Cost-effectiveness model of a novel multi-mRNA assay for diagnosis and risk assessment of acute respiratory tract infections and sepsis in the emergency department

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Background
Sepsis is a life threatening and high burden organ dysfunction caused by a dysregulated host response to infection. In the United States alone, over 15 million patient are assessed annually for acute infection and sepsis in the Emergency Department, with Acute Respiratory Tract Infections (ARTI) accounting for approximately 35% of testing burden. Early identification of acute infection and suspected sepsis and initiation of appropriate treatment saves lives. However, diagnosis and risk stratification remain challenging leading to overtreatment in many cases and undertreatment in some cases.

HostDx™ Sepsis, developed by Inflammatix, is a novel diagnostic that measures 30 host genes to accurately estimate the separately likelihoods of bacterial infection, viral infection, and severity (30-day mortality).

This study reports a United States cost-effectiveness model of how a test like HostDx Sepsis may impact clinical care compared to standard-of-care diagnostic accuracy.

Methods
To establish the cost per patient treated from a payer perspective, we first established a baseline model of how physicians may treat patients judged to be at low, moderate, or high risk of bacterial infections, viral infections, and 30-day mortality. We first combined each possible likelihood band for the three axes of bacterial infection, viral infection, and 30-day mortality, resulting in 18 diagnostic possibilities (Figure 1). Each diagnostic possibility was assigned a base case in ED (e.g. treatment vs. no treatment with antibiotics and anti-virals; Figure 1).

For each combination of three diagnostic bands (bacterial/viral/severity), $2^3 = 8$ true states are possible (for instance, a simulated patient could have a true state of non-bacterial, non-viral, and non-mortality). We thus evaluated 8 * 144 = 1152 possible states within this model, each of the 8 true states were possible. Each scenario of the 144 scenarios were thus given outcomes according to whether the action (based on the diagnostic) was right according to the true state (Table 1).

The costs and clinical parameters associated with each action were derived from literature (Table 2).

Proportions of patients assigned to each diagnostic band were based on ROC curves estimated from AUROCs. This yielded a vector of expected patient assignments per band for each of the 144 scenarios associated with a given ROC curve (in other words, how many of 1000 simulated patients ended up in each band). We then used a multinomial distribution to model thousands of possible patient assignment scenarios based on estimated probabilities.

The 30-day outcomes considered in the study for each of the 144 scenarios were expected total cost, incremental cost per life-year saved, antibiotics-free days, and hospital length of stay (HLOS). The cost per scenario was multiplied by the patient assignments (for each of 1000 models) to yield final estimates of costs and clinical outcomes.

For outcomes of standard of care and HostDx Sepsis were directly compared in the same model by varying estimated AUROCs for the three diagnostic axes (bacterial, viral, and mortality).

We performed sensitivity analysis over patient, test, and cost assumptions.

Results
We ran 1,000 versions of the model for standard-of-care and HostDx Sepsis arms. The primary effects of improved AUROCs in the HostDx Sepsis case were to move patients out of a non-informative ‘moderate infection’ band into informative bands (Figure 2). Compared to the base case, HostDx Sepsis resulted in 0.8 fewer hospital days, 1.5 more antibiotics-free days, a 1.6% reduction in mortality; and a cost savings of $1957 compared to standard of care assuming a $200 test price (Table 3). In sensitivity analysis, cost results were most sensitive to the HLOS and estimated hospital costs per day (Figure 3).

Table 1. Example of outcome of actions based on true latent class for the ‘low/low/low’ band

Table 2. Cost & clinical parameter inputs

Table 3. Overall results for the model demonstrating effectiveness of HostDx Sepsis over base case scenario

Limitations
This model lacks intervention clinical trial data. Model assumptions are partially based on market research data. HostDx Sepsis accuracy is based on retrospective data. Treatment assumptions based on a key-opinion-leader input only.

Conclusions
In our model, we compared HostDx Sepsis to standard of care in terms of improved ability to diagnose bacterial and viral infections and to appropriately judge level-of-care needs. The HostDx Sepsis arm demonstrated clinical utility and cost effectiveness versus the current standard of care arm. Improved care is reflected by fewer unnecessary antibiotic prescriptions and side effects and shorter HLOS. Interventional studies are necessary to evaluate the effects of HostDx Sepsis on clinical practice.

Key References