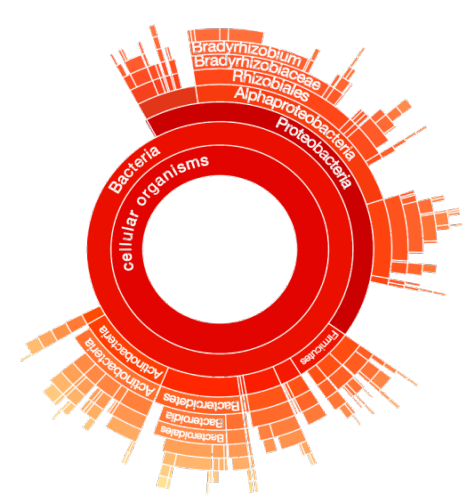


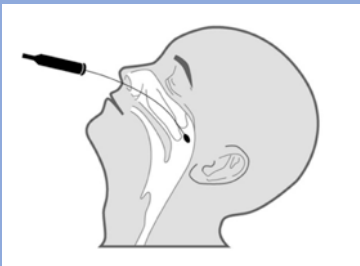


Detection of previously missed pathogens by a fully-validated metagenomics-based test

Robert Schlager, MD, Dr Med, MPH
Assistant Professor (University of Utah)
Medical Director (ARUP Laboratories)
Chief Medical Officer (IDbyDNA Inc.)

From Case Reports to Analytical Performance and Clinical Utility

NP Swabs ($n=109$)



PCR Panel (RVP)



I. Positives ($n=42$)

II. Unselected ($n=67$)

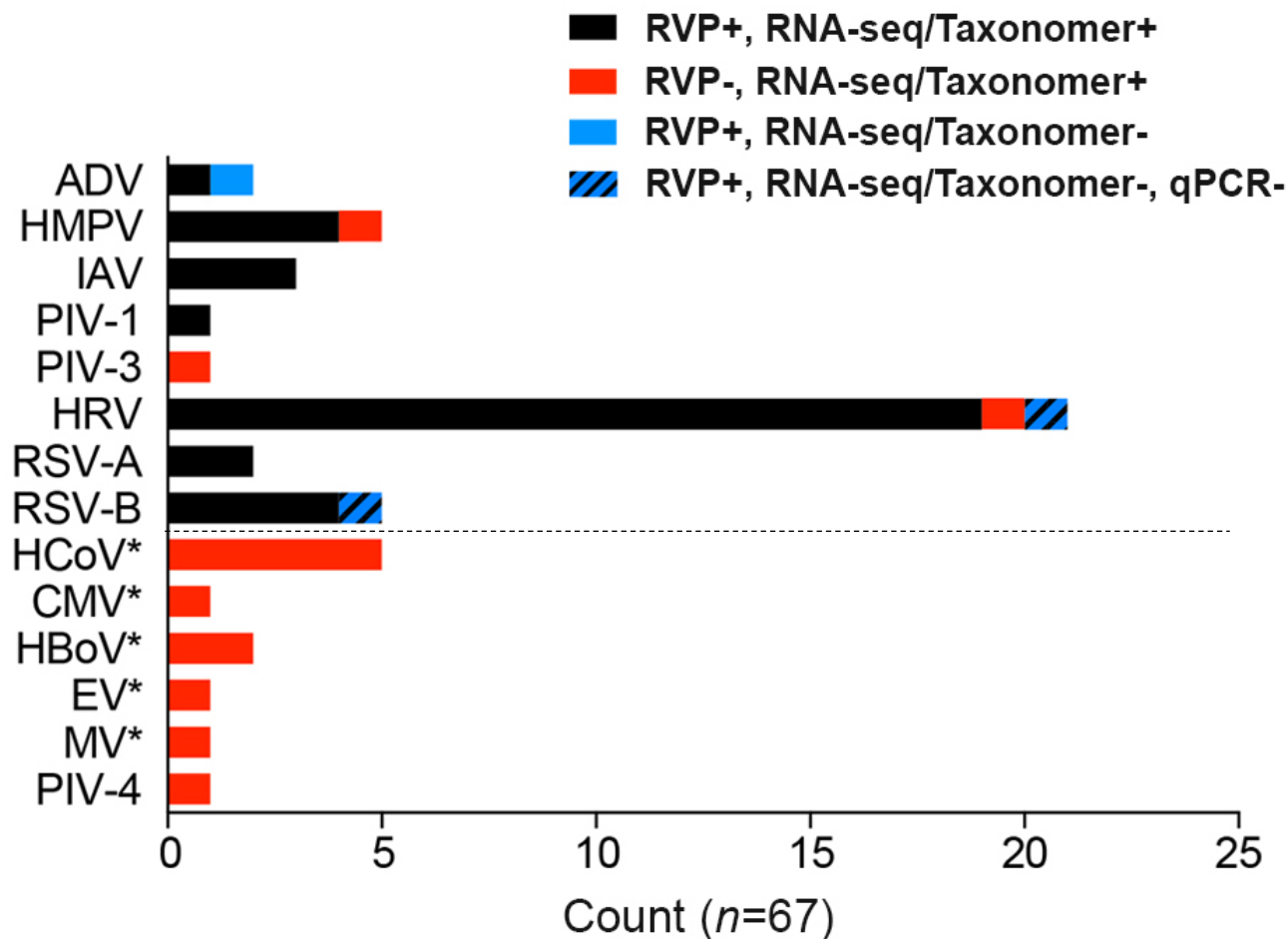
RNA-seq (HiSeq)

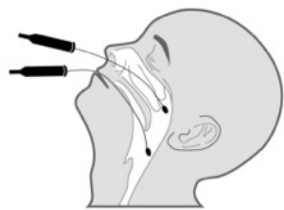


5-10 M reads/sample

>90% Agreement with PCR Panel

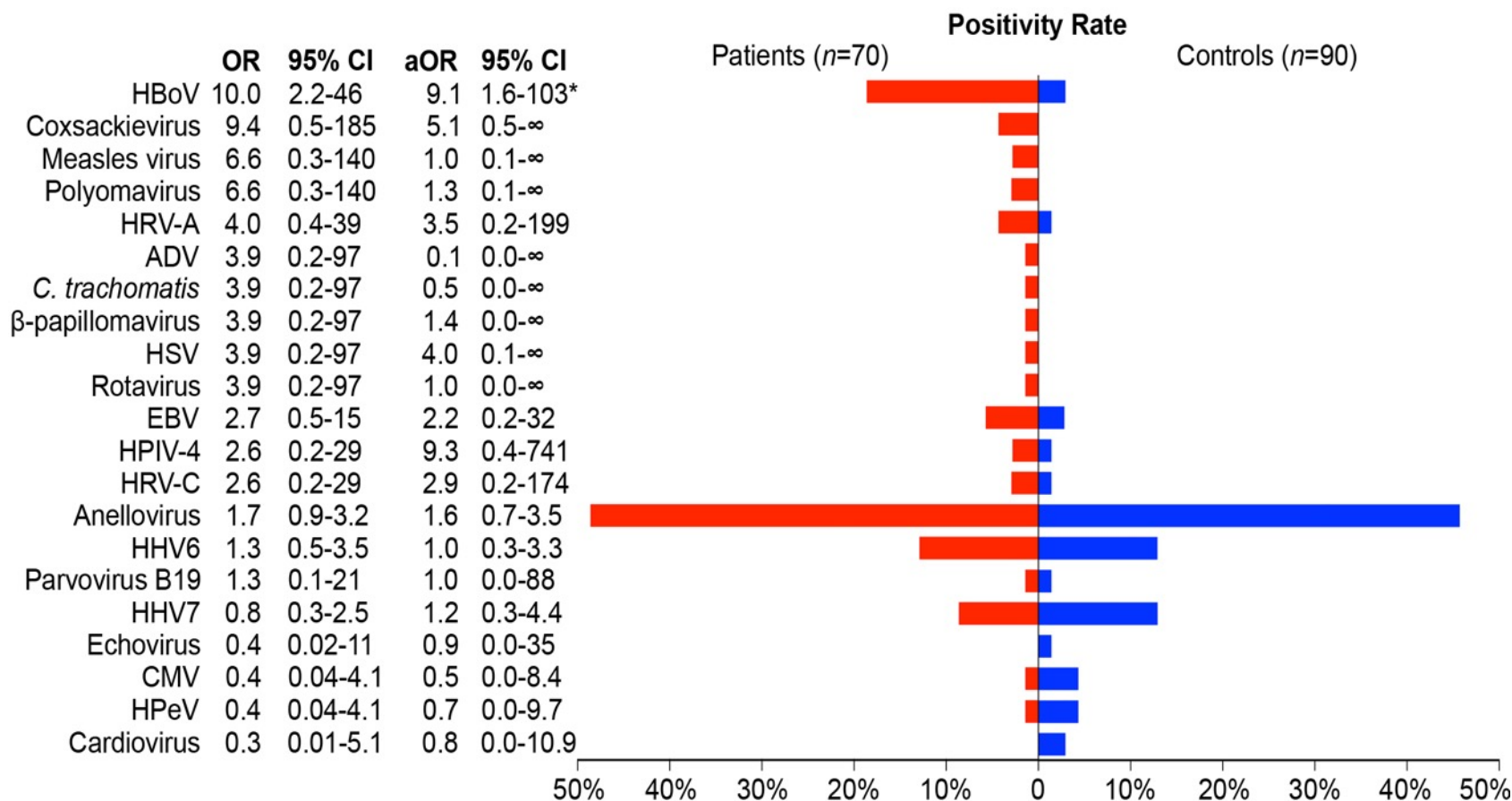
NP/OP Swabs (Viral Pathogens), RNA-seq & Taxonomer





Putative Pathogens in 30% of Children with Pneumonia of Previously Unknown Etiology

NP/OP Swabs (Viral Pathogens), RNAseq & Taxonomer



Putting it Together

A First **Validated Test**

ARUP Laboratories

3500+ Employees
~50,000 Samples per Day



Enterprise of the University of Utah



Anatomic Pathology



Infectious Disease



Genetics



Oncology



Hemostasis



Pain Management



Immunology



Pediatrics

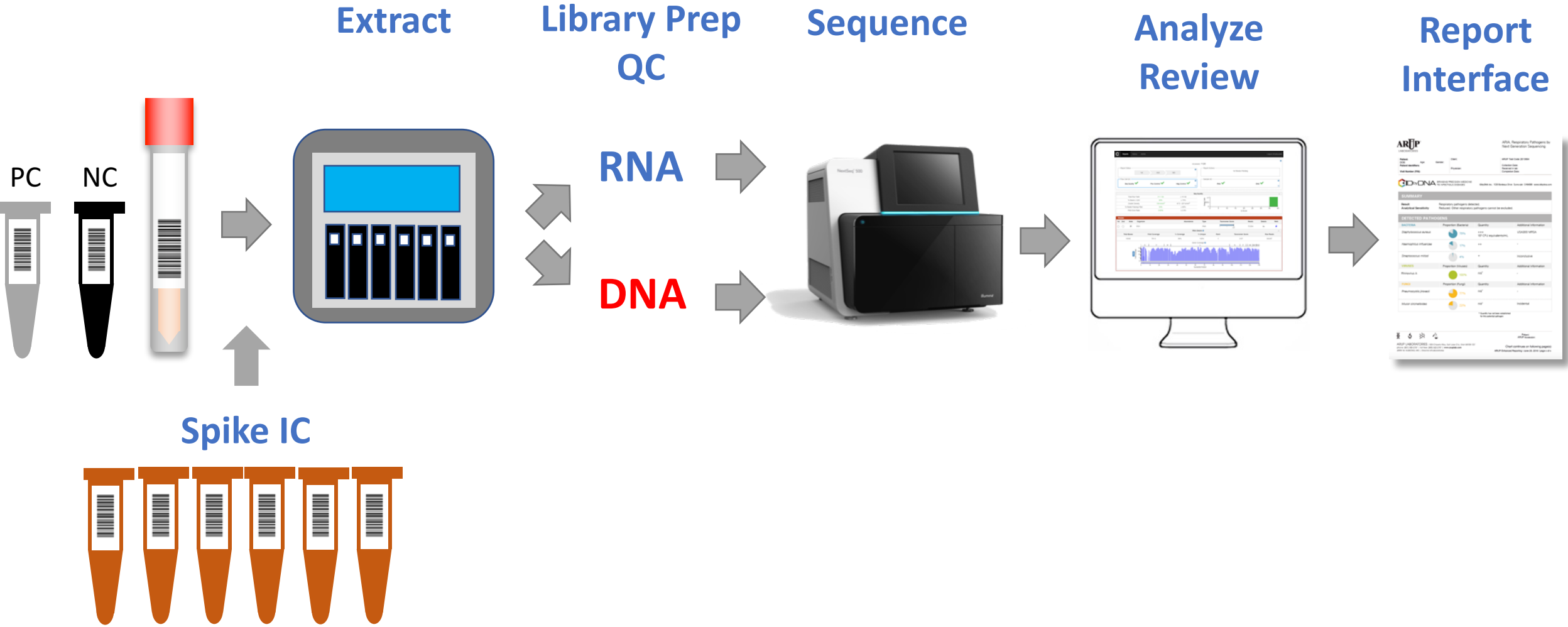
Strong Focus on Quality



Automated Sample Handling



Workflow



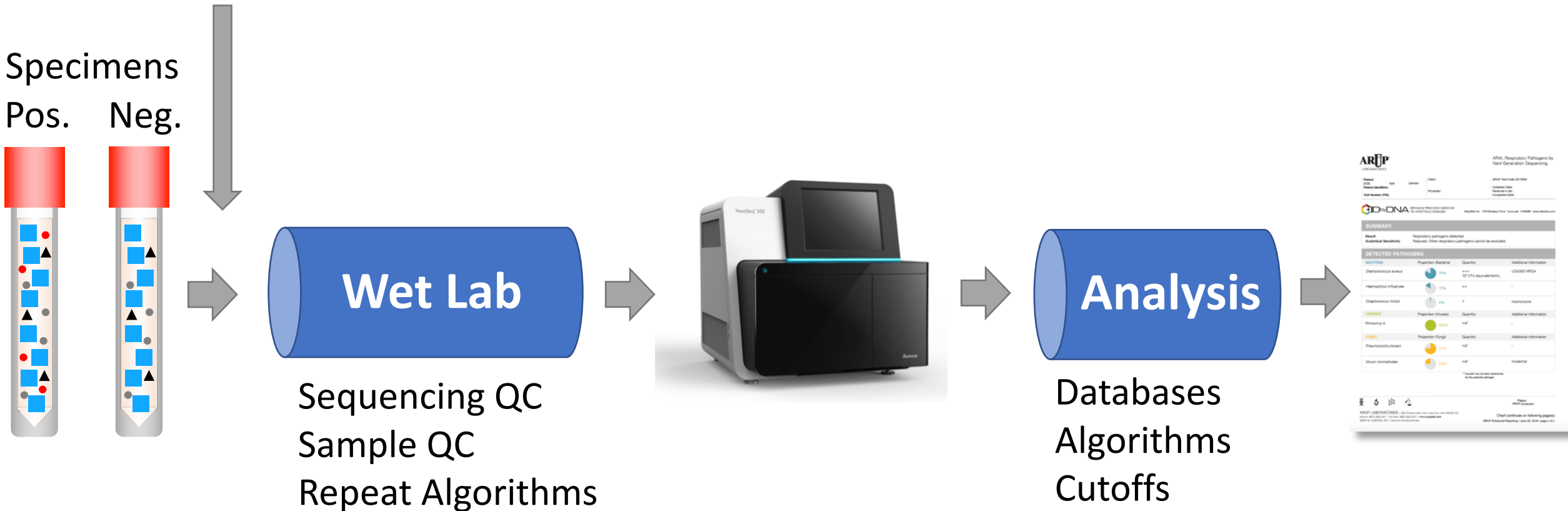
Validated: End-to-End Workflow

- ❑ Sensitivity
- ❑ Specificity
- ❑ Accuracy
- ✓ Reproducibility
- ✓ Stability

External Controls

Internal Controls

Specimens	Pos.	Neg.
1		
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100		



Validated: Virtual Specimens

- ✓ Sensitivity
- ✓ Specificity
- ✓ Accuracy
- ✓ Reproducibility
- ✓ Stability

Pathogens
Near neighbors
Commensals
Contaminants

Virtual
Specimen
x1000's

Virtual Matrix

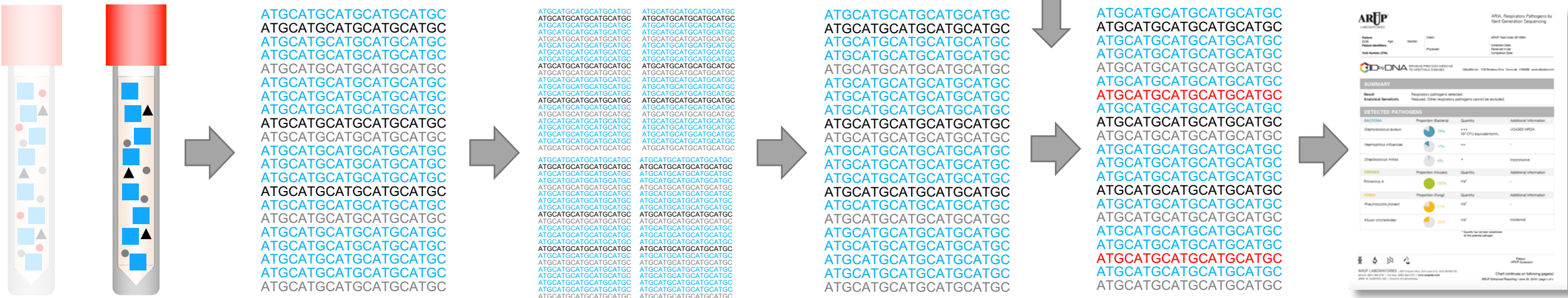
x10s

Data

Neg.

Pos.

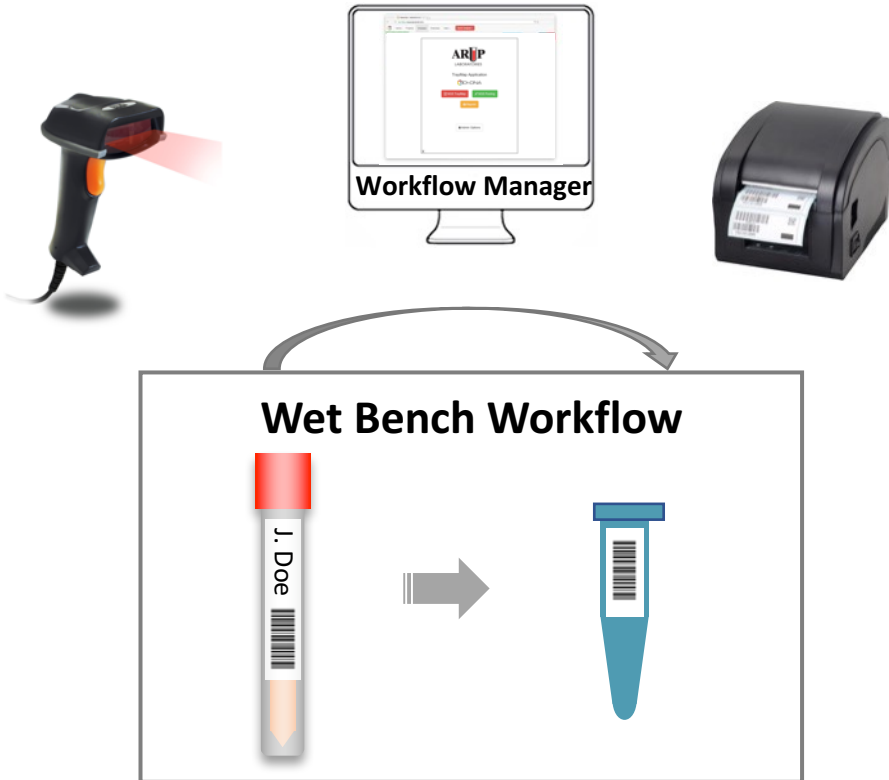
Specimens



Diagnostic-Grade Sample-to-Report Metagenomics

Simplifying Workflows for Diagnostic Labs

Sample & Library Prep



Sequencing

Validated

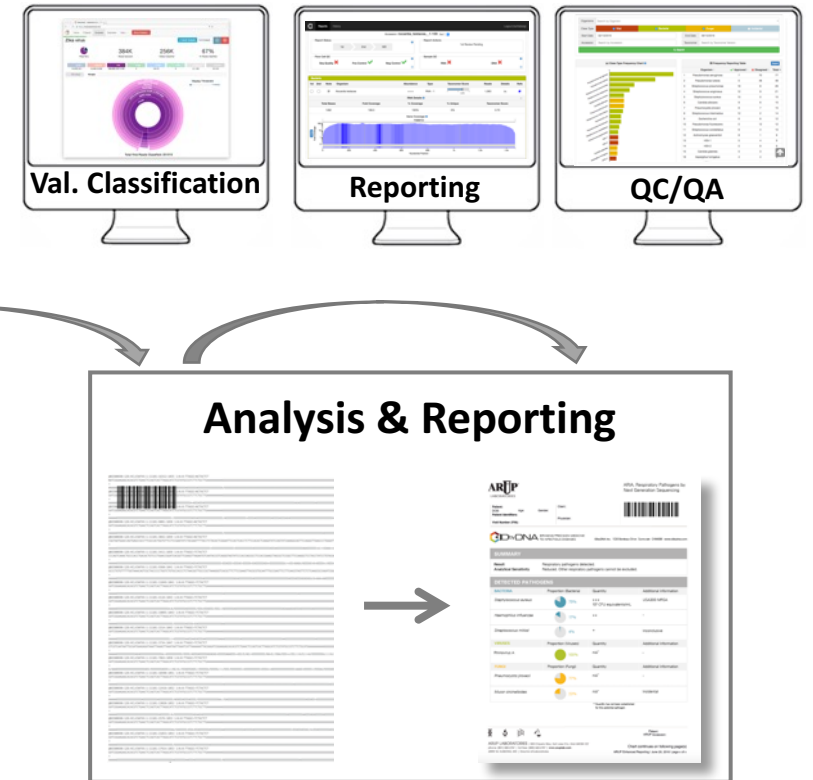
- Databases
- Algorithms
- Cutoffs

Unbiased Sequencing

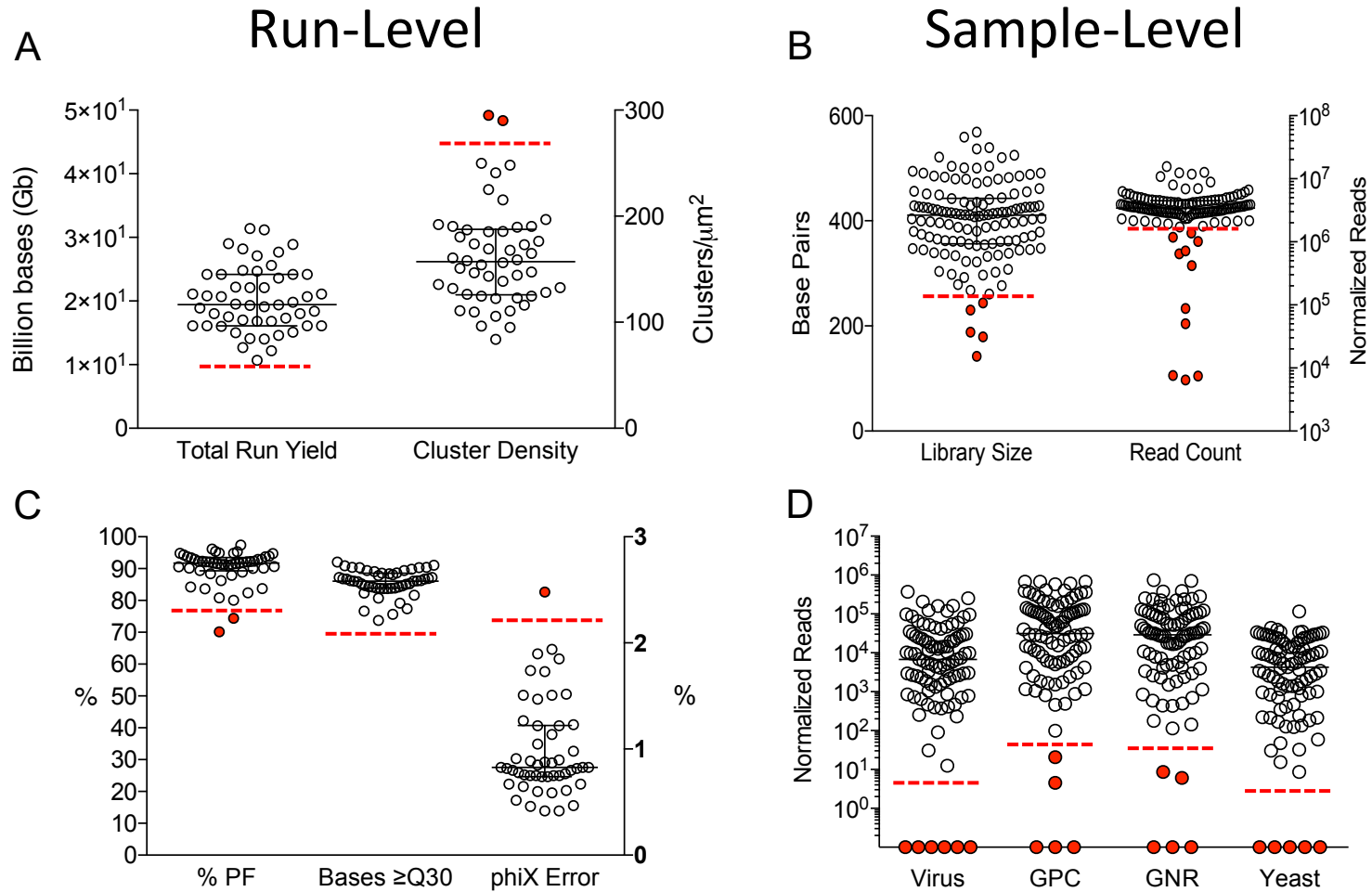


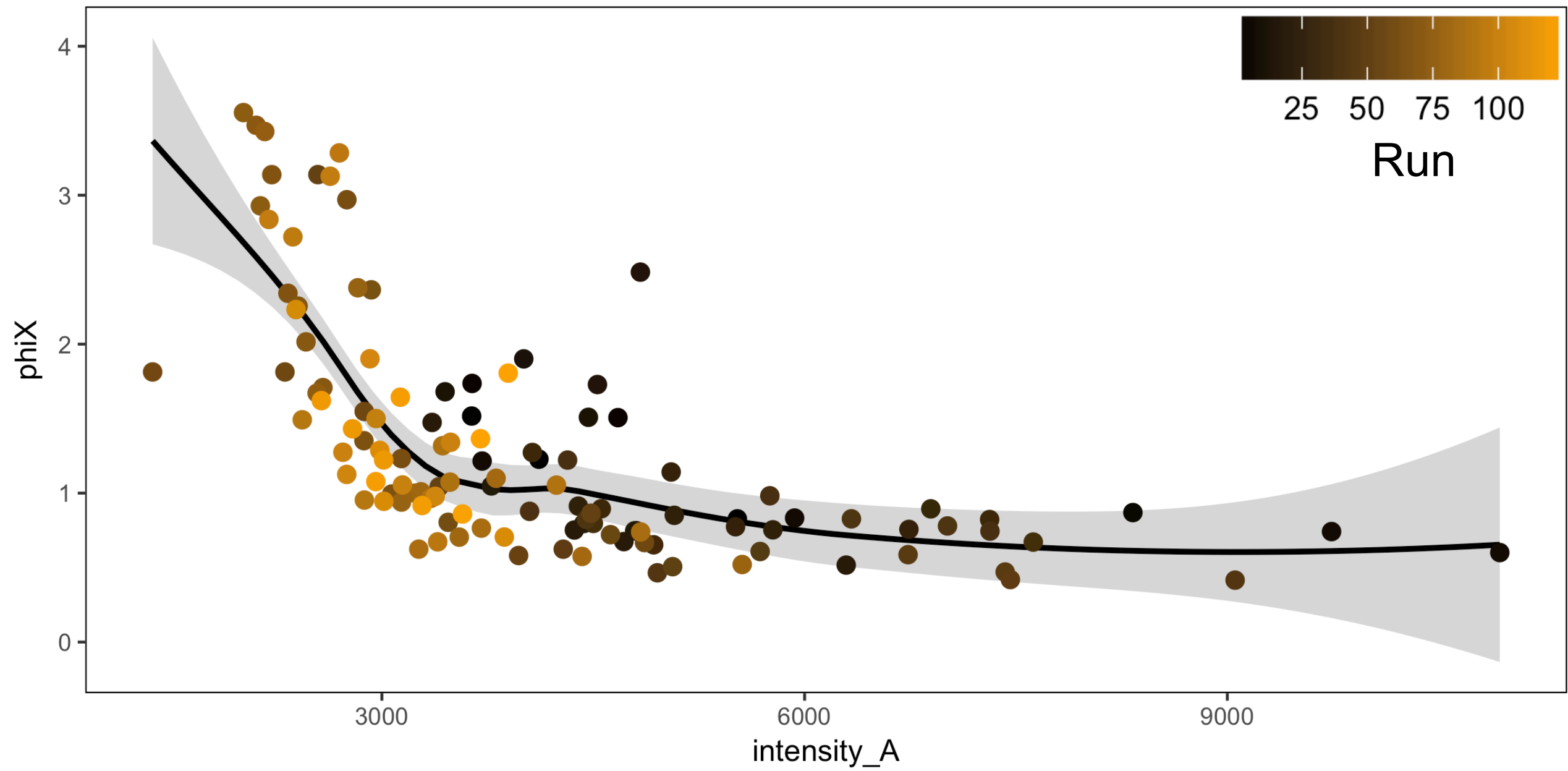
Analysis

Report

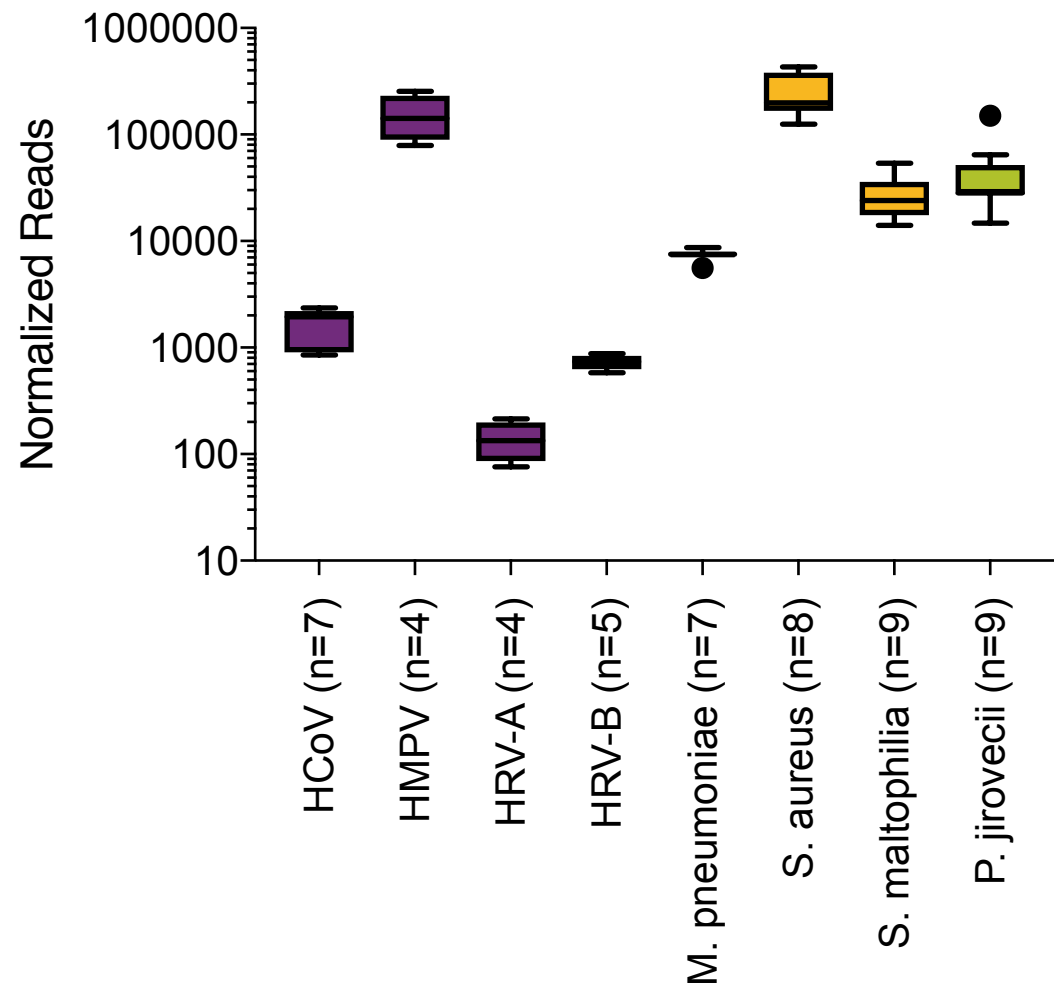


Validated Quality Control Parameters





Normalization Improves Reproducibility

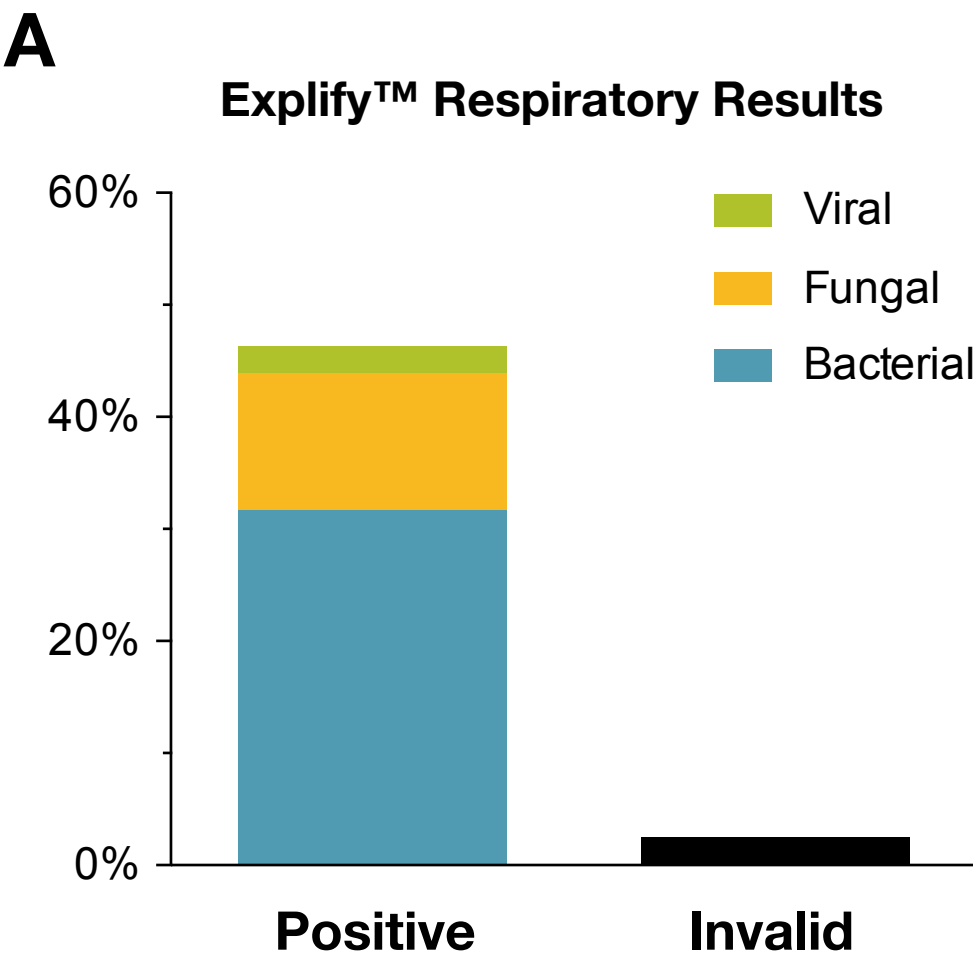


Diagnostic Yield

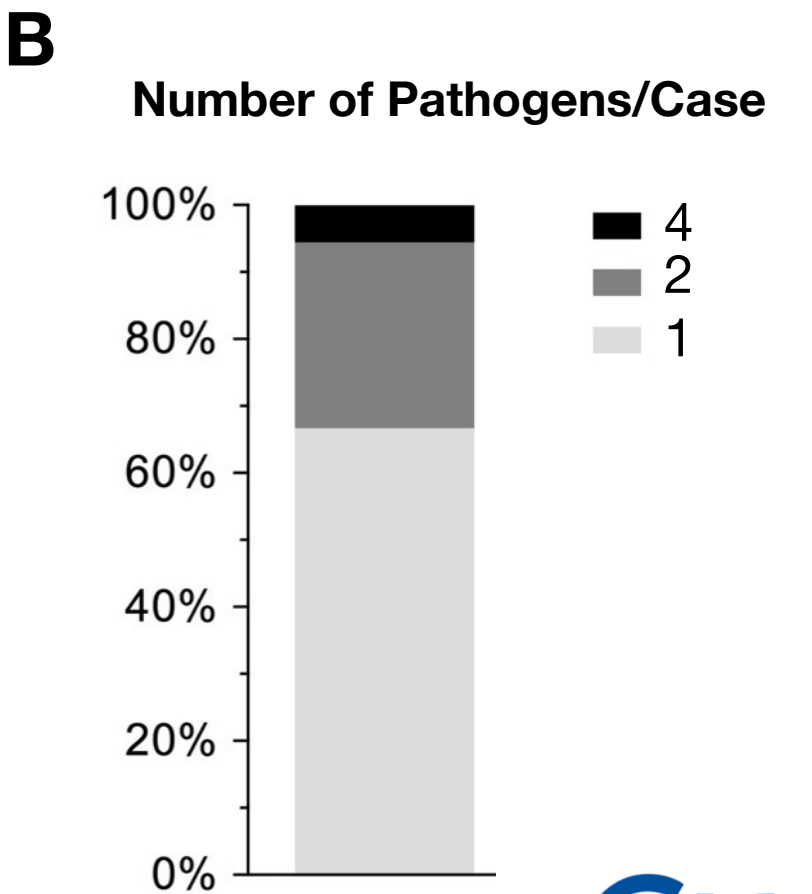
A First **Application Study**

Previously Missed Pathogens in ~40% of Children

Immunocompromised, Pneumonia, ICU



Viruses	Parainfluenza virus Human Bocavirus Rhinovirus
Fungi	<i>Pneumocystis</i> <i>Mucor</i> <i>Fusarium</i>
Bacteria	<i>Staph. aureus</i> <i>Strep. pneumoniae</i> <i>S. maltophilia</i>



Adding Additional Layers of Information

