Remote login software and other innovations to enhance scale-up of point-of-care HPV testing in high-burden, low-income settings

Steven Badman
Kirby Institute, University of New South Wales, Sydney, Australia

Abstract
Molecular diagnosis of HPV at the point of care (POC) is an important technological development because the highest rates of HPV infection are often found in low-resource settings (LRS) or very remote locations in high-resource settings (HRS). The burden of HPV-related morbidity and mortality in LRS is high and requires immediate action in order to be contained or eliminated. However, accurate estimates of prevalence and risk factors are not available in many countries, and current HPV testing capacity varies considerably.

Background
Molecular diagnosis of HPV at the point of care (POC) is an important technological development because the highest rates of HPV infection are often found in low-resource settings (LRS) or very remote locations in high-resource settings (HRS). The burden of HPV-related morbidity and mortality in LRS is high and requires immediate action in order to be contained or eliminated. However, accurate estimates of prevalence and risk factors are not available in many countries, and current HPV testing capacity varies considerably.

The scope for same-day HPV test and treat strategies in LRS is often constrained by climate, geography, logistics, infrastructure and funding. However, faster and more portable forms of nucleic acid amplification test (NAAT) technology are now available and can provide molecular POC systems that are able to enhance new approaches to HPV POC test and treat methods. Xpert® (Cepheid, Sunnyvale, CA, USA) is one such system and has demonstrated feasibility in a number of high-burden low-resource settings. Nonetheless, upscaling their use in LRS and very remote HRS presents several major challenges, including:

- Considerable planning and resources are required, plus centralised POC monitoring, data transfer and management;
- Remote locations can make POC test site set-up, training of lay providers and maintenance difficult;
- In-country transport may be unreliable, whether by road or air;
- Constant forward planning is needed to maintain testing continuity and prevent stock-outs;
- Unreliable 110/240v electrical power supply creates frequent disruption of molecular POC testing or related equipment.

These challenges are further exacerbated if travel-test-travel arrangements (or pop-up testing) at different POC clinics/sites on different days is required. While this method is feasible, using this approach requires additional care to preserve the integrity of test instruments and HPV test cartridges.

Based on our experience in remote Australia, Papua New Guinea, the South Pacific region and Myanmar, some innovations aimed at improving the upscaling of POC test and treat strategies in clinic- or community-based settings are presented.

Innovation 1: remote log-in software
We initially trialled the use of a commercial remote access tool (LogMeln, Boston, MA, USA; www.logmein.com) in 2013–2015 during the Ttango 1 trial. Molecular POC testing for chlamydia and gonorrhoea on Xpert® was conducted in 12 remote Indigenous health services in Australia, and it has since been used to good effect in other studies including Ttango 2, which is an upscaled version of the trial, and is now present in 35 remote Indigenous health services. This preloaded secure software provides centralised, secure, internet access to POC testing laptops in real-time. Test operator performance, technical support and data transfer can be actioned as required from hundreds or thousands of kilometres away. A central dashboard provides 24-hour access for other activities such as software upgrades and review of test errors. Internet connectivity can be established using a 3G mobile phone hotspot, in–house WiFi or ethernet cable. In addition, live training sessions are possible via Skype (www.skype.com), GoToMeeting (www.gotomeeting.com) or a dedicated support phone number. Access to additional POC training materials and updates for the Ttango2 programme is provided via a participant log-in section on the study website (Figure 1).

Innovation 2: maintaining power supply in LRS
Currently many LRS locations using Cepheid Xpert® for POC testing rely on uninterruptible power supplies (UPS) to prevent loss of power to assay instruments, but these have several constraints. Examples of the limitations of UPS systems include, but are not limited to:

- The need for one large (sinewave) UPS system to support a single Xpert® IV assay instrument – this provides 1 kW power but weighs 15–30 kg, creating transport problems, especially for pop-up testing events;
- A limited reserve battery time of approximately 90 minutes;
- Significant cost/wastage as lead acid batteries only discharge to 50% of stored capacity and have a 2–3 year life span;
- The requirement for 110/240v mains power as the only method of recharging the UPS.

At present, a small portable lithium–ion power pack (Figure 2) for Xpert® POC testing as an alternative to UPS is being evaluated. The unit (35 x 30 x 15 cm) can power two Xpert® IV assay...
Figure 1. The TTANGO2 study website home page

Figure 2. A small portable lithium-ion power pack for Xpert® POC testing is being used as an alternative to larger uninterruptible power supplies

Software and other innovations

instruments for 5.5 hours, plus concurrent items such as a centrifuge or printer. This approach offers other significant advantages:

- The system has multiple recharging options, such as 110/240v mains electricity, in-car charging, solar or wind power;
- It is easy to connect additional power packs in parallel to provide emergency power to larger lab instruments, including the Xpert® XV1 or other NAAT platforms;
- 12v LED lighting can be plugged in to extend POC care testing after nightfall or during blackouts with minimal power drain;
- The unit includes a centralised management system to prevent over-charging and weighs only 10 kg.

The next step will be to evaluate outreach POC testing in areas without 110–240v mains power, using portable solar/wind power generation for power-pack recharging. The aim is to make Xpert® HPV and other screening accessible for the first time for populations who may have previously been considered too hard to reach or service.

Innovation 3: HPV sample pooling evaluation

We are currently undertaking an HPV pooling evaluation to determine whether two or more HPV samples can be combined into one Xpert® test cartridge. The aim is to see whether HPV screening can be accelerated given the number of negative samples present in any given population and reduce testing costs without a loss of test sensitivity. If HPV sample pooling is successful, we intend to design a model to predict how many HPV samples can be pooled in one cartridge (X axis) based on population prevalence estimates (Y axis). This could result in a sliding scale of pooled samples, with more samples being pooled per cartridge in situations of lower HPV prevalence. A similar model could be applied to pooling some other bloodborne or sexually-transmitted infection sample types for molecular POC testing.

Innovation 4: is there an alternative to ThinPrep® PreservCyt solution?

ThinPrep® PreservCyt is currently used for sample preparation for Xpert® HPV screening; however, it is a flammable methanol-based product and quantities over 500 mL often result in this medium being classified as a dangerous good. This classification requires additional safety packaging and makes shipping by air more difficult and expensive in many countries. Some airlines may refuse to carry this product in large quantities and road transport to testing locations may not always be a viable alternative. Hence the use of ThinPrep® PreservCyt represents a potential barrier to upscaling HPV POC screening, especially in LRS. We are therefore examining alternative HPV cell-stabilising media and are planning to conduct a series of evaluations to determine whether non-volatile media can be used instead for testing HPV samples at the POC. HPV samples sent for cytology may still require preservation in ThinPrep® PreservCyt and guidelines should be followed in accordance with specific country testing policies.

Cepheid does not endorse the testing of alternate specimen types (specimen types that are not cleared/approved/registered by any regulatory body, per the package insert). If you choose to use the assay with alternate testing types, it is your laboratory’s responsibility to validate the assay for each alternate specimen type in accordance with federal, state, and local laws.