Cost Savings of Paper Analytical Devices (PADs) to Detect Substandard and Falsified Antibiotics: Kenya Case Study

Supplementary File

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Appendix 1: Detailed Agent-Based Model Methods

1.1 Modeled batches, brands and sampling

The agent-based model simulated a three-year time period, drawing on the estimated timeline from sampling to removal of substandard and falsified drugs from the market in Kenya and the estimated amount of time amoxicillin can remain on the market before expiration.[1]

Each drug-agent was given a brand, batch, and quality attributes, based on the distribution identified from a prior study on amoxicillin quality in Kenya.[2] Modeled drug-agents were first assigned their brand based on the market share proportion of the 13 brands commonly found in Kenya. Then, each brand was broken up into 36 batches, representing the breakdown of the market into one batch per brand each month over 3 years. The sizes of batches varied, where batch size was determined based on how much of the market each brand occupied, resulting in a market breakdown by brand as seen in manuscript Table 1. Each batch was determined to be a poor-quality batch or a good-quality batch based on the prevalence of tested quality for that brand. We modeled the prevalence of substandard and falsified amoxicillin for each brand based on data from samples collected in 2014-2017 in Western Kenya.[2] Every month over three years, each brand was simulated to release a new batch onto the market. At the end of every month, the expired batches (batches that have been on the market for 3 years) left the market, assuming they have been consumed or removed from the shelf.

We simulated medicine quality sampling by randomly selecting medicines to test in the model. In months 1 to 3 of the model time frame, 40 samples of 100 pills each were selected at random from each of the 13 brands. This quantity of samples is based on the minimum number needed for a lot-quality assurance sampling (LQAS) that would with 95% confidence detect a substandard or falsified product at 10% prevalence.[3-6]

1.2 Estimating Model Outputs

Health outcomes

We used the number of pneumonia cases among children under five in Kenya and rates of care-seeking to estimate the monthly number of pediatric pneumonia treatments with amoxicillin. Then, using the prevalence of substandard or falsified amoxicillin in each scenario we estimated the number of pneumonia treatments using either legitimate or poor-quality amoxicillin.

We simulated that patients who sought care received antibiotic treatment either in a hospital or community setting, resulting in differential costs and case fatality rates.[7] In both locations, we assumed that patients who received poor-quality medicines faced twice the case-fatality rate of those who received legitimate treatments.[7, 8] We also assumed that antibiotic treatment for patients who used medications that were substandard or falsified were prolonged by 5 extra days.[9] We kept track of the number

of deaths, substandard or falsified treatments, and legitimate treatments each month in each scenario.

1.3 Calculating Cost Savings

Cost savings were derived by estimating the difference in costs of testing between using PADs/aPADs versus HPLC. Similarly, incremental returns were estimated by taking the difference of the sum of treatment costs and productivity losses between each scenario and the reference HPLC scenario. We also derived costs per death averted and costs per substandard or falsified treatment averted, with and without productivity losses, as well as the cost per substandard or falsified amoxicillin removed from the market. All cost data were adjusted using inflation rates to represent 2018 US dollars. Future productivity losses were discounted at 3%.

1.4 Sensitivity analyses

We conducted probabilistic sensitivity analysis by varying inputs over 10,000 runs of the model to provide ranges around outputs. We applied three distributional assumptions for data input ranges: 1) beta distribution for probabilities, 2) gamma distribution for costs and treatment lengths, and 3) a triangular distribution for the rate of utilization. Uncertainty ranges of each input parameter were extracted from the literature where available for distributional assumptions. For parameters that did not report uncertainty ranges, we assumed their standard errors at 25% of the mean. We compared the investment costs and health and economic outcomes across scenarios. We report a 90% uncertainty range represented by the 5^{th} and 95^{th} percentiles of the model outpts. This demonstrates the range of possible outcomes one can expect while ranging model inputs.

Appendix 2: Paper Analytical Devices (PADs) Addendum

The color barcode output of the PADs allows for a single device to identify over sixty different drugs allowing for collaborators to select pharmaceuticals of interest to focus on. The barcode is compared to a standard image used to qualitatively identify if the correct API is present. Training on interpretation of these color barcodes is currently required for analysis and is conducted via presentation and demonstration with 10 blinded certification samples and takes about 2 hours to complete. In order to assist with this training requirement, the authors' institution is developing a mobile phone app that captures an image of the PAD for analysis via a neural network. The PADs have been used in Bangladesh, Ethiopia, Kenya, Laos, Malawi, and Tanzania to screen antibiotics, antimalarials, and chemotherapy drugs.[10-13]

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