Impact of a Multiplex Respiratory PCR Test on Outcomes for Patients Presenting with Respiratory Illness in the Urgent Care Setting: A Hybrid-Effectiveness Quasi-Experimental Trial

BioMérieux-Initiated Research Project

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This protocol has been read and approved by:

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INVESTIGATOR PROTOCOL SIGNATURE PAGE

I have read and understand this protocol and will conduct the study in accordance with this protocol, all attachments and amendments, applicable Food and Drug Administration regulations, HIPAA, IRB requirements, and the policies of the institutions where the study will take place.

In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision and providing bioMérieux with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site.

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Investigator:

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(Print Name)

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(Signature) Date (dd/mmm/yyyy)

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(Print Name)

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(Signature) Date (dd/mmm/yyyy)

Upon signing, send a copy of this page to bioMérieux and retain a copy for your files

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1. INTRODUCTION

Antimicrobial resistance (AMR) is a critical public health challenge and a significant global burden.[1] In the United States, most antibiotics are prescribed in outpatient settings, with suspicion or confirmation of a respiratory infection serving as a primary driver of unnecessary antibiotic use. This use is deemed inappropriate in approximately 30% of cases [2]. This estimate differs based on setting and patient population. For example, a study assessing antibiotic use in a Veterans Affairs (VA) hospital demonstrated that 64.2% of patients received unnecessary antibiotics, with diagnoses such as bronchitis or nonspecific upper respiratory infections being the most likely to result in antibiotic use.[3] Importantly, antibiotic overuse is not without consequences, as it is associated with adverse events that frequently lead to emergency department (ED) visits.[2] Regardless of setting, acute respiratory conditions, such as acute bronchitis and rhinosinusitis are associated with the highest rates of inappropriate antibiotic prescribing.[4] In cases of pharyngitis, similar trends have been observed. A 2020 study by Shapiro et al. revealed that while Group A streptococcus (GAS) pharyngitis prevalence is 20-30% in children and 5-15% in adults, antibiotics were prescribed in 57% of cases across these groups. Notably, 50% of patients received antibiotics without prior GAS testing, even though laboratory testing is linked to more appropriate prescribing.[5] In a pediatric study, unnecessary antibiotic prescribing occurred in 58% of outpatient visits for bronchitis or bronchiolitis, with diagnostic uncertainty identified as a key factor driving inappropriate use.[6]

The role of multiplex rapid diagnostic tests (mRDTs) in the inpatient setting has been the focus of many studies. Its role on the outpatient care setting remains less studied. In outpatient settings, prescribing behaviors are influenced by factors such as the lack of an established patient-provider relationship, time constraints, patient satisfaction, and medicolegal considerations.[7] Early evidence from studies implementing mRDTs suggests that molecular respiratory rapid diagnostic tests have the potential to positively impact patient care. In ED settings, studies have demonstrated benefits such as decreased test turnaround times (TAT), reduced lengths of stay, and more appropriate antiviral use.[8],[9],[10] However, the impact on antibiotic use and ED length of stay remains mixed, with clinical decision-making and contextual factors playing crucial roles.[11],[12]

The Centers for Disease Control and Prevention (CDC) provides core elements for outpatient antibiotic stewardship programs (ASP) [13], and studies performed in outpatient settings that leverage elements of these recommendations within multifactorial interventions have shown promise in improving stewardship outcomes. Gerber et al. demonstrated that clinician education combined with audit and feedback improved adherence to prescribing guidelines for bacterial acute respiratory tract infections.[14] Similarly, Finkelstein et al. highlighted the effectiveness of a physician behavior change strategy paired with parental education in reducing antibiotic use.[15] More recently, Stenehjem et al. demonstrated that a multifaceted stewardship approach—including education for both providers and

patients, electronic health record tools, benchmarking, and media campaigns—led to reduced antibiotic prescribing for respiratory infections in urgent care settings.[16]

Performance metrics, such as those from the Healthcare Effectiveness Data and Information Set (HEDIS), play a vital role in evaluating antibiotic stewardship efforts. HEDIS measures, used by over 90% of U.S. health plans, help identify performance gaps. Analysis of 2008-2012 HEDIS data that described antibiotic prescribing for acute bronchitis demonstrated poor performance across insurance plans, with antibiotics prescribed in 80% of adult cases.[17] Recently, a newly validated HEDIS measure has been introduced to assess antibiotic use for respiratory conditions, emphasizing “measurement” (i.e., utilization, improvement) as a core element of outpatient stewardship.[18] This measure has broad support among antibiotic stewardship programs and health plan stakeholders and is used to evaluate care quality for over 200 million individuals.

Implementation science is a relatively recent arm of clinical research that aims to increase the adoption and sustainability of evidence-based interventions.[19],[20] Years of research has demonstrated that innovation uptake relies on contextual factors in addition to effectiveness. To fully understand the impact of diagnostic innovation on clinical outcomes, it is important to consider these elements together.

2. DEFINITIONS

- ABX: Antibiotics
- AMR: Antimicrobial Resistance
- ASP: Antibiotic Stewardship Programs
- CAHPS: Consumer Assessment of Healthcare Providers and Systems, a program developed by the Agency for Healthcare Research and Quality.
- CDC: Centers for Disease Control and Prevention
- CFR: Code of Federal Regulations
- CLIA: Clinical Laboratory Improvement Amendments
- DID: Difference-in-Differences
- DO: Doctor of Osteopathic Medicine
- ED: Emergency Department
- EMR: Electronic Medical Record
- GAS: Group A Streptococcus
- GCP: Good Clinical Practices
- GDP: Good Documentation Practices
- GLP: Good Laboratory Practices
- GMP: Good Manufacturing Practices
- HEDIS: Healthcare Effectiveness Data and Information Set, a set of standardized performance measures used to assess the quality of care provided by health plans.

- IFU: Instructions for Use
- MD: Medical Doctor
- mRDT: Multiplex Rapid Diagnostic Tests
- NCQA: National Committee for Quality Assurance
- NP: Nurse Practitioner
- NPS: Nasopharyngeal Swab
- PA: Physician Assistant
- QC: Quality Control
- R: Respiratory
- PCR: Polymerase Chain Reaction
- SOC: Standard of Care
- ST: Sore Throat
- TAT: Turnaround Time
- TS: Throat Swab
- VA: Veterans Affairs

3. PRODUCT

3.1 Product Name and Intended Use

The BIOFIRE® SPOTFIRE® Respiratory/Sore Throat (R/ST) Panel is a multiplexed polymerase chain reaction (PCR) test intended for use with the BIOFIRE® SPOTFIRE® System for the simultaneous, qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swab (NPS) specimens obtained from individuals with signs and symptoms of respiratory tract infection, including COVID-19; (Respiratory menu) or in throat swab (TS) specimens from individuals with signs and symptoms of pharyngitis (Sore Throat menu). Time from test initiation to result is approximately 15 minutes.

3.2 Product Description

The SPOTFIRE R/ST Panel, designed for use with the SPOTFIRE System, is a PCR based sample-to-answer diagnostic test that simultaneously identifies nucleic acids from 15 different bacterial and viral organisms from nasopharyngeal swab (NPS) specimens, or 14 different bacterial and viral organisms from TS specimens, in transport media collected from individuals with signs and symptoms of respiratory infection or pharyngitis, respectively. The SPOTFIRE R/ST Panel uses a single instrument protocol with different reporting of analytes for the two sample types. Sample type is selected at the time of testing and the system's software controls the analyte reporting based on the selected sample type.

Nucleic acids from the viral and bacterial organisms identified by this test are generally detectable in NPS/TS specimens during the acute phase of infection. The detection and identification of specific viral

and bacterial nucleic acids from individuals exhibiting signs and symptoms of respiratory infection and/or pharyngitis are indicative of the presence of the identified microorganism and aids in diagnosis if used in conjunction with other clinical and epidemiological information, and laboratory findings. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Negative results in the setting of a respiratory illness and/or pharyngitis may be due to infection with pathogens that are not detected by this test, or a respiratory tract infection that may not be detected by an NPS or TS specimen. Positive results do not rule out the possibility of coinfection with other organisms. The agent(s) detected by the SPOTFIRE R/ST Panel may not be the definite cause of disease.

At the clinician's discretion, additional laboratory testing (e.g., bacterial and viral culture, immunofluorescence, and radiography) may be performed when evaluating a patient with possible respiratory tract infection and/or pharyngitis.

The SPOTFIRE R/ST Panel is intended for use by non-laboratory trained healthcare professionals in a facility holding a CLIA Certificate of Waiver (in the United States) or it may also be used by trained medical and laboratory professionals in a laboratory setting or under the supervision of a trained laboratory professional.

The SPOTFIRE R/ST Panel identifies and differentiates the following organism types and subtypes:

Respiratory Menu	**Sore Throat Menu**
Viruses	**Viruses**
Adenovirus	Adenovirus
Coronavirus SARS-CoV-2	Coronavirus (seasonal)
Coronavirus (seasonal)	Human metapneumovirus
Human metapneumovirus	Human rhinovirus/enterovirus
Human rhinovirus/enterovirus	Influenza A virus
Influenza A virus	Influenza A virus/ H1-2009
Influenza A virus/ H1-2009	Influenza A virus/ H3
Influenza A virus/ H3	Influenza B virus
Influenza B virus	Parainfluenza virus
Parainfluenza virus	Respiratory syncytial virus
Respiratory syncytial virus	
Bacteria	**Bacteria**
Bordetella parapertussis	*Chlamydia pneumoniae*
Bordetella pertussis	*Mycoplasma pneumoniae*
Chlamydia pneumoniae	*Streptococcus dysgalactiae* (Group C/G Strep)

Mycoplasma pneumoniae	*Streptococcus pyogenes* (Group A Strep)

4. OBJECTIVES

This research study will use a hybrid effectiveness-implementation type 1 design to assess effectiveness of the Spotfire R/ST assay in the urgent care setting. A hybrid effectiveness-implementation type 1 study primarily focuses on the effectiveness of an intervention (e.g., use of Spotfire R/ST) but also simultaneously allows for the collection of data on the barriers and facilitators of implementing the Spotfire R/ST test in the real-world urgent care setting.

Primary Research Aims of the study are as follows:

Aim 1: Assess the impact of the Spotfire R/ST assay on antibiotic prescribing practices, , patient, and workflow in the urgent care setting.

Aim 2: Identify barriers and facilitators to the adoption and implementation of Spotfire R/ST in the urgent care setting.

In addition to clinical impact data, the study aims to also address the following questions:

1. What barriers and facilitators affect the real-world implementation of the Spotfire R/ST assay when combined with provider and patient education?
2. What challenges arise in delivering the Spotfire R/ST intervention (i.e., Spotfire R/ST + medical education and patient education), and how might they inform broader implementation?
3. What modifications to practice could enhance Spotfire R/ST adoption and effectiveness?
4. What implementation strategies are most promising?

Primary outcome: Antibiotic utilization for respiratory conditions (HEDIS AXR) – The % of episodes for patients one year and older with a diagnosis of a respiratory condition that results in an antibiotic prescribing event. (*Note: while the HEDIS measure includes all patients greater than 3 months of age, AFC's electronic health record (EHR) stores age as whole years. Excluding patients with a reported age of 0 from the baseline data resulted in only 0.03% of observations lost.)*

Secondary outcomes:

- Effectiveness and utilization outcomes:
    - Percentage of episodes for patients one year and older with a diagnosis of acute bronchitis/bronchiolitis that did not result in an antibiotic prescribing event (i.e., the percentage of episodes that were not prescribed an antibiotic) (HEDIS AAB)

- Percentage of episodes for members 3 years of age and older with a diagnosis of pharyngitis, dispensed an antibiotic and received a group A streptococcus test for the episode (HEDIS CWP)
- Percentage of episodes for patients 3 years of age or older with a positive Group A Strep (GAS) test and prescribed an antibiotic
- Percentage of patients with a positive influenza test who receive an antiviral for influenza
- Percentage of patients without a positive influenza test with a clinical diagnosis of influenza who receive an antiviral for influenza
- CAHPS clinician and group survey (patient satisfaction)
- Workflow (specific measures to be determined from pre-intervention qualitative survey with AFC urgent care providers)
- Length of patient visit (from check-in to discharge)

- Implementation outcomes:
  - Reach, effectiveness, adoption, implementation, maintenance (RE-AIM) outcomes

5. BIOETHICS REQUIREMENTS

Pursuant to 21 Code of Federal Regulations (CFR) 56, the study must be registered with and obtain IRB approval or waiver prior to beginning testing. The IRB letter must be provided to bioMérieux, Inc. and a copy retained at the site. No Resistance Consulting Group will be primarily responsible for obtaining this documentation and managing ongoing communications with the IRB as needed.

The BIOFIRE SPOTFIRE system and panels will be manufactured in compliance with Good Manufacturing Practices (GMPs). The study will be conducted in compliance with Good Clinical Practices (GCPs), Good Documentation Practices (GDPs), and Good Laboratory Practices (GLPs).

Protected Health Information (PHI) must not be provided to bioMérieux. Electronic Medical Record (EMR) and survey data shared with bioMérieux must be deidentified and linked by a study-specific identifier as specified in Data Capture Plan.

6. STUDY SCHEDULE

6.1 Pre-Implementation

The pre-implementation portion of the study, including the development and administration of the provider pre-implementation survey, development of the urgent care stewardship intervention, and work with the onsite clinical champion to understand clinic workflow, will take an estimated total of 4 weeks. Additionally, during this period, a bioMérieux Field Application Specialist will install the SPOTFIRE system at the intervention site and provide training of on-site users. Concurrently, members of the bioMérieux Global Medical Affairs and US Medical Affairs teams will provide general and non-product focused educational content on respiratory diagnosis and ASP/antibiotic prescribing best practices. This content will be reviewed and adapted by the AFC team and will be reviewed with the AFC Providers at the intervention site prior to the start of the active intervention phase.

Based on the results of the provider pre-survey, site visit, and discussions with the clinical champion, members of the AFC and bioMérieux research teams will design an AMS intervention bundle to be implemented with the Spotfire assay at the intervention site. This intervention will likely include a bi-weekly audit and feedback process providing peer comparison on antibiotic prescribing to providers, as well as the development of a diagnostic testing and prescribing algorithm designed by AFC to be used by providers in the intervention clinic. Additional AMS or implementation science elements may be included as needed based on the results of the pre-implementation work (i.e., based on barriers and facilitators to adoption that are identified during the pre-intervention period).

6.2 Active Intervention

Patients at both the intervention and control sites will be prospectively enrolled in the study over the course of 12 weeks during peak respiratory season

At the intervention site, subjects meeting the inclusion and exclusion criteria, and who provide consent to participate in the study, will have a respiratory sample tested on the SPOTFIRE R/ST Panel, with results used by the treating clinician to guide management. At the end of the visit, enrolled patients will take a satisfaction survey, based on the AHRQ-validated CAHPS survey. Providers at the intervention site will participate in the AMS and implementation science interventions designed in the pre-implementation phase. Clinicians will be encouraged to perform intervention testing only before considering SOC testing for enrolled patients.

Patients who do not meet inclusion and exclusion criteria or those who do meet inclusion and exclusion criteria but decline participation in the study will receive SOC antigen testing as per standard clinic procedure. Additionally, due to the high volume of patients presenting to the clinics, a monthly enrollment cap will be set to ensure even distribution of patients across the enrollment period. Patients meeting inclusion and exclusion criteria who present to the clinic after monthly enrollment targets have been met will not be enrolled in the study and will be treated according to SOC.

In the instance that providers choose to run SOC testing on intervention group patients (in addition to intervention SPOTFIRE R/ST testing), this data will be collected and analyzed along with all other data

listed in the table below. Clinicians will be encouraged to perform intervention testing before considering SOC testing for enrolled patients.

At the control site and at the discretion of the treating clinician, patients will have their respiratory samples tested on the clinic's usual standard of care (SOC) respiratory antigen tests, with results used by the treating clinician to guide management. Patients at the control site who meet inclusion and exclusion criteria and agree to participate will also take the CAHPS-based satisfaction survey.

See appendix 3 for study flow diagram.

6.3 Post-Implementation

After patient enrollment is completed at the end of January 2026, the medical records of participating subjects (from both the control and interventional sites) will be collated into a report by an AFC bioinformatics team who will extract/collate the relevant data points required for results analysis.

6.4 Study Schedule of Activities

See Appendix 4 for full schedule of activities

7. METHODS

7.1 Site-Specific Information

7.1.1 Description of Study Sites

Two urgent care sites within the American Family Care (AFC) Alabama system were selected for participation. Sites were chosen based in part on baseline comparability (e.g., similar baseline demographics, prescribing rates, policies and procedures, standard of care methods) and geographic distance apart, to reduce contamination of the intervention. Additionally, the baseline antibiotic prescribing rate for each site was compared to confirm that the parallel trends assumption (required for a difference-in-differences analysis) was met. Based on these criteria, the Gardendale and Grove AFC sites were selected. In the baseline period (October 2024 – January 2025), the average antibiotic prescribing rate for Gardendale was 58.0% [95% CI: 56.4%, 59.6%], and the average antibiotic prescribing rate for Grove was 77.4% [95% CI: 75.6%, 79.1%]. The correlation coefficient between the monthly average antibiotic prescribing rate for the two sites was 0.56. Due to the high rate of prescribing at Grove, this was identified as the intervention site.

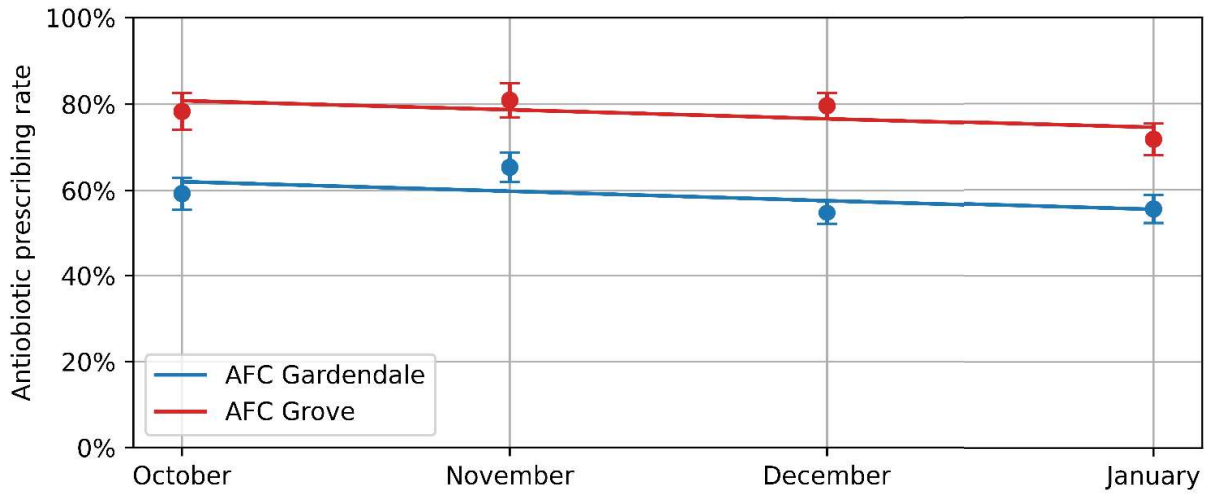


Figure 1: Antibiotic prescribing trends at Gardendale and Grove urgent care sites during the baseline period.

7.1.2 Site-Specific Data Collection

The following information will be collected from each site:

- Information collected via EMR:
  - See Study Data Table in Appendix 5

- Information Collected via provider survey:
  - See Appendix 6
- Information collected via patient survey:
  - See Appendix 7
- General Site Information to be collected:

Implementation Outcomes	
Domain	**Measurement**
Reach	Quantitative: • Total number of consistently employed (non-float) employees that prescribe antimicrobials at the intervention site • Proportion of staff members who participate in the pre-intervention educational session(s) Qualitative • Pre-survey to understand attitudes around both prescribing practices and respiratory mPCR diagnostics, willingness to adopt new technologies and processes/ participate in implementation program.
Effectiveness	Quantitative: • See primary and secondary outcomes for the study (e.g., antibiotic prescribing rates) Qualitative: • Patient satisfaction scores at the control and intervention sites
Adoption	Quantitative: • Porportion of staff at the intervention site who participate in the education session • Results of audit and feedback process pre/post in the intervention site Qualitative • Provider satisfaction, willingness to adopt new technology for respiratory infection diagnosis
Implementation	Acceptability (mixed methods) • The information from the pre survey will be used to inform the bundled intervention and make modifications as necessary during the passive

	implementation period. Pre and post survey results will be compared to assess implementation success •

7.2 Inclusion Criteria

- Patients older than 1 year
- Patients presenting with signs and symptoms of acute respiratory illness including but not limited to bronchitis, bronchiolitis, rhinitis, pharyngitis, tonsillitis, and laryngitis
- First visit for respiratory indication within the study period

7.3 Exclusion Criteria

- Patients younger than 1 year
- Patients for which there is a clinical suspicion of pneumonia (i.e., severe illness on presentation requiring hospitalization or not eligible for urgent care)
- Patients experiencing symptoms for > 10 days
- Patients with significant respiratory comorbidities, including COPD, emphysema, pulmonary fibrosis, diseases causing chronic respiratory tract inflammation, and other conditions
- Patients with other significant oropharyngeal or upper respiratory comorbidities or conditions, including but not limited to nasal deformations, peritonsillar abscess
- Had a previous visit for respiratory indication within the study period

7.4 Subject Enrollment

Subjects who consent to participate shall be assigned a unique Subject Identification Number to de-identify their information. This Subject Identification Number will be captured on the Screening & Enrollment Log and used to identify them on all source documents thereafter.

A record of all screened subjects will be maintained in a Screening/Enrollment Log. The date of screening, results of screening (included or not) and, if not eligible, the primary reason for excluding the subject, enrollment status (enrolled or not) and, if not enrolled, the primary reason will be recorded.

Please note, for the purposes of the study population a subject is considered enrolled at the time in which the informed consent is signed.

7.5 Screen Failures

Subjects that do not meet the eligibility criteria for this study will be considered as screen failures, including subjects who withdraw consent prior to or during specimen collection, and subjects who are withdrawn from the study prior to or during specimen collection by the Investigator for any reason.

If a subject signs the Informed consent form (ICF) but is found ineligible for inclusion in the study prior to or during the specimen collection procedure, the subject will not be advanced any further in this clinical investigation and will receive appropriate alternative care as identified by the Investigator. The subject's signed ICF and completed inclusion/exclusion criteria will be retained by the Investigator and the subject will be notified of their ineligibility.

Screening data, including the reason for exclusion, demographics, informed consent date and adverse event, if applicable, will be collected. The subject's informed consent date, demographics, and reason for exclusion will be documented in the Case Report Form (CRF) and Screening & Enrollment Log.

7.6 Informed Consent

The ICF conforms to 21 CFR Part 50, Protection of Human Subjects. Each subject must read, understand, have an opportunity to have any questions addressed, and sign this form prior to being enrolled in the study. The ICF does not contain exculpatory language.

The Principal Investigator (PI), or a site representative who is appropriately qualified under national law and who has been trained on the protocol, will approach subjects who are potential candidates for participation. They will explain and verify that the subject understands the nature and scope of the study, the procedures to be performed as part of the study, the potential risks and benefits of participation, implications, expected duration, possible treatment alternatives, and follow-up measures if the participation of the subject in the clinical investigation is discontinued. The subject's rights and the applicable damage compensation system will also be explained, and any questions the subject has will be answered. The study will be explained to the subject in lay terms and adequate time will be allowed for the subject to ask questions.

Interested subjects will be invited to participate in the study and will be asked to provide written informed consent prior to initiation of any study-related procedures. Subjects will be assured that they may withdraw from the study at any time and for any reason, without repercussion. If the subject agrees to participate, the ICF must be signed and dated by the subject and by the person who obtained informed consent.

The general process for obtaining informed consent shall:

- avoid any coercion of or undue influence of subjects to participate;
- not waive or appear to waive subject's legal rights;

- use native language that is non-technical and understandable to the subject or his/her legal representative; and
- include personally dated signatures of the subject and the Investigator or a designee responsible for conducting the informed consent process.

The ICF that is used must be approved by the IRB. A dated and signed copy of the ICF will be given to the subject and the original dated and signed consent will be placed in the study binder kept by NRCG.

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the subjects affected in written form. If relevant, all affected subjects shall be asked to confirm their continuing informed consent in writing.

A signed ICF must be obtained from every subject before any study-related procedures beyond Standard of Care (SOC) are performed.

Failure to obtain a signed and dated informed consent form prior to performing study-related procedures constitutes a protocol violation, which must be reported in accordance with all applicable regulations.

7.7 Intervention Sample Collection and Handling

- Sample Requirements
    - Specimen Type
        - NPS collected according to standard technique and immediately placed in 3 mL of transport media.
        - TS collected according to standard technique and immediately placed in 1 mL of transport media.
        - Detailed NPS and TS specimen collection instructions can be found in the SPOTFIRE R/ST Panel Quick Guide.
    - Minimum Sample Volume
        - 0.3 mL (300 µL)
- Sample Storage
    - Patient samples will be labeled and stored per IFU and clinic standard practice after testing has been initiated. Once test results, and a re-test is confirmed as unnecessary, patient samples will be destroyed per clinic procedures.
- Sample Testing
    - All NP or throat swabs collected for the SPOTFIRE R/ST panel will be tested at the collection sites. All specimens should be tested according to the instructions provided with the BIOFIRE SPOTFIRE R/ST Panel test by qualified and trained staff.
- Testing Results
    - All SPOTFIRE R/ST results will be uploaded into the approproate area of the patient's EMR for provider review. Printouts/documentation, including all results (e.g. test records and output files) will be maintained by the intervention site.

7.8 Quality Control Testing

All testing will be accompanied by adequate quality control to verify the accuracy of the test procedure and to monitor performance of various components. bioMérieux will provide quality control from Maine Molecular Quality Controls, Inc., specifically the SPOTFIRE® RSP Negative Control and SPOTFIRE® RSP Positive Control M42638. QC tests should be performed as indicated in the IFU. Any unexpected QC results should be repeated. If the repeat testing still reports unexpected results, the use of the module should be paused, and the site should notify bioMérieux immediately.

Positive and negative QC testing should be performed when:

- Training a new operator
- Receiving a new shipment or lot of SPOTFIRE R/ST Panels test kits
- Receiving a new SPOTFIRE control station or module

A negative QC test should be run monthly to monitor for environmental contamination or more frequently if contamination is suspected. All QC testing and results should be logged in the study binder.

7.9 Diagnostic and Treatment Algorithm

- Using evidence-based medicine and the SPOTFIRE R/ST IFU, AFC will develop a treatment algorithm to assist treating providers in deciding which test the patient's specimen should be run on. Prior to study initiation, AFC will also develop a treatment algorithm based on relevant specialty treatment guidelines (CDC/IDSA/Etc.) which will assist the providers in how best to treat the pathogen(s) identified by the SPOTFIRE R/ST test.
- See Appendix 7 for developed treatment algorithm.

7.10 Data Capture Plan

- All subjects enrolled in the study at the interventional clinic will be de-identified and assigned a single numerical identifier chosen by NRCG. Samples will be numbered incrementally and sequentially, e.g., 001, 002, 003… NRCG will be responsible for maintaining a study enrollment log linking enrolled patient EMR information to patient de-identified study number. No protected health information (PHI) will be provided to bioMérieux. See data table in section 7.1 for a comprehensive list of all information extracted from patient medical records.
- Study-related EMR data will be extracted by the AFC Bioinformatics team for review on a regular basis. The AFC study team will review each dataset to ensure compliance with applicable laws, regulations, completeness, consistency, and accuracy, including a review for missing values and potential deviations from the study protocol. If discrepancies or deviations are identified during this review, AFC will notify bioMérieux and NRCG staff. NRCG will be responsible for evaluating

the issue, documenting any protocol deviations, and initiating corrective and preventive actions as needed. NRCG will involve AFC and bioMérieux staff when necessary.

- Patient surveys will be collected at both control and intervention sites via an iPad (or similar tablet device) and securely transferred and stored via bioMérieux-housed CFR-compliant Microsoft Forms. Provider surveys will only be collected at the intervention site. They will be built and administered within Microsoft Forms and distributed to providers via email.

7.11 Data Analysis Plan

7.11.1 Sample Size and Power Calculation

Based on current literature, a decrease of 10% or more in antibiotic prescribing is considered a clinically meaningful decrease. Additionally, National Committee for Quality Assurance (NCQA) considers a detectable difference for most HEDIS measures to be 10 percentage points (102024 Quality Rating System Measure Technical Specifications). The sample size for this study was calculated using existing AFC data on prescribing rates and patient volume, anticipating an effect size of 10%. A review of historical NCQA HEDIS reports demonstrates that the median AXR (inappropriate prescribing for respiratory infections) and median URI (appropriate prescribing) are approximately 26% and 73%, respectively. The Urgent Care Association estimates that the median patient volume in US urgent cares is 56 patients a day, 45% of which are due to respiratory illness. Preliminary data of antibiotic prescribing in the baseline period were utilized to simulate the sample size required to observe a 10% decrease in antibiotic prescribing at the intervention site using a DID approach. A sample size of at least 350 patients from each site was estimated to be sufficient (approximately 80% power), assuming active intervention results are as stable as the baseline period. To account for attrition, we will aim to enroll 400 patients at both the intervention and control sites.

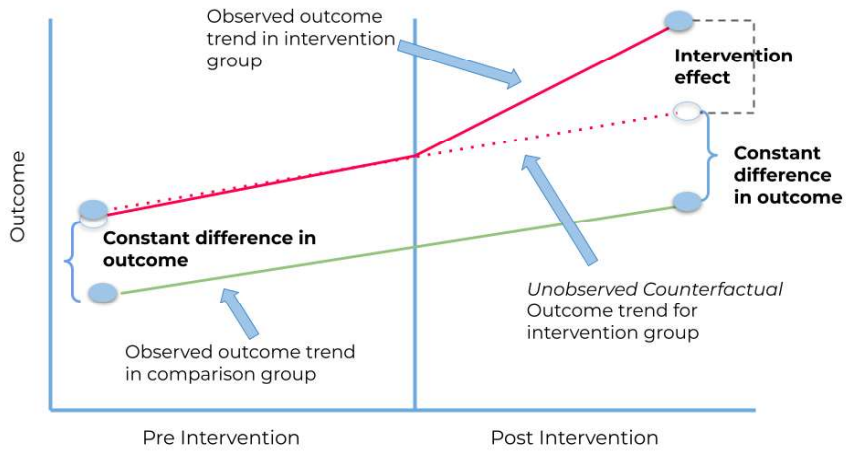
7.12 Statistical Analysis

Data analysis will be performed by bioMérieux.

This study employs a pre-post design with a difference-in-differences (DID) analysis to estimate the treatment effect of implementing the Spotfire R/ST assay paired with training and education. The DID approach compares changes in outcomes over time between the intervention and control groups, accounting for baseline differences and secular trends.

The DID model will estimate the causal effect of the intervention (Spotfire) using an interaction term between time (pre- vs. post-intervention) and treatment group (Spotfire vs. standard of care):

$$Y=\beta0+\beta1[Time]+\beta2[Intervention]+\beta3[Time*Intervention]+\beta4[Covariates]+\epsilon$$



Linear regression will be used for continuous outcomes, model will be adjusted for differing types of outcomes as necessary (e.g., dichotomous outcome = logistic regression, count data or rates = poisson and/or negative binomial)

Covariates will adjust for potential confounders such as demographic and site-specific factors, as appropriate. Likelihood ratio testing will evaluate covariates for confounding effects, ensuring the final model includes only relevant predictors.

Several key assumptions must be met in order to determine appropriateness of DID analysis. The common shocks assumption holds that other phenomena occurring at the same time or after the start of treatment will equally affect the treatment and comparison groups. The parallel trends assumption says that, although treatment and comparison groups may have different levels of the outcome prior to the start of treatment, their trends in pretreatment outcomes should be the same. The parallel trends assumption implies that, absent treatment, outcomes for the treatment and comparison groups are expected to change at the same rate. Thus, any difference in the differences in outcomes between groups can be attributed to the intervention, rather than to differential pre-existing trends in outcomes. The stable composition assumption states that the populations in treatment and control groups must remain consistent across pre- and post-intervention periods and the assumption of no spillover effects states intervention's impact on one group does not influence outcomes in the other group.

The below checklist shares elements of DID analysis that will be tested prior to the final analysis of the model, and how each deviation will be addressed, if necessary.

Confirm that	How to test	What to do if violated
Data exists on study outcomes for at least one observation	Direct observation	N/A

period among groups exposed and not exposed to an intervention, both before and after intervention was implemented		
Trends in outcome performance prior to an intervention are "parallel" between treatment and comparison groups	Test equivalence of linear trends between treatment and comparison groups prior to intervention by testing the significance of the interaction term between the time trend and the treatment group	If multiple comparison groups are available, match treatment to comparison units
Baseline outcome levels are unrelated to expectations for changes in outcomes	For both treatment and comparison groups, test whether baseline outcome is correlated with change in performance across the study period	If multiple comparison groups are available, match treatment to comparison units
Violations to standard statistical assumptions are appropriately addressed	Test for violations of homoscedasticity of standard errors. (Breusch and Pagan 1979; Drukker 2003)	Permutation tests or clustered standard errors will likely result in the most accurate statistical inference when using difference-indifference analysis
Events or factors other than treatment, occurring at the time of treatment, do not differentially affect outcomes for treatment and comparison groups	Not directly testable	N/A
The composition of treatment and comparison groups does not change over the course of the study	Test for difference in observed covariates between treatment and comparison rates before and after the intervention. Test for differential drop-out rates between treatment and comparison groups. (Hausman and Wise 1979)	Control for differences in observed covariates between treatment and comparison rates before and after the intervention
Treatment does not "spill-over" from treatment group to comparison group	Test whether comparison group experiences deviation from existing trend concurrent with intervention	If multiple comparison groups are available, choose alternative comparison group that is not subject to spillovers

Table adapted from HSR: Health Services Research 50:4 (August 2015)

Secondary analysis will apply mixed-methods concepts to combine qualitative survey findings with quantitative outcomes to explore associations and identify barriers and facilitators to implementation.

Subgroup analyses will evaluate intervention effects across demographic and clinical subcategories to detect heterogeneity of treatment effects. Specifically, a subgroup analysis of asthma patients will be conducted.

Metrics specific to the intervention site will be described using RE-AIM dimensions: Reach (proportion of eligible providers and patients exposed to the intervention), Effectiveness (impact on prescribing and satisfaction outcomes), Adoption (proportion of sites/providers implementing the intervention), Implementation fidelity (extent to which the intervention was delivered as intended), and Maintenance (sustainability of the intervention over time).

8. STUDY SUSPENSION OR EARLY TERMINATION

8.1 Procedure for Suspension or Early Termination

The Sponsor may suspend or prematurely terminate this clinical investigation either at an individual investigational site or at all sites. A Principal Investigator, IRB, or regulatory authority may suspend or prematurely terminate participation in this clinical investigation at the investigational sites for which they are responsible.

If suspicion of an unacceptable risk to subjects arises during the clinical investigation, or when so instructed by the IRB or regulatory authorities, the Sponsor will suspend the clinical investigation while the risk is assessed. If an unacceptable risk is confirmed, the Sponsor will terminate the clinical investigation.

The Sponsor will consider terminating or suspending the participation of a particular investigational site or Investigator if monitoring or auditing identifies serious or repeated deviations on the part of an Investigator.

If suspension or premature termination occurs, the terminating party will justify its decision in writing and promptly inform the other parties with whom they are in direct communication.

If suspension or premature termination occurs:

The Sponsor will remain responsible for providing resources to fulfill the obligations from this protocol and existing agreements for following the subjects enrolled in the clinical investigation, and the site's Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her investigational site.

If the study is terminated, bioMérieux must comply with all applicable government regulations. If discontinuation of the study should occur, the Principal Investigator must return all clinical investigation materials, if applicable, to the Sponsor and provide a written statement to the IRB explaining the reasons for the premature termination.

8.2 Procedure for Resuming the Clinical Investigation After Temporary Suspension

When the Sponsor concludes an analysis of the reason(s) for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the Sponsor will inform the relevant parties of the rationale and provide them with the relevant data supporting this decision. Concurrence will be obtained from the IRBs and, where appropriate, regulatory authorities before the clinical investigation resumes. If subjects have been informed of the suspension, the Principal Investigator or authorized designee will inform them of the reasons for resumption.

8.3 Close Out Activities

Close-out activities will be conducted to ensure that the Principal Investigator's records are accurate and complete, all documents needed for the Sponsor's files are retrieved, remaining clinical investigation materials are disposed of, previously identified issues have been resolved, and all parties are notified.

9. MATERIALS/EQUIPMENT

9.1 Provided by bioMérieux:

- 15 kits (each containing 30 pouches and 30 Sample Preparation Reagent Kits)
- 1 BIOFIRE® SPOTFIRE® Control Station
- 2 BIOFIRE® SPOTFIRE® Modules
- BIOFIRE® Pouch Loading Station
- SPOTFIRE® RSP Negative Control M42738 (sufficient quantity for duration of study)
- SPOTFIRE® RSP Positive Control M42638 (sufficient quantity for duration of study)

9.2 Provided by Site:

Supplies necessary for testing that are not specifically listed in **Section 9.1** are the responsibility of the testing site. Supplies and equipment used, but not provided by bioMérieux, Inc., must be within specifications and records must be available upon request (e.g., refrigerator and incubator temperatures, pipettors within calibration, media within expiration dates, etc.). Examples of such materials include, but are not limited to:

- Material to be used for the collection of NPS and TS samples, as defined in the IFU
- 10% bleach or similar disinfectant for cleaning of the Pouch Loading Station and SPOTFIRE system
- 2 tablets for patient surveys

10. TRAINING REQUIREMENT

Training on the protocol, data capture method, and the conduct of the study will be provided by a representative of bioMérieux's Global Medical Affairs department for site personnel involved in the study.

Training on the BIOFIRE SPOTFIRE system and panels will be performed by a representative of bioMérieux field service team.

All training of site and study staff should be logged as deemed appropriate in the study binder.

11. PROTOCOL DEVIATIONS

Conformance to the protocol is essential to the quality and integrity of the clinical study. Every effort should be made to avoid any deviation from the clinical protocol. A protocol deviation is an event whereby the clinical investigator or site personnel did not conduct the study according to the protocol.

Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of human subjects may proceed without prior approval of the Sponsor and the IRB. Such deviations shall be documented and reported to the Sponsor in the EDC within 5 days of knowledge. The IRB should be notified of the deviation as required by IRB reporting guidance.

12. ADVERSE EVENTS

1. **Adverse Events, Serious Adverse Events, and Serious Incidents**

    a. **Definitions**

        i. **Adverse Event (AE):**
        Any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including abnormal laboratory findings) in a subject or user, whether directly related to the investigational device or not. For IVD-MD studies, AEs may arise from:

- Procedures associated with sample collection, i.e.: Nasopharyngeal swab.
- Psychological distress due to study participation or communication of results,
- Inaccurate, delayed, or misinterpreted results that may impact patient management.

        ii. **Serious Adverse Event (SAE):**
        Any untoward medical occurrence that:

- Results in death,
- Is life-threatening,
- Required inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Is a congenital anomaly/birth defect, or
- Represents a serious deterioration in the health of the subject or user, which may include:
- A life-threatening illness or injury,
- Permanent impairment of a body structure or a body function,
- Hospitalization or prolongation of patient management in hospital,
- Medical or surgical intervention to prevent life-threatening illness or permanent impairment.

iii. **Serious Incident:**
In the context of an IVD-MD, a serious incident is any incident that directly or indirectly led, might have led, or might lead to death, serious deterioration in health of a subject, user, or other person or a serious public health threat. This includes incidents resulting from device malfunction, user error due to ergonomic or design issues, or incorrect, delayed, or missed results that have significant clinical consequences.

iv. **Field Safety Corrective Action (FSCA)**
A corrective action taken for technical or medical reasons to prevent or reduce the risk of a serious incident related to an IVD-MD already in use.

b. **Recording of Adverse Event**
All AEs will be recorded in the Case Report Form (CRF) from the time the Informed Consent Form is obtained until the end of the study. The investigator will document onset date/time, resolution date/time, severity, seriousness, relationship to the SPOTFIRE R/ST or related study procedures (e.g.: procedure discomfort), action taken and outcome.

c. **Reporting of Serious Adverse Events and Serious Incidents**

i. **To the Sponsor**
All SAEs and serious incidents, regardless of their relationship to the SPOTFIRE R/ST must be reported to the sponsor within 24 hours of the investigator's first awareness.

ii. **To Regulatory Authorities**
The sponsor is responsible for timely reporting of SAE and FSCA to competent authorities with IVRD Art.82 and applicable national requirements.

iii. **To Ethics Committees/IRBs**
The investigator must report SAEs and serious incidents in compliance with applicable local requirements and EC/IRB policies.

d. **Causality and Expectedness Assessment**
Causality (relationship to the SPOTFIRE R/ST or study related procedures) will be assessed by the investigator using predefined categories (e.g., not related, unlikely related, possibly related, probably related, definitely related). bioMérieux will determine whether the event was expected or unexpected based on Device Risk Analysis and Instructions for Use (IFU).

e. **Follow-up of Adverse Event and Serious Incidents**
All AEs, SAEs, and serious incidents will be followed until resolution, stabilization, or return to baseline, or until they can no longer be reasonably monitored.

13. CLINICAL MONITORING

13.1 Site Monitoring

The study will be monitored to ensure that it is conducted in conformance with the agreed upon Clinical Monitoring Plan to assess continued compliance with the protocol, recognized Good Clinical Practices, FDA's IDE guidance documents, and federal regulations outlined in 21 CFR Part 812. In addition, the monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively.

The study may also be subject to a quality assurance audit by the Sponsor or its designees, as well as inspection by appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during monitoring visits or audits and that sufficient time is devoted to the process.

13.2 Monitoring Activities

Onsite monitoring visits will include Site Initiation Visit and Interim Monitoring Visit.

The intervention site's Investigator will allocate adequate time for monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to the study-related documents and study-related facilities and has adequate space to conduct the monitoring visit.

Monitoring visits will be documented on monitoring visit reports as per Monitoring Plan, and will aim to verify that:

- Compliance with the clinical protocol and applicable regulations is being maintained
- Enrolled subjects are eligible for study participation
- Signed and dated IRB approved ICF's have been obtained from each prospective subject
- Source data is verified and signed-off upon as accurate
- Subject records are accurate and complete
- Subject withdrawal has been documented (if applicable)
- The Investigator and site staff are informed and knowledgeable of all relevant document updates concerning the clinical investigation
- Only authorized individuals are performing study-related functions
- Adequacy of staffing and facilities
- All adverse events are reported to the Sponsor (if applicable)
- All serious and unanticipated adverse device events are reported to the Sponsor and the IRB
- All other required IRB reports, notifications, applications, submissions, and correspondence are maintained in the Investigator's files and are accurate
- Corrective and preventive actions have been implemented (if applicable)
- Maintenance and calibration of equipment relevant to clinical assessments is appropriately performed and documented

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15. APPENDICES

Appendix 1: SPOTFIRE RST IFU
Appendix 2: SPOTFIRE RST Quick Guide
Appendix 3: Study Flow Diagram
Appendix 4: Study Schedule of Activities
Appendix 5: Study Data Table
Appendix 6: Provider Survey
Appendix 7: Patient Survey
Appendix 8: Diagnostic Treatment Algorithm

APPENDIX 1: BIOFIRE® SPOTFIRE® Respiratory/Sore Throat (R/ST) Panel IFU

Document version: 02

Document Date: 07/09/2024

See attached for full document.

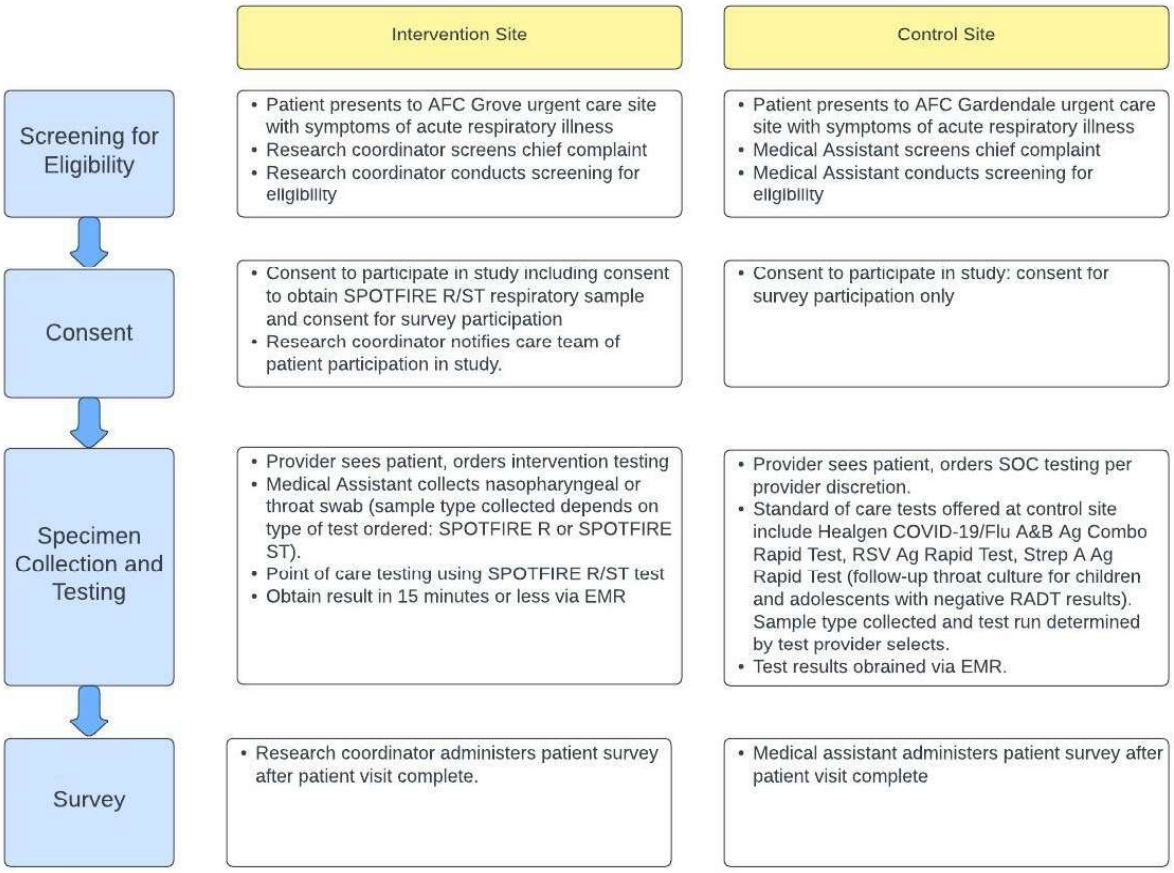
APPENDIX 2: BIOFIRE® SPOTFIRE® Respiratory/Sore Throat (R/ST) Panel Quick Guide

Document version: 02

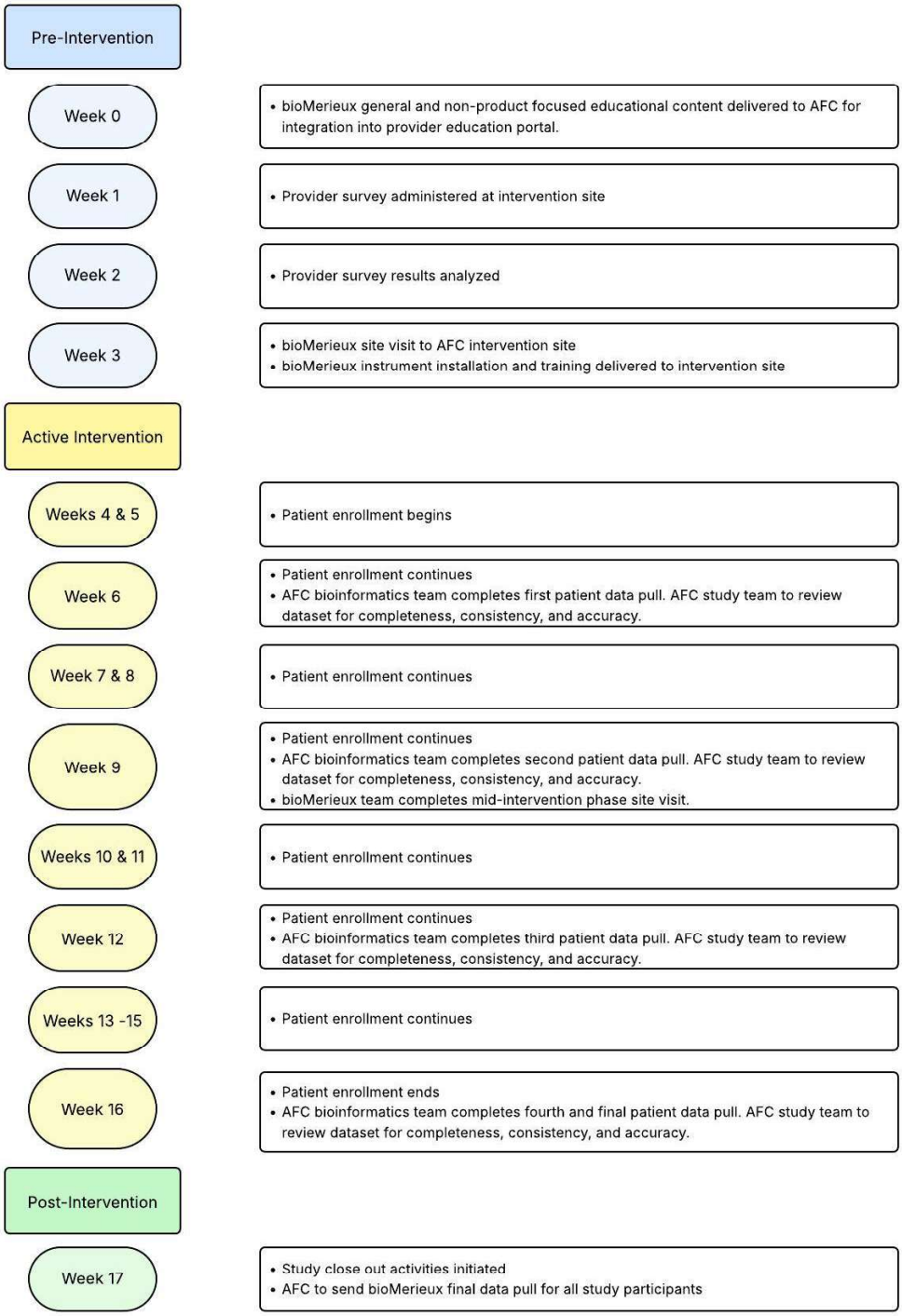
Document Date: 07/09/2024

See attached for full document

APPENDIX 3: Study Flow Diagram



APPENDIX 4: Study Schedule of Activities


Pre-Intervention
Week 0
• bioMerieux general and non-product focused educational content delivered to AFC for integration into provider education portal.
Week 1
• Provider survey administered at intervention site
Week 2
• Provider survey results analyzed
Week 3
• bioMerieux site visit to AFC intervention site
• bioMerieux instrument installation and training delivered to intervention site
Active Intervention
Weeks 4 & 5
• Patient enrollment begins
Week 6
• Patient enrollment continues
• AFC bioinformatics team completes first patient data pull. AFC study team to review dataset for completeness, consistency, and accuracy.
Week 7 & 8
• Patient enrollment continues
Week 9
• Patient enrollment continues
• AFC bioinformatics team completes second patient data pull. AFC study team to review dataset for completeness, consistency, and accuracy.
• bioMerieux team completes mid-intervention phase site visit.
Weeks 10 & 11
• Patient enrollment continues
Week 12
• Patient enrollment continues
• AFC bioinformatics team completes third patient data pull. AFC study team to review dataset for completeness, consistency, and accuracy.
Weeks 13 -15
• Patient enrollment continues
Week 16
• Patient enrollment ends
• AFC bioinformatics team completes fourth and final patient data pull. AFC study team to review dataset for completeness, consistency, and accuracy.
Post-Intervention
Week 17
• Study close out activities initiated
• AFC to send bioMerieux final data pull for all study participants

Appendix 5: Study Data Table

bioMérieux/AFC SPOTFIRE Study Data Table		
Variable	**Unit of Measurement**	**Definition**
Subject ID	As assigned by NRCG	De-identified study subject ID as assigned by NRCG
Site	Gardendale, Grove	Location patient was seen at as reported in EMR
Date of visit	DD/MM/YYYY	Date patient was seen in clinic and enrolled in study as reported in EMR
Patient Age	Years	Patient age at time of visit, recorded in whole years, as reported in EMR
Patient Race	White, Black/African American, Native Hawaiian/Pacific Islander, Asian, American Indian/Alaska Native, Other	Patient race as reported in EMR at time of visit
Patient Ethnicity	Hispanic/Latino, NOT Hispanic/Latino	Patient ethnicity as reported in EMR at time of visit
Patient biological sex	M, F	Patient 's biological sex as reported in EMR
Time of arrival	hh:mm	Patient check-in time
SPOTFIRE test run	SPOTFIRE R or SPOTFIRE ST	SPOTFIRE test (R or ST) run for patient at time of study visit as reported in EMR.
Adenovirus	Positive, Negative	Result of SPOTFIRE test: Adenovirus target detected. Positive = detected. Negative = not detected
Coronavirus SARS-CoV-2	Positive, Negative, Not Tested	Result of SPOTFIRE test: Coronavirus SARS-CoV-2 target detected. Positive = detected. Negative = not detected. Not tested = target not offered on test used for patient.
Coronavirus (seasonal)	Positive, Negative	Result of SPOTFIRE test: Coronavirus (seasonal) target detected. Positive = detected. Negative = not detected
Human metapneumovirus	Positive, Negative	Result of SPOTFIRE test: Human metapneumovirus target detected. Positive = detected. Negative = not detected

Human rhinovirus/enterovirus	Positive, Negative	Result of SPOTFIRE test: Human rhinovirus/enterovirus target detected. Positive = detected. Negative = not detected
Influenza A Virus	Positive, Negative	Result of SPOTFIRE test: Influenza A Virus target detected. Positive = detected. Negative = not detected
Influenza A virus/ H1-2009	Positive, Negative	Result of SPOTFIRE test: Influenza A virus/ H1-2009 target detected. Positive = detected. Negative = not detected
Influenza A virus/ H3	Positive, Negative	Result of SPOTFIRE test: Influenza A virus/ H3 target detected. Positive = detected. Negative = not detected
Influenza B virus	Positive, Negative	Result of SPOTFIRE test: Influenza B virus target detected. Positive = detected. Negative = not detected
Parainfluenza virus	Positive, Negative	Result of SPOTFIRE test: Parainfluenza virus target detected. Positive = detected. Negative = not detected
Respiratory syncytial virus	Positive, Negative	Result of SPOTFIRE test: Respiratory syncytial virus target detected. Positive = detected. Negative = not detected
Bordetella parapertussis	Positive, Negative, Not Tested	Result of SPOTFIRE test: Bordetella parapertussis target detected. Positive = detected. Negative = not detected. Not tested = target not offered on test used for patient.
Bordetella pertussis	Positive, Negative, Not Tested	Result of SPOTFIRE test: Bordetella pertussis target detected. Positive = detected. Negative = not detected. Not tested = target not offered on test used for patient.
Chlamydia pneumoniae	Positive, Negative	Result of SPOTFIRE test: Chlamydia pneumoniae target detected. Positive = detected. Negative = not detected
Mycoplasma pneumoniae	Positive, Negative	Result of SPOTFIRE test: Mycoplasma pneumoniae virus target detected. Positive = detected. Negative = not detected

Streptococcus dysgalactiae (Group C/G Strep)	Positive, Negative, Not Tested	Result of SPOTFIRE test: Streptococcus dysgalactiae (Group C/G Strep) target detected. Positive = detected. Negative = not detected. Not tested = target not offered on test used for patient.
Streptococcus pyogenes (Group A Strep)	Positive, Negative, Not Tested	Result of SPOTFIRE test: Streptococcus pyogenes (Group A Strep) target detected. Positive = detected. Negative = not detected. Not tested = target not offered on test used for patient.
SOC test run	Healgen COVID-19/Flu A&B Ag Combo Rapid Test, RSV Ag Rapid Test, Strep A Ag Rapid Test (follow-up throat culture for children and adolescents with negative RADT results)	SOC test run on control group or intervention group patient at time of visit as reported in EMR.
SOC respiratory test result	Organism detected	SOC respiratory test result for control group patient at study visit as reported in EMR. No organism detected = neg test result. Organism detected = positive test result.
SOC test run on study patient at intervention site?	Y/N	Y/N on if patient seen at intervention site had SOC test run in addition to SPOTFIRE test. This is a variable that will not be directly collected via EMR, but will be a binary variable developed by the bioMérieux biomathematics team based on site of visit and type of testing performed as reported via patient EMR.
SOC respiratory test result (intervention group)	Organism detected	If Y to SOC respiratory test being run on intervention group patient - SOC respiratory test result for intervention group patient at study visit as reported in EMR. No organism detected = neg test result. Organism detected = positive test result.
Recorded ongoing diagnoses	Diagnosis ICD-10 code	Any relevant persistent or ongoing patient diagnoses as reported in EMR for study subject at time of study visit.

Asthma at presentation	Y/N	Y/N bioMérieux created binary variable on whether pt has ICD-10 code associated with asthma at time of visit.
Study visit diagnosis	Diagnosis ICD-10 code	Patient diagnosis as reported in EMR for study visit.
ABX prescribed?	Y/N	Y/N on if study subject was prescribed at least one antibiotic for diagnosis at time of study visit. , as reported in EMR (variable that bioMérieux creates based on what patient was prescribed)
ABX 1 type	name, class	If Y to patient being prescribed ABX at time of study visit - name and class of antibiotic 1 prescribed, as reported in EMR. Antibiotic class will be determined by trained pharmacists during the analysis phase. This information is not reported in the EMR.
ABX 1 dose	dosage	If Y to patient being prescribed ABX at time of study visit - dosage of antibiotic 1 prescribed, as reported in EMR
ABX 1 duration	days	If Y to patient being prescribed ABX at time of study visit - number of days patient is prescribed antibiotic 1 for, as reported in EMR
ABX 2 type	name, class	If Y to patient being prescribed ABX at time of study visit - name and class of antibiotic 2 prescribed, as reported in EMR
ABX 2 dose	dosage	If Y to patient being prescribed ABX at time of study visit - dosage of antibiotic 2 prescribed, as reported in EMR
ABX 2 duration	days	If Y to patient being prescribed ABX at time of study visit - number of days patient is prescribed antibiotic 2 for, as reported in EMR
ABX 3 type	name, class	If Y to patient being prescribed ABX at time of study visit - name and class of antibiotic 3 prescribed, as reported in EMR
ABX 3 dose	dosage	If Y to patient being prescribed ABX at time of study visit - dosage of antibiotic 3prescribed, as reported in EMR

ABX 3 duration	days	If Y to patient being prescribed ABX at time of study visit - number of days patient is prescribed antibiotic 3 for, as reported in EMR
Antiviral prescribed?	Y/N	Y/N on if study subject was prescribed at least one antiviral for diagnosis at time of study visit. , as reported in EMR (variable that bioMérieux creates based on what patient was prescribed)
Antiviral 1 type	name, class	If Y to patient being prescribed antiviral at time of study visit - name and class of antiviral 1 prescribed, as reported in EMR
Antiviral 1 dose	dosage	If Y to patient being prescribed antiviral at time of study visit - dosage of antiviral 1 prescribed, as reported in EMR
Antiviral 1 duration	days	If Y to patient being prescribed antivirals at time of study visit - number of days patient is prescribed antiviral 1 for, as reported in EMR
Antiviral 2 type	name, class	If Y to patient being prescribed antiviral at time of study visit - name and class of antiviral 2 prescribed, as reported in EMR
Antiviral 2 dose	dosage	If Y to patient being prescribed antiviral at time of study visit - dosage of antiviral 2 prescribed, as reported in EMR
Antiviral 2 duration	days	If Y to patient being prescribed antivirals at time of study visit - number of days patient is prescribed antiviral 2 for, as reported in EMR
Antiviral 3 type	name, class	If Y to patient being prescribed antiviral at time of study visit - name and class of antiviral 3 prescribed, as reported in EMR
Antiviral 3 dose	dosage	If Y to patient being prescribed antiviral at time of study visit - dosage of antiviral 3 prescribed, as reported in EMR
Antiviral 3 duration	days	If Y to patient being prescribed antivirals at time of study visit - number of days patient is prescribed antiviral 3 for, as reported in EMR
Prescribing Provider Type	PA, NP, MD, DO	Prescribing provider license type according to registered NPI number

Appropriateness of Treatment	Y/N	Was treatment prescribed appropriate? Y = Antibiotic prescribed for bacterial infection OR antiviral prescribed for viral infection. N = Antibiotic prescribed for anything other than bacterial infection OR antiviral prescribed for anything other than viral infection.
Did patient receive test result prior to discharge?	Y/N	Y/N on if patient received test result prior to discharge from clinic.
Time of discharge	hh:mm	Time patient discharged from clinic on the day of study visit, as reported in EMR

APPENDIX 6: Provider Survey

APPENDIX 7: Patient Survey

APPENDIX 8: Diagnostic Treatment Algorithm