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Evidence of temperature cycling in laboratories and clinics located in low-resource settings, and its potential impact on HIV rapid diagnostic tests

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Introduction

Rapid diagnostic tests (RDTs) are low-cost diagnostic methods suitable for use in areas lacking infrastructure such as clean water, electricity, and refrigeration. For this reason, the World Health Organization recommends that RDTs not require refrigeration and be able to tolerate temperatures of at least 40°C and peaks of up to 50°C, which may not only occur during storage but also prolonged transport under tropical conditions.[1] HIV RDTs are commonly specified by the manufacturer for storage between 15°C and 30°C. High temperatures and humidity have been identified as key contributors to the decline in sensitivity of RDTs over time.[2] In low-resource settings, diagnostic kits are typically stored at ambient temperature until use. We tracked actual temperature occurrences over one to two years by placing temperature data loggers in laboratory and clinic locations at eight locations in three developing countries (India, Nicaragua, and Uganda). Our data demonstrate that temperatures frequently rose above 30°C and in many cases remained above 30°C for prolonged periods of time.

Methods

Temperature loggers were placed at eight study sites. At each site, one temperature monitor was placed in a laboratory where diagnostic tests are performed, and another logger was placed in the clinic where patients are treated and samples are collected. A total of four hospital sites were selected in three countries: two locations in India (New Delhi, Hyderabad) and one each in Nicaragua and Uganda. Temperature data were recorded by temperature loggers at intervals that varied from every two minutes to hourly. All data were collected automatically and relayed to PATH headquarters in Seattle, Washington, USA. Two types of temperature data loggers were used: Temperature Data Logger (SM300, Dickson Data) and Track-It™ Data Logger (5396-0101, Monarch Instrument). All data were analyzed by a statistician consultant (Tsuga Analytics, LLC).

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Results

Over 7.5 million data points were analyzed. Ten summary statistics were generated from each of the eight data sets: 1) maximum temperature, 2) minimum temperature, 3) mean, 4) median, 5) standard deviation of temperature data, 6) variance or square value of the standard deviation, 7) total number of data points collected, 8) number of data points above 30°C, 9) percent of data points above 30°C, 10) average duration of time above 30°C. Tables 1 through 4 show summary statistics and box plots of the data.

Table 1: Summary statistics—Nicaragua study site

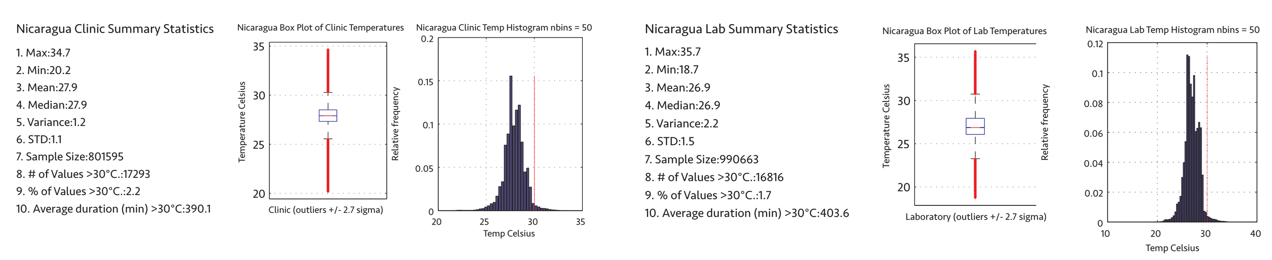


Table 2: Summary statistics—Uganda study site

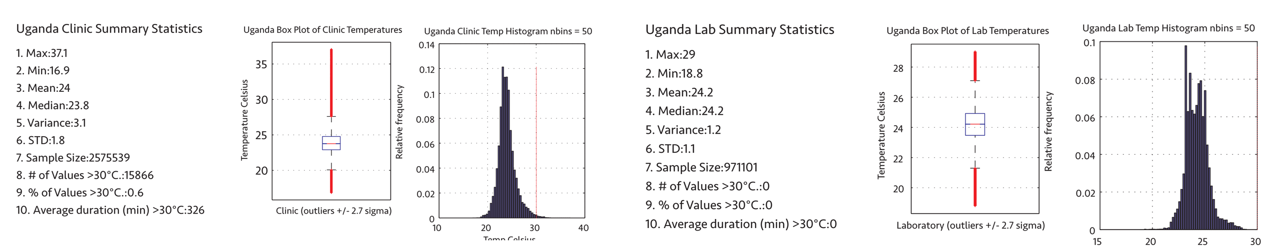


Table 3: Summary statistics—India/Hyderabad study site

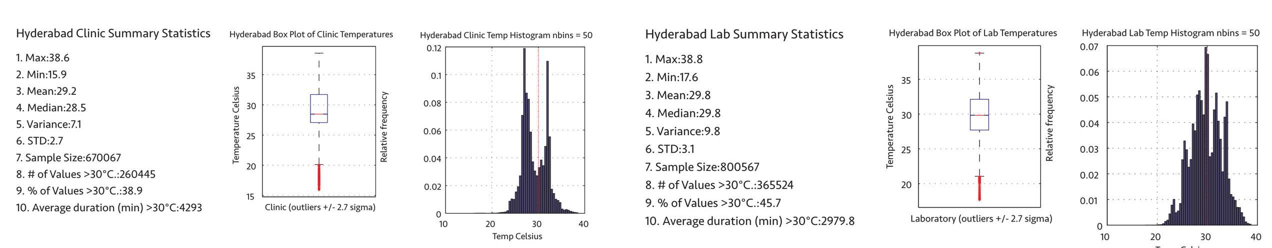
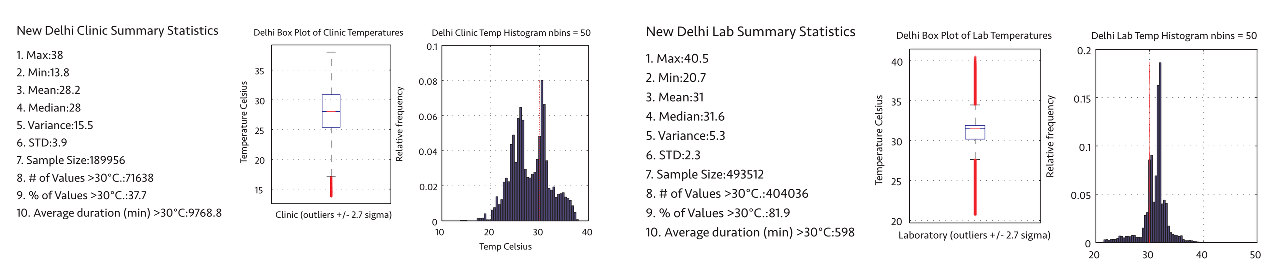
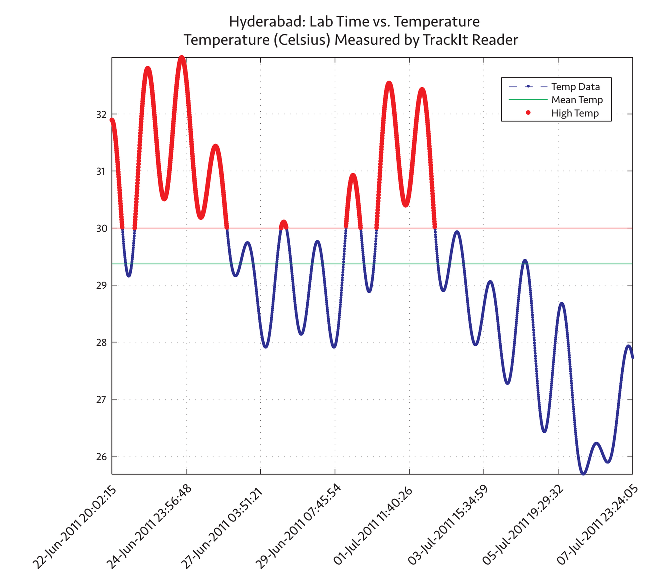


Table 4: Summary statistics—India/New Delhi study site



Results (continued)

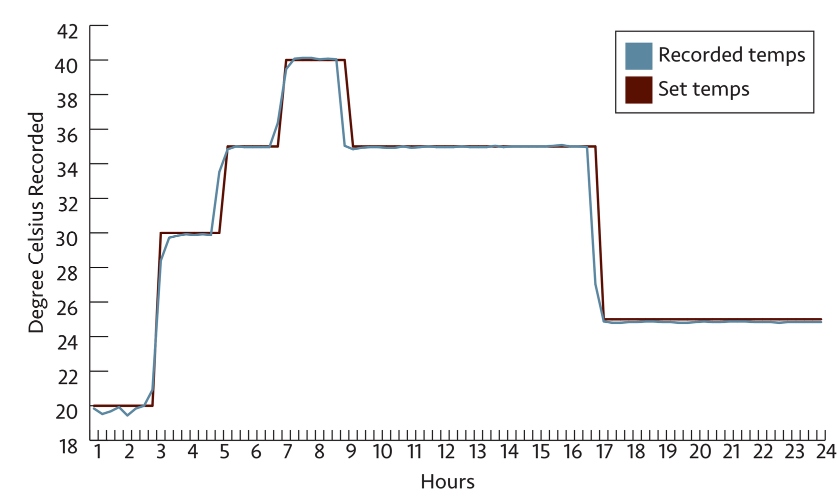
Figure 1: Example of laboratory time versus temperature



The temperature data shown in Figure 1 illustrate that cyclical fluctuations of temperatures are common in these settings. Stability testing and product claims for diagnostic tests intended for use in low-resource settings should be expanded to include temperature cycling and elevated temperatures (up to at least 40°C at the minimum).

Currently our team is investigating HIV RDT performance, both user operation and RDT stress testing. We are conducting stakeholder interviews and running field tests of user assessments. We are also conducting laboratory-based stability and guardbanding studies on HIV RDTs. For example, HIV RDTs are being subjected to a temperature cycling regimen and evaluated for performance. Figure 2 shows the temperature cycling profile currently being used.

Figure 2: Temperature cycling profile—laboratory-based evaluation of HIV RDTs



Discussion

Previous evidence suggests that improperly stored RDTs may underperform in the field and fail to accurately diagnose patients.[3] Ambient temperature in sub-Saharan Africa frequently and routinely goes above the recommended storage temperature for the tests.[4] Potential degradation of RDTs may occur at distribution centers and during transport.[5] The danger of underperforming diagnostic tests is grave, as a 1% error rate in testing one million people could result in misdiagnosis of 10,000 cases.[6] Our collected data demonstrate that temperatures not only reach higher than manufacturers' recommended upper limit of 30°C but can also remain above 30°C for prolonged periods of time. In particular, sites demonstrated an average duration of temperatures above 30°C from 10 hours to 167 hours. While all locations demonstrated a diurnal pattern of temperature fluctuation, some sites consistently showed a slow cooling with elevated temperatures (greater than 30°C) lasting well past midnight. As illustrated in Figure 1, prolonged periods of temperatures greater than 30°C took place for consecutive days and nights.

References

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