obtained from a centralized, enterprise data warehouse. The study was approved by the University of Tennessee Health Science Center Institutional Review Board.

Results. A total of 1,005,377 patients on antibiotics from 136 facilities were included. Procalcitonin levels were evaluated for 103,913 of these patients. Within the procalcitonin group, 96% had their first procalcitonin drawn within 36 hours of the first antibiotic dose and 70% of patients had a single procalcitonin level drawn. Of those with multiple levels, 23% had levels drawn 24–72 hours apart. Only 32% had antibiotic therapy discontinued within 36 hours of meeting threshold.

Conclusion. There is wide variability among facilities regarding procalcitonin use and monitoring. Baseline procalcitonin levels were drawn appropriately for most patients. Opportunities exist to standardize monitoring and encourage discontinuation of antibiotics when thresholds are reached. The findings of this analysis will be used to aid efforts to establish a health-system wide procalcitonin monitoring protocol to support antibiotic and laboratory stewardship.

Disclosures. **All authors:** No reported disclosures.

2014. TLDA Validation of a Host Response Signature to Discriminate Bacterial, Viral, and Non-infectious Causes of Illness

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Background. Bacterial and viral infections are difficult to clinically distinguish, leading to antibiotic overuse and resistance. Host response signatures are an alternative to traditional pathogen-detection methods to differentiate these etiologies. Several gene expression signatures have been described although performance in ambiguous clinical phenotypes is unknown. Here, we validate a host response signature and explore its performance in microbiology-negative and co-infection cases.

Methods. RT-PCR taqman low-density array (TLDA) was used to measure 87 gene targets in a training cohort of 151 samples from patients with microbiologically confirmed and clinically adjudicated phenotypes (48 bacterial; 54 viral; 49 non-infectious illness [NI]). This data were used to construct three distinct classifiers: bacterial vs. nonbacterial; viral vs. nonviral; and non-infectious vs. infectious. This model was then applied to 75 subjects with co-infection and 40 suspected bacterial cases without microbiological confirmation.

Results. Leave-one-out cross validation on the training cohort demonstrated AUC values of 0.85, 0.89, and 0.88 for bacterial, viral, and NI, respectively. In 40 subjects with microbiology-negative bacterial infections, a bacterial or co-infection signature was present in 72%. Of 75 subjects with co-infection, 53 included a bacterial infection following recent viral infection and 22 were bacterial infections in patients with chronic viral infection (e.g., HCV, HIV). Bacterial infection and co-infection were successfully identified in these varied scenarios.

Conclusion. This gene expression signature distinguished bacterial, viral, and noninfectious causes of illness. The host response was able to confirm the majority of suspected bacterial infection without confirmatory microbiology but also highlighted a viral response in many. Furthermore, the use of distinct viral and bacterial signatures was capable of identifying co-infection. Such a host gene expression strategy, when translated to a clinically useful platform, can offer new insights into the etiology of both simple and complex cases that are not currently available.

Disclosures. **G. S. Ginsburg**, Host Response Inc.: Board Member, Founder, Scientific Advisor and Shareholder, Stock (currently worth <$100). **C. W. Woods**, Host Response: Founder, Licensing agreement or royalty; Qvella: Collaborator, Research support; BioFire: Collaborator, none. **E. L. Tsalik**, Host Response, Inc..: Founder, Equity.

2015. Host Gene Expression Identifies Infectious Triggers of Asthma Exacerbation

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Background. Asthma exacerbations often occur due to infectious triggers. However, determining whether an infection is present and whether it is bacterial or viral remains clinically challenging leading to antibiotic overuse. A diagnostic strategy that clarifies these uncertainties can enable personalized asthma treatment and mitigate antibiotic resistance. Host gene expression is a promising alternative to pathogen-detection methods.

Methods. Forty-six patients presenting to the emergency department with asthma exacerbations were enrolled. Cases were clinically adjudicated as having bacterial, viral, or non-infectious etiologies. RT-PCR taqman low density array (TLDA) was used to quantify 87 gene targets, followed by logistic regression modeling to define class. Etiologies were correlated with clinical information including symptoms and antibiotic prescriptions.

Results. Most clinical parameters were similar between groups including duration of symptoms, presence of sick contacts, and severity of nasal symptoms, cough, headache, throat discomfort, and malaise. Only fever/chills ($P = 0.006$) and a composite of all symptoms ($P = 0.02$) were significantly different. In contrast to clinically adjudicated phenotypes, host response signatures identified very few bacterial triggers. Notably, none of the adjudicated bacterial cases had positive confirmatory microbiology. Instead, 29 and 57% were identified as having a viral infection or no infection, respectively. Despite the absence of bacterial infections identified using host gene expression, antibiotics were prescribed in 47.8% of all cases.

Conclusion. Host response signatures indicated that asthma exacerbation is infrequently caused by bacterial infections, even when clinical adjudications suggest this to be the case. Instead, most are either of viral or non-infectious etiologies. Despite most cases being classified as nonbacterial, empiric antibiotics were prescribed nearly half the time. A host gene expression approach can offer clinically useful diagnostic information to guide more appropriate antibiotic use among patients with asthma exacerbation.

Disclosures. **G. S. Ginsburg**, Host Response Inc.: Board Member, Founder, Scientific Advisor and Shareholder, Stock (currently worth < $100). **C. W. Woods**, Host Response: Founder, Licensing agreement or royalty; Qvella: Collaborator, Research support; BioFire: Collaborator, none. **E. L. Tsalik**, Host Response, Inc.: Founder, Equity.

2016. TaqMan Multiplex PCR of a Seven-Gene Host Biomarker to Discriminate Bacterial from Viral Infections

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Background. Acute infections are among the most frequent diagnoses in outpatient care settings. Early, accurate and rapid differentiation between viral and bacterial infections is critical to guide the choice of antimicrobial treatment, improve patient outcome, and to ensure antimicrobial stewardship. Current microbiological offerings rely on direct pathogen detection, which is limited by insufficient accuracy. Recently, host response-based molecular diagnostics have been considered as a novel alternative or complimentary approach. We have previously developed and validated a seven-gene signature set (higher in viral infections (*IFI27*, *JUP*, and *LAX1*) and higher in bacterial infection (*HK3*, *TNIP1*, *GPAA1*, and *CTSB*) that accurately discriminated between viral and bacterial infections (in six validation cohorts, summary ROC AUC of 0.91 (95% CI, 0.82–0.96). We here describe the development of a rapid multiplex HostDx™ Fever, a seven-gene host response biomarker PCR assay that discriminates bacterial from viral infections.

Methods. To translate the microarray-derived gene set into a rapid and easy to use assay to be run on an automated PCR instrument, TaqMan® assays were designed, multiplexed and optimized for each of the seven targets. Data were then compared with NanoString® and an ultrafast qPCR platform, respectively.

Results. Seven TaqMan assays were divided into two multiplex reactions, one 5-plex and one 4-plex. KPNA6 was included as housekeeping control in each of the two multiplexes. Ten clinical samples from healthy subjects (3) or patients with confirmed viral (4) or bacterial (3) infections were tested in parallel on three platforms: regular qPCR, an ultrafast qPCR and NanoString platform. We found a high degree of concordance with $R > 0.95$ between TaqMan and NanoString platforms, and $R > 0.94$ between TaqMan and the ultrafast qPCR platform. Ultrafast qPCR results were obtained in 12 minutes.

Conclusion. The discovered seven-gene set was validated and allows for robust discrimination between bacterial and viral infections. Multiplexing permits are more cost-effective method of testing. As a rapid test, HostDx™ Fever could assist in improved decision making for outpatients with suspected acute infections.

Disclosures. **W. Nie**, Inflammatix Inc.: Employee, Salary. **D. Rawling**, Inflammatix Inc.: Employee, Salary. **M. Eshoo**, Inflammatix Inc.: Employee, Salary. **P. Khatri**, Inflammatix Inc.: Board Member, Equity. **J. Romanowsky**, Inflammatix Inc.: Employee, Salary. **O. Liesenfeld**, Inflammatix Inc.: Employee, Salary. **T. Sweeney**, Inflammatix Inc.: Employee, Salary.

2017. Improving Timely Diagnosis of Meningitis and Encephalitis: The Effectiveness of Online CME

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Background. Timely and accurate diagnosis of meningitis and encephalitis not only guides the patient care strategy, but can reduce inappropriate antibiotic use, support antimicrobial stewardship, shorten hospital stays, and decrease morbidity and mortality.

Methods. To address knowledge and competence gaps among ID specialists, a CME/CE-certified. Thrity-minute, video-based, multidisciplinary panel discussion

was developed and posted online on August 2, 2017. Featuring three faculties with therapeutic expertise, the activity addressed: Distinguishing characteristics of various diagnostic methods; considerations when interpreting test results; and applying findings to patient care decisions Educational effectiveness was assessed with a repeated-pairs pre-/post-assessment study design, in which each individual served as his/her own control. Responses to three multiple-choice, knowledge/competence questions and 1 self-efficacy confidence question were analyzed. A chi-squared test assessed changes pre- to post-assessment. *P* value of <0.05 is statistically significant. Effect sizes were evaluated using Cramer's V (<0.05 modest; 0.06–0.15 noticeable effect; 0.16–0.26 considerable effect; >0.26 extensive effect). Data were collected through September 7, 2017.

Results. A total of 4,712 healthcare providers, including 3,317 physicians have participated in the activity. Data from ID specialists (n = 266) who answered all pre-/post-assessment questions during the study period were analyzed. Significant improvements were observed overall (P = 0.0002; V = 0.156) and in several specific areas of assessment (figure). Following activity participation, 29% of ID specialists indicated increased confidence in diagnosing meningitis and encephalitis using rapid molecular tests and 89% of ID specialists indicated a commitment to incorporate one or more changes into practice. Finally, the findings also uncovered educational needs that are the focus of ongoing interventions.

Conclusion. Participation in this online education significantly improved ID specialists' knowledge and competence with regard to using rapid molecular tests to diagnose meningitis and encephalitis. These findings highlight the positive impact of well-designed online education.

Assessment of Educational Effectiveness			
Area of Assessment	% relative improvement (% of ID specialists selecting the correct response at pre- vs post-assessment)	*P*-value for change	Cramer's V for the magnitude of the change
Evaluate the clinical implications of findings from single- vs multiple-pathogen tests	8% improvement (86% vs 93%)	*P*=NS	V=0.103 (Noticeable)
Interpret diagnostic findings and recognize the need for follow-up testing to distinguish between latent and active infections	25% improvement (59% vs 74%)	*P*=.0205	V=.169 (Considerable)
Identify key characteristics that differentiate rapid molecular tests from traditional diagnostic methods for meningitis and encephalitis	29% improvement (62% vs 80%)	*P*=.0064	V=.169 (Considerable)

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2018. Host Gene Expression Classifiers Distinguish Bacterial and Viral Infections in Sri Lankan Patients with Acute Febrile Respiratory Illness

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Background. Acute febrile illness is a frequent cause of hospitalization in the tropics and often presents with respiratory symptoms, even when caused by non-respiratory pathogens. Previously, host-based gene expression signatures accurately identified acute respiratory infections as being bacterial or viral in a U.S. cohort. We determined signature performance in a Sri Lankan cohort with acute febrile respiratory illness (AFRI).

Methods. We enrolled patients with AFRI in Sri Lanka from July 2012 to May 2013 and collected nasopharygeal swabs, acute/ convalescent sera, and blood in PAXgene RNA tubes. Bacterial (*Orientia tsutsugamushi*, *Leptospira* spp.) and viral (influenza A/B, dengue) infections were confirmed using polymerase chain reaction, virus isolation, enzyme immunoassay, and/or microscopic agglutination testing. We extracted total RNA and performed host RNA sequencing (Illumina). We aligned reads to hg38 reference genome using Bowtie2, quantified at isoform level using Express version 1.5.1, and normalized using trimmed-mean normalization. The original model estimated three classes and separate signatures predicted bacterial infections, viral infections, and non-infectious illnesses. Regularized regression was used to predict bacterial and viral infections based on prior signatures. Accuracy was estimated using leave-one-out cross-validation.

Results. Among 43 patients with viral infections (14 dengue, 29 influenza) and 16 patients with bacterial infections (six *Leptospira* spp., 10 *O. tsutsumagushi*), median age was 37 years (IQR 23–51) and 49% were male. Of five respiratory symptoms (cough, sore throat, rhinitis/ congestion, shortness of breath, and pain with breathing), median (IQR) number of symptoms was 2 (1–2) for influenza, 2 (1–2) for dengue, 2 (2–3) for *Leptospira* spp., and 1.5 (1–2) for *O. tsutsumagushi*. We observed high predictive accuracy in discriminating bacterial and viral infections: AUROC 0.91 for the bacterial and AUROC 0.81 for the viral model. At enrollment, 65% of viral and 50% of bacterial AFRI patients received antibiotics.

Conclusion. Host gene expression classifiers performed well in a Sri Lankan population with AFRI, even with nonrespiratory pathogens that may not be readily identified. Host-based diagnostics may play a critical role in improving diagnostic ability and antibiotic use globally.

Disclosures. **E. L. Tsalik**, Host Response, Inc.: Founder, Equity. **G. S. Ginsburg**, Host Response Inc.: Board Member, Founder, Scientific Advisor and Shareholder, Stock (currently worth <$100). **C. W. Woods**, Host Response, Inc.: Founder, Equity.

2019. Host Gene Expression Signatures for Diagnosis of Acute Respiratory Infections in the Elderly

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Background. Despite advances in molecular techniques the etiology of acute respiratory infections (ARIs) is often difficult to differentiate either at the point of care or with advanced microbiological techniques. There is growing interest in host biomarker assays, including those based on gene expression patterns in circulating cells, to aid in differentiation of viral and bacterial diseases. However, there are concerns about how such tests perform in vulnerable aging populations where host responses are often muted.

Methods. In order to assess performance of gene expression-based biomarkers, we enrolled patients presenting to the emergency department with clinical ARI and selected 184 individuals aged ≤25 and ≥60 years old with proven viral or bacterial ARI. Gene expression in peripheral blood was measured with Affymetrix microarrays. Published viral and bacterial signatures were applied to the data and Bayesian approaches were used to develop novel discriminative models.

Results. We noted a marked decline in signature performance between younger and older individuals in both viral (AUC 0.90 vs. 0.64) and bacterial (AUC 0.91 vs. 0.50) infections. Incorporation of age-related genomic changes was able to restore much of the signature performance in older individuals. When examining the genomic differences driving the drop in signature performance, we found marked perturbations in expression of immunoglobulin genes and pathways driving known immunoregulatory mechanisms that provide novel insights into an age-related decline in ARI-focused immunity.

Conclusion. Pathogen class-specific host-based gene expression signatures offer great promise as diagnostic tools. However, altered immune responses in vulnerable populations such as the elderly are also manifested at the genomic level and can affect diagnostic signature performance. Age-specific alterations in the components of a diagnostic signature can minimize much of this effect, however this work highlights the need for consideration of age during biomarker development for infectious diseases. Furthermore, studies of age-related differences in biomarker performance can lead to important breakthroughs in our understanding of age-associated alterations in immunity.

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2020. Concordance of Direct vs. Indirect Pathogen Detection Using the BioFire® System

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Background. Polymerase chain reaction (PCR) is a highly sensitive and specific method for pathogen detection. While direct methods enable rapid identification, they are limited by pathogen titer, available assays, or sample matrix. Transcriptomic analysis addresses these limitations by measuring systemic host gene expression changes to infections. The BioFire System uses sample-to-answer multiplex PCR that was adapted to detect 42 transcripts differentially expressed during viral and bacterial infections. Here we report concordance between indirect detection of viral respiratory pathogens and the FDA-cleared BioFire® Respiratory Panel 2 (RP2).

Methods. Paired nasal pharyngeal swabs and blood samples were obtained by informed consent from patients with suspected acute respiratory illness. Swabs (COPAN FLOQSwab™) were collected and stored in viral transport media (BD) for BioFire RP2 testing and peripheral blood samples were collected in PAXgene tubes (Qiagen) for testing with the research use only human response (HR) panel. A logistic regression model was developed to classify viral and nonviral positive samples using normalized quantification cycles for each assay. Probabilities of viral infection for each