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Considerations for the design and implementation of point-of-care technology for use in low- and middle-income countries

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Designing technology for point-of-care use in low- and middle-income countries requires understanding of the underlying barriers that contribute to recalcitrant global problems. The only way to understand those barriers is to work with local experts, otherwise you may wind up solving the wrong problem.

There is no shortage of new point-of-care (POC) devices being developed for use in low- and middle-income countries (LMICs). More than 3,000 articles have been published in the past 10 years describing such technologies, but many factors determine whether a POC technology can be applied to real-world problems.

We sought to create a device for assessing the quality of pharmaceuticals in LMICs, where 10.5–13.6% of finished medicines are estimated to be substandard or falsified pharmaceuticals (SFPs). Upwards of US$30 billion per year is wasted on these products, which harm patients and health-care systems[1,2]. The technology used for the pharmaceutical analysis of SFPs requires expensive instruments and supplies, laboratory space and trained users — things not readily available in many LMICs. Our challenge was to create a technology that could be used outside a laboratory setting, by virtually anyone, to identify SFPs.

Considerations for design

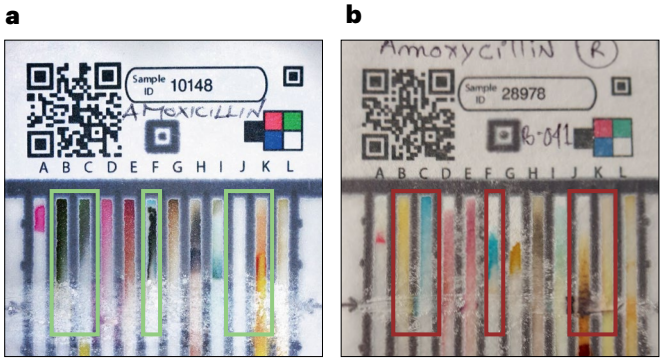
Clearly identifying the questions a POC technology must answer is critical for its successful implementation. For example, many analytical methods are designed to produce accurate results at low detection level. However, pharmaceuticals are high purity products, so low limit of detection is almost never a critical metric for quality assessment. To ensure you are answering the right questions, it is crucial to engage with local experts. Through working with local professionals, we learned about the fragmentation of the supply chains and markets for pharmaceuticals. For example, different batches of one brand of a medicine could contain pills produced by different manufacturers. Additionally, patients often had to buy their own antibiotics or chemotherapy drugs from shops outside of the hospital; those medicines might be unregistered or grey market products. We realized that we would have to develop a method that did not rely on packaging features or libraries of authentic products. Throughout the development and implementation of our screening device we have been fortunate to collaborate with pharmacists, clinicians, drug regulators, health economists, industrial designers, app programmers and computer scientists in the USA, Kenya, Malawi, Ethiopia, Tanzania and Cameroon. Their contributions have allowed us to create together an effective approach to find SFPs in low-resource settings.

Considerations for implementation

Keeping the World Health Organization's REASSURED guidelines for LMIC diagnostic devices[3] in mind, we developed a paper analytical device (PAD) for rapid screening of pharmaceutical dosage forms. The PAD gives results in 3–5 minutes, costs about $0.50 to manufacture and is shelf-stable for months. The PAD has 12 lanes separated by hydrophobic barriers; each lane contains different reagents dried onto the paper, which react with specific functional groups present in the samples. The user rubs the sample across all 12 lanes, then dips the edge of the PAD into water to activate the different colour tests in each lane. This generates a colour barcode that can be compared with standard barcodes. The absence of expected colours indicates a SFP, while the presence of unexpected colours indicates cutting agents like starch[4]. The PAD was assessed by the US Pharmacopeia (USP) Technology Review Program in 2020 and determined to be effective for identifying active pharmaceutical ingredients and detecting fillers. Testers in Ghana and Uganda found it gave reproducible results after minimal training but pointed out that interpreting the colour barcodes was difficult; testers in Laos gave similar feedback[5,6]. To eliminate the need for human interpretation of results, we introduced a mobile app (PADreader for Android) that captures PAD images and uses a neural network to classify drug identity with 97% accuracy[7].

Solving the recalcitrant problem of SFPs is not just about creating a field screening device, but about creating a continuum of analysis from field screening to laboratory testing. To date, thousands of samples have been screened with PADs in LMICs. The Distributed Pharmaceutical Analysis Laboratory (DPAL) connects these samples with high-performance liquid chromatography analysis capacity at dozens of colleges and universities across the world. DPAL has notified regulatory authorities of more than 160 failed products. In one case, capsules labelled as amoxicillin were flagged as suspicious due to the absence of the expected PAD colour barcode for amoxicillin and the presence of starch; subsequent laboratory testing showed that the product contained chalk and starch instead of antibiotics (Fig. 1). In 2019, the PAD flagged three lots of cisplatin in Ethiopia as suspiciously low in cisplatin; laboratory testing confirmed the product had only half of the stated amount of cisplatin[8].

Developing PADs to screen inadequately regulated pharmaceuticals in LMICs positioned us for a reciprocal innovation in the USA, where



Good dosage form | Suspicious dosage form

Fig. 1 | Falsified amoxicillin dosage forms detected by the PAD. Dosage forms of amoxicillin from East Asia were screened on the paper analytical device (PAD). **a**, A good quality dosage form produced characteristic colour responses in lanes B, C, F and K. **b**, A falsified dosage form does not give the expected colour responses, and the black colour in lane J indicates the presence of starch. Follow-up testing confirmed this sample contained no amoxicillin.

unregulated illicit drugs kill more than 100,000 people every year. Harm reduction organizations want to identify super-potent opioids associated with fatal overdoses, but they face a familiar suite of problems: they are not trained chemists, they have limited access to scientific instrumentation and laboratories, and they do not have a lot of money to solve the problem. We developed the idPAD for testing common street drugs in our region; used in conjunction with a fentanyl test strip, it can identify major drug classes and drugs spiked with fentanyl. This technology is being field tested in several cities in the Midwest.

Let the problem lead the research

The PAD has been more successfully applied to real-world problems than most of the hundreds of sensor prototypes published yearly. It was a risky departure from the existing research activities in our laboratory, but we think that taking that risk was a key element behind the project's success. Our goal was to solve a real-world problem, not to advance an academic research programme — although that eventually happened too, because researchers in paper microfluidics and pharmaceutical analysis were generous in sharing their expertise and welcoming us into their research communities. The key to getting beyond academic endpoints was our LMIC partners, who helped us to understand the right questions and constraints to tackle. By letting the problem lead the research, we were able to select appropriate technology at the design stage and find good collaborators for the implementation stage, which has contributed to the success of the PAD in LMIC settings.

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Competing interests

M.L. is an inventor of the PAD (US 9,354,181 B2 issued 31 May 2016) and is the owner of Paper Analytics LLC. K.L.H. declares no competing interests.