameter) to be used in the force choice questions.10 Discrete choice experiment is a subset of DOEs originally used to develop market surveys. Using $2 \times 2$ matrix factorial design for all the attribute levels listed in Table 1, 648 test points ($2^3 \times 2^2 \times 2^2 \times 2^2 \times 2^2 \times 2^2$) could be represented in as few as 16 choices. Forced choice surveys by design need to be limited to approximately 20 questions because participant fatigue is a key consideration in the use of DCE.11 Most of the choice pairs contained 2 least ideal combinations, and survey participants were forced to select the better of the 2 less desirable choices.

Data Analysis
Data were collected electronically and analyzed using JMP version 8 (SAS Institute, Inc, Cary, NC) with application of Firth’s unbiased estimator. The analysis was conducted by applying Firth’s unbiased estimator available in JMP software, and the results are shown in Figure 2.12 Choice modeling, a form of conditional logistic regression, is a method to use a linear model to model choices based on response attributes and not solely on subject characteristics.13 The effect of likelihood is a graphical tool for ranking causes from most significant (low probability relative to $\chi^2$ value) to least significant (high probability relative to $\chi^2$). The effect likelihood ratio test, similar to a Pareto chart, addresses the factors that have the greatest impact on outcome. In this test, however, the null hypothesis states that the attribute or variable has no effect on the probability of success of a POCT.

Prediction Profiler is a JMP graphical representation of utility and allows one to look for variation in each attribute as an independent and interdependent variable.12 To address the interdependence of each attribute and the effect of compromise, analysis of survey data was evaluated based on its desirability as independent and dependent conditions. Desirability as defined by JMP software is a technique by which multiple attributes can be optimized to obtain the best characteristics for as many attributes simultaneously. As independent variables, desirability for each individual attribute was determined at maximum desirability (1.0). For interdependent variables, desirability is allowed to vary to the optimal level for all factors even if desirability for a single factor is less than its optimal independent value.

RESULTS
Summary of WALEX Discussion Points
Characteristics and associated attributes for use in the choice surveys were selected from inputs obtained from focus groups conducted among health professionals.4 The focus of the WALEX and forced choice surveys was POCT for chlamydia. In prior work, physicians from public and private sector laboratories selected the need for rapid tests for this organism as the top need.5 Under each set of choice questions, Table 1 summarizes the feedback that we received from choices made by health professionals, clinical laboratorians, and companies regarding acceptable features of POCT. In each case, we included the percent of choices from all participants. An example of this is reflected in the choices for instrument assay time or the time from sample to result. One participant stated that “most focus groups say, yeah, they’d like to have five minutes [for a POCT but], 20 minutes is acceptable. But we all know that people sit in emergency

| TABLE 1. Key POCT Characteristics and Their Attributes as Identified by STD Focus Groups |
|----------------------------------|----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Sample Type                      | Hands-on Time, min               | Instrument Process Time | No. Samples per Batch | Instrument Setup Cost, US $ | Cost per Assay, US $ |
| Vaginal swab                     | 5 min                            | 5 min               | 1                | 5000             | 10              |
| Urine                            | 10 min                           | 20 min              | 2                | 10,000           | 25              |
| Cervical/urethral swab           | 1 h/4 h                          | 1                  | 4                | 20,000           | 50              |

© 2012 Lippincott Williams & Wilkins
departments for four hours. [In addition,] “the outside requirement of four hours [gives] a lot more acceptability to different manufacturers”.

The target for populating the WALEX was 20 to 40 participants inclusive of test developers (research engineers and scientists), end users (clinical laboratory directors and physicians), and those who regulate test development (experts with current and past experience with FDA and sponsoring agencies). A total of 27 experts participated in the WALEX. The percentages of attendees who self-identified in the categories of research engineers and research scientists, clinical laboratory directors and physicians, regulatory personnel and government

<table>
<thead>
<tr>
<th>Choice Set No.</th>
<th>Participant Choice Frequency, %</th>
<th>Sample Type</th>
<th>Hands-on Time, min</th>
<th>Instrument Time</th>
<th>Samples per Batch</th>
<th>Instrument Setup Cost, US $</th>
<th>Assay Cost, US $</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>91</td>
<td>Cervical/urethral swab</td>
<td>5</td>
<td>20 min</td>
<td>1</td>
<td>20,000</td>
<td>10.00</td>
</tr>
<tr>
<td>1</td>
<td>9</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>5 min</td>
<td>1</td>
<td>5000</td>
<td>50.00</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>20 min</td>
<td>4</td>
<td>5000</td>
<td>25.00</td>
</tr>
<tr>
<td>2</td>
<td>82</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>4 h</td>
<td>1</td>
<td>20,000</td>
<td>10.00</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>Vaginal swab</td>
<td>5</td>
<td>5 min</td>
<td>1</td>
<td>5000</td>
<td>50.00</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>5 min</td>
<td>4</td>
<td>5000</td>
<td>50.00</td>
</tr>
<tr>
<td>4</td>
<td>48</td>
<td>Cervical/urethral swab</td>
<td>5</td>
<td>4 h</td>
<td>1</td>
<td>10,000</td>
<td>25.00</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>Urine</td>
<td>10</td>
<td>1 h</td>
<td>1</td>
<td>10,000</td>
<td>10.00</td>
</tr>
<tr>
<td>5</td>
<td>64</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>5 min</td>
<td>2</td>
<td>5000</td>
<td>10.00</td>
</tr>
<tr>
<td>5</td>
<td>36</td>
<td>Vaginal swab</td>
<td>10</td>
<td>5 min</td>
<td>4</td>
<td>20,000</td>
<td>50.00</td>
</tr>
<tr>
<td>6</td>
<td>95</td>
<td>Urine</td>
<td>10</td>
<td>5 min</td>
<td>1</td>
<td>5000</td>
<td>25.00</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>Cervical/urethral swab</td>
<td>5</td>
<td>1 h</td>
<td>1</td>
<td>10,000</td>
<td>25.00</td>
</tr>
<tr>
<td>7</td>
<td>95</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>5 min</td>
<td>2</td>
<td>10,000</td>
<td>25.00</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>Urine</td>
<td>5</td>
<td>5 min</td>
<td>4</td>
<td>5000</td>
<td>25.00</td>
</tr>
<tr>
<td>8</td>
<td>14</td>
<td>Cervical/urethral swab</td>
<td>5</td>
<td>5 min</td>
<td>4</td>
<td>5000</td>
<td>10.00</td>
</tr>
<tr>
<td>8</td>
<td>86</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>20 min</td>
<td>2</td>
<td>10,000</td>
<td>10.00</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>Urine</td>
<td>10</td>
<td>5 min</td>
<td>2</td>
<td>20,000</td>
<td>10.00</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>Urine</td>
<td>5</td>
<td>5 min</td>
<td>1</td>
<td>10,000</td>
<td>50.00</td>
</tr>
<tr>
<td>10</td>
<td>38</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>4 h</td>
<td>1</td>
<td>10,000</td>
<td>50.00</td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>Urine</td>
<td>5</td>
<td>4 h</td>
<td>1</td>
<td>20,000</td>
<td>25.00</td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>1 h</td>
<td>2</td>
<td>20,000</td>
<td>50.00</td>
</tr>
<tr>
<td>11</td>
<td>71</td>
<td>Vaginal swab</td>
<td>10</td>
<td>4 h</td>
<td>2</td>
<td>5000</td>
<td>10.00</td>
</tr>
<tr>
<td>12</td>
<td>73</td>
<td>Cervical/urethral swab</td>
<td>10</td>
<td>1 h</td>
<td>4</td>
<td>10,000</td>
<td>25.00</td>
</tr>
<tr>
<td>12</td>
<td>27</td>
<td>Vaginal swab</td>
<td>10</td>
<td>20 min</td>
<td>2</td>
<td>20,000</td>
<td>25.00</td>
</tr>
<tr>
<td>13</td>
<td>5</td>
<td>Vaginal swab</td>
<td>5</td>
<td>1 h</td>
<td>1</td>
<td>20,000</td>
<td>10.00</td>
</tr>
<tr>
<td>13</td>
<td>95</td>
<td>Urine</td>
<td>10</td>
<td>1 h</td>
<td>4</td>
<td>20,000</td>
<td>50.00</td>
</tr>
<tr>
<td>14</td>
<td>41</td>
<td>Cervical/urethral swab</td>
<td>5</td>
<td>1 h</td>
<td>1</td>
<td>20,000</td>
<td>25.00</td>
</tr>
<tr>
<td>14</td>
<td>59</td>
<td>Urine</td>
<td>5</td>
<td>4 h</td>
<td>2</td>
<td>20,000</td>
<td>50.00</td>
</tr>
<tr>
<td>15</td>
<td>86</td>
<td>Urine</td>
<td>5</td>
<td>1 h</td>
<td>2</td>
<td>5000</td>
<td>50.00</td>
</tr>
<tr>
<td>15</td>
<td>14</td>
<td>Urine</td>
<td>10</td>
<td>20 min</td>
<td>1</td>
<td>5000</td>
<td>50.00</td>
</tr>
<tr>
<td>16</td>
<td>14</td>
<td>Vaginal swab</td>
<td>10</td>
<td>1 h</td>
<td>1</td>
<td>5000</td>
<td>25.00</td>
</tr>
<tr>
<td>16</td>
<td>86</td>
<td>Vaginal swab</td>
<td>5</td>
<td>20 min</td>
<td>2</td>
<td>5000</td>
<td>50.00</td>
</tr>
</tbody>
</table>
sponsors, or other were 26%, 18%, 33%, and 22%, respectively. Those who identified themselves in the category of “other” included clinical laboratorians, and industry representatives. Owing to conflict of interest restrictions, 5 of the government sponsors were not permitted to provide responses to the survey questions. Therefore, there is a slight difference in the makeup of the groups who participated in the WALEX and those who responded to the survey questions (33% vs 18%). The other 3 groups consisted of researchers, physicians, and other participants averaged 6 participant per group ±1; thus, their contributions to the survey provided nearly equivalent inputs of 31%, 23%, and 27%, respectively.

Finally, we evaluated the familiarity of the survey participants (n = 22) with the issues associated with chlamydia diagnostics, point-of-care diagnostics, and diagnostic testing. For the most part, the participants stated they were familiar with the use of or the design of point-of-care tests (52%). However, a much smaller percentage of participants were familiar with Chlamydia; 22% of the survey participants were specifically familiar with Chlamydia as represented by those clinicians (9%) and researchers (13%) with expertise in the treatment or study of this organism. The remaining survey participants (26%) were familiar with requirements for acceptance of diagnostistics assays in clinical settings. Before administration of the survey questions shown in Table 2, the WALEX was conducted to address specific topics associated with the development and transition of successful assays to the clinical market. Shown below are the results from the 4 topic areas discussed in detail: technical design of POCT, transition from research and development to testing and manufacturing, risk assessment, and market acceptance.

**Technical Design of POCT**

Key factors discussed included patient acceptance of sampling location and patient willingness to self-sample, sensitivity of sample types based on organism load associated with sampling location, differences in processing requirements based on site, sensitivity versus specificity, and time to result (Table 3). The interdependency of these factors in the design of an appropriate test was evident from the ensuing discussion. Sampling location (vaginal, cervical, penile, urine) and type (swab vs liquid) were affected by inferred sensitivity owing to organism load and dilution factor. Urine, although preferred by the patient community and for the home POCT, was not ideal for chlamydia testing as stated by clinical professionals. To obtain the necessary sensitivity, the urine concentration or the fractionated sample collection (mid stream, first burst, or total) is needed, which adds to the complexity, equipment, and training needed to administer the POCT. Sensitivity and time to result are also affected by administration of Chlamydia POCT as a screen or for confirmation of a diagnosis as acknowledged by participants. A 2-tier test composed of a rapid but less sensitive POCT followed by a slower but more sensitive confirmatory test for all first-tier-negative samples to be modeled after the methodology used for “streptococcal” testing was suggested. An assumption of this model was that higher false-positive rates would be tolerated; this assumption was rejected by some participants because of variations in geographic prevalence rates and because of higher costs. One participant stated “using a specificity under 96% and a prevalence of 1% resulted “in an estimated PPV of 26%,” making “the value of such a test nearly irrelevant.” A final viewpoint expressed was that a “one-size-fits-all” Chlamydia POCT may not be the correct solution.

**Transition From Research and Development to Testing and Manufacturing**

In the next part of the WALEX, the regulatory requirement and preferences regarding the format in which tests are packaged was the focus (Table 3). The most important detail regarding the approval and clearance of the test by FDA is the newest requirements for medical devices inclusive of Clinical Laboratory Improvement Amendments (CLIA)–waived test to exhibit a performance of at least 95% of a currently accepted reference test. Therefore, an assumption of this model was that higher false-positive rates would be tolerated; this assumption was rejected by some participants because of variations in geographic prevalence rates and because of higher costs. One participant stated “using a specificity under 96% and a prevalence of 1% resulted “in an estimated PPV of 26%,” making “the value of such a test nearly irrelevant.” A final viewpoint expressed was that a “one-size-fits-all” Chlamydia POCT may not be the correct solution.

**Risk Assessment and Cost**

Risk in the development and marketing of POCT for Chlamydia was not seen as an issue, although cost per test was
<table>
<thead>
<tr>
<th>Topic Area: POCT Technical Requirements</th>
<th>Variables Discussed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient acceptance of sampling location</td>
<td>Cervix, vaginal, penile, urethral and urine as sites</td>
</tr>
<tr>
<td>Male preference for urine</td>
<td></td>
</tr>
<tr>
<td>Patient willingness to self-sample</td>
<td>Acceptance of self-collection of vaginal swabs by women</td>
</tr>
<tr>
<td>Acceptance and preference of urine (in a cup) by men</td>
<td></td>
</tr>
<tr>
<td>Fewer bathrooms for collection in clinics for urine</td>
<td></td>
</tr>
<tr>
<td>Home testing acceptance of urine</td>
<td></td>
</tr>
<tr>
<td>Sensitivity of sampling site</td>
<td>Organism load of urine, cervical swabs</td>
</tr>
<tr>
<td>Organism load associated with first urine vs entire urine stream</td>
<td></td>
</tr>
<tr>
<td>Glans (male) is an insensitive site to collect by swab</td>
<td></td>
</tr>
<tr>
<td>Sample processing</td>
<td>Requirements for concentration of urine: more equipment, more steps, more training</td>
</tr>
<tr>
<td>Use of self-collection sponge or urine pellet on swab</td>
<td></td>
</tr>
<tr>
<td>Specificity and sensitivity</td>
<td>FDA regulates test approval</td>
</tr>
<tr>
<td>FDA states new test must perform $&gt;95%$ sensitivity of current NAAT Chlamydia test $^{15}$</td>
<td></td>
</tr>
<tr>
<td>Use 2-test system to capture and immediately treat positives and confirm negatives by a more sensitive test</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic nature of Chlamydia is problematic in physician’s choice for testing and syndromic treatment model</td>
<td></td>
</tr>
<tr>
<td>Lower specificity tests may result in faster detection and treatment of positives</td>
<td></td>
</tr>
<tr>
<td>No false-positives required for fast test for Chlamydia</td>
<td></td>
</tr>
<tr>
<td>False-positive and -negative rates are driven by the prevalence of disease in population</td>
<td></td>
</tr>
<tr>
<td>Different Chlamydia disease prevalence rates need different specificity and sensitivities</td>
<td></td>
</tr>
<tr>
<td>Time to result</td>
<td>Patients want result in 5 min but will accept 20 min</td>
</tr>
<tr>
<td>Emergency department physicians will accept up to 4 h to fit with clinic flow</td>
<td></td>
</tr>
<tr>
<td>Public health laboratories want POCT to fit with clinic visit flow ($&lt;1$ h)</td>
<td></td>
</tr>
<tr>
<td>Many patients tested for Chlamydia do not return for results</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Use of screening tests vs confirmatory testing</td>
</tr>
</tbody>
</table>

(Continued on next page)
seen as a significant factor in successful test development (Table 3). Cost per tests in the US $20 to $30 range per sample or for multiplex tests per analyte suggested by developers was summarily rejected by clinicians as unacceptable, particularly if the test was used as a screening test. It was noted by clinician laboratorians that the current NAATs were approximately US $15 per test. Multiplexing analytes as presented by developers as a way to reduce costs was not universally accepted by clinicians attending the WALEX. One clinician noted that, unless disease prevalence was similar for all the analytes, multiplex POCT would not be advantageous and could be difficult to justify for cost savings.

**Market Acceptance**

When queried, the WALEX group, defined as the end user of POCT as clinicians, clinical laboratories, and patients indicating that the design of POCT for Chlamydia, has many potential targets (Table 1). One research stated that adolescent focus groups indicated that they would accept POCT for Chlamydia even if they had higher false-positive rates. Patient privacy issues were noted to be a key driver for POCT acceptance and home testing. Participants described the potential complications of patient-based home testing as a concern when patients self-medicated based on the outcome of home tests. The potential for misinterpretation and the operator errors were seen as negative influences on home testing for Chlamydia. Notably, home sampling with mail in-testing at established centers was viewed as a favorable solution.

**Forced Choice Survey Results**

The frequency of each forced choice within the pair is shown in the second column and reflects the selection by all WALEX survey participants (Table 2). The survey data were modeled using Firth’s unbiased estimator (JMP version 8.0; SAS, Inc) (Fig. 2). By posing a set of choices, which carefully balances the choices in a balanced designed matrix of questions, a quantitative statistical evaluation of the respondents’ true desires is estimated using the bias-corrected maximum likelihood estimator. The parameter estimate indicating the coefficients on a linear regression and the \( \chi^2 \) probability are shown in the lower table. As can be seen in the effect likelihood ratio tests, the smallest \( \chi^2 \) > probability is assigned to the cost per assay, followed by instrument processing time, number of samples per batch (also defined in WALEX as run), and instrument setup cost, and sample type hands-on time just barely made the cutoff for significance (<0.05), although sample type was not determined to be a significant factor based on its attribute choices of 5 or 10 minutes.

The largest negative coefficient in the parameter estimates table is shown for urine as a sample type. This negative bias may be reflective of the WALEX discussion in which the value of urine samples may be compromised by the absence of clinical data indicative of sufficient organism load and absence of appropriate sampling preparation methods for current POCT.

As shown in Figure 2, statistically significant characteristics (<0.05), based on failure of the null hypothesis for each encompass choice variation, according the attributes listed in Table 1, are likely candidates to affect the success of a POCT. The independent effect for the choices of each variable are often called marginals. The sum of the marginals in a particular combination of variables chosen is called the utility of that choice. A graphical representation of this utility function is called the prediction profiler, shown in Figure 3. The prediction profile calculates the utility of a choice set by being able to interactively change the test variables or factors independently from each other in JMP 8. Thus, for this analysis, the following 6 characteristics were the most desirable independent attribute levels (Fig. 3A): vaginal swab, a 5-minute hands-on time, a 5-minute instrument process time, 4 samples per batch, a $5000 instrument setup cost, and a $10 cost per assay, the utility (also called response), were calculated as:

\[
\text{Utility} = 5.209893 - 0.272061 \times (5) - 0.07308899 \times (5) + 5.3264127 \times (4) - 0.00051979 \times (5000) - 0.5308509 \times (10) = 16.88.
\]

In contrast, when choices were forced to select the best combination of attributes, survey participants made their selections based on compromise. Less important ideal attributes were sacrificed to preserve key characteristics. This compromise is represented by the prediction profiler graph shown in Figure 3B. In this case, the maximum utility for the attributes of vaginal swab, a 10-minute hands-on time, a 240-minute instrument process time, 4 samples per batch, a $10,000 instrument setup cost, and a $10 cost per assay were selected. When desirability was maximized, there is no compromise for the desired attributes of higher
throughput (4 samples per batch), lower cost per assay (<$10), and sample type (vaginal swab). In contrast, survey takers were willing to compromise where acceptance of hands-on time increased to 10 minutes, overall assay time (instrument process time) increased to 240 minutes, and instrument costs acceptability slightly increased to $10,000.

Essentially, this tool provided a means to determine exactly where the WALEX participants drew “a line in the sand” beyond which POCTs lacking essential attributes would be rejected and provided a “broader bull’s-eye” for developers to target an acceptable POCT. The idea of a “broader bull’s-eye” is illustrated in a spider chart, which provides a graphical representation of

![Spider chart](link)

**FIGURE 3.** Prediction profiler of the STD survey with the settings for the maximum utility. A, Independent attribute choices (no compromise). B, Interdependent attribute choices (with compromise).

**FIGURE 4.** Spider chart of participant preference for Chlamydia POCT: Each characteristic is shown as a spoke on the wheel. Spokes are organized by preferences where 6 is the most preferred or most significant choice and 1 is the least preferred choice.
relative target size for an acceptable POCT (Fig. 4). The areas within the boundaries define the ranges of attributes or trade space for assay development. Notably, the configuration and area bounded in the spider chart varied by expertise, supporting the WALEX quote that a “one-size-fits-all” Chlamydia POCT may not be the correct solution.

DISCUSSION

Our studies demonstrate 1 approach that can be used to (1) address the causes for the gap between technology solutions and needs and (2) find practical and acceptable solutions by partnering industry, regulatory, and health professionals as unified stakeholders in identifying the most practical path forward. On the basis of our research focus, we used the process of WALEX in combination with DCE to address the needs for better Chlamydia tests. The need for improved methods for detection of chlamydial infections has been well established by our center and a number of other groups for the last decade. The recommendation for POCT has been described, and the implementation of more robust screening has been addressed as a national priority. A key advantage of the WALEX is the opportunity provided to the participants to educate and inform each other from different expert viewpoints. For the WALEX to be successful, the right number and mix of people is critical to a successful outcome. This tool can provide participants with a better understanding of the issues or restrictions faced by developers (industry) and end users (clinicians), while giving sponsors (funding agencies, payers) a voice in the development of a solution. Rigid adherence to narrow performance characteristics by the user community is likely off-putting to commercial developers and may well be a significant cause for the gap between the need for and the development of POCTs. The addition of DCE to the WALEX assisted us in capturing the process of consensus and in validating key parameters in potential technical solutions. In this way, the WALEX process combined with DCE developers may view the challenge of POCT development for targets like chlamydia more favorably, thus attracting more developers and promoting greater success.

Unlike focus groups, the WALEX intentionally mixes experts with differing and sometimes opposing views not for the purpose of “group thinking” but for the purpose of achieving consensus on the best solution or path forward. As a result, the solutions achieved in the WALEX may be different from those of a focus group as demonstrated by our WALEX and DCE methods. As described in our study, acceptable test characteristics could support testing times of up to 4 hours if the cost of the test could be kept to less than US $10. In contrast, our center has conducted studies among focus groups and used surveys conducted among clinicians involved in STI testing who indicated a time window of only 20 minutes. This difference may be attributed to the interaction among WALEX members to compromise on the best practical solution rather than the ideal solution. This trade-off provides developers flexibility during the development process to select the most cost-effective technology options and guidance with regard to technical decisions not only in making a test but also in market acceptance in an appropriate target population.

In summary, we have described a new methodology for developing compromise concessions to a problem using inputs from diverse viewpoints in the affected community. To use this tool effectively, it is important to do adequate preparation before the actual WALEX and include all who may be stakeholders in the outcome. All survey participants had the basis for an in-depth understanding of the characteristics of diagnostic tests, and 74% of the participants were specifically familiar with the needs for POCT or POCT for Chlamydia.

Our study has limitations. One caveat to our studies is that payers (ie, health maintenance organizations, federal medical insurance programs, and insurers) who are stakeholders in this process were not included in our WALEX. We recognize their absence as a source of potential bias in the outcome and are attempting to include them in future WALEX.

We conclude that the WALEX process combined with forced choice surveys (1) is an effective means to rapidly evaluate technological gaps, (2) provides an opportunity for cross-fertilization and better understanding of technology needs from multiple viewpoints, and (3) helps focus a multidisciplinary team on providing practice solutions to technology challenges. Although this WALEX focused participants on the needs of 1 particular POCT technology under development, we will investigate the appropriateness of this tool in providing broader industry guidance and education on critical test attributes by including multiple developers in future WALEX meetings with the possibility that the best solutions may lie in the innovation among multiple technologies. It is hoped that this tool will prove to be accurate and useful in bridging the technology gaps that are inhibiting adoption of successful POCT for targets important to public health such as chlamydia.

REFERENCES