P-457

Distinct Respiratory Pathogen Profiles in Transplant Recipients and Improved Detection Beyond Culture with ONETest™

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INTRODUCTION

Lower respiratory tract infections are a major cause of morbidity in transplant recipients, yet conventional culture may have reduced sensitivity, particularly following antimicrobial exposure. This diagnostic challenge may be especially important in immunocompromised patients, in whom timely and comprehensive pathogen detection can influence clinical management.

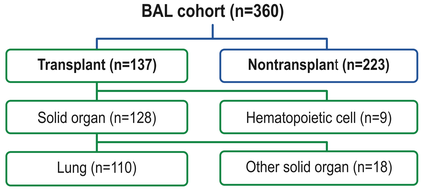
Targeted metagenomic sequencing offers broader microbial profiling and may complement conventional diagnostic approaches. We evaluated ONETest (OT), a targeted metagenomic sequencing assay, in bronchoalveolar lavage (BAL) specimens to compare respiratory pathogen profiles and diagnostic performance between transplant and non-transplant patients.

OBJECTIVES

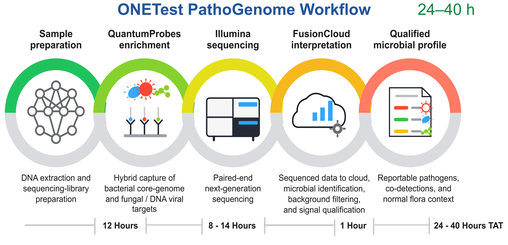
1. **Culture-referenced agreement**
   Sample- and species-level metrics
2. **Transplant-stratified profiles**
   Microbial distributions of culture-confirmed detections
3. **Additional-detection review**
   Orthogonal PCR where available

METHODS

Study Design and Population

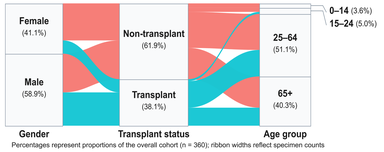


How ONETest works



RESULTS

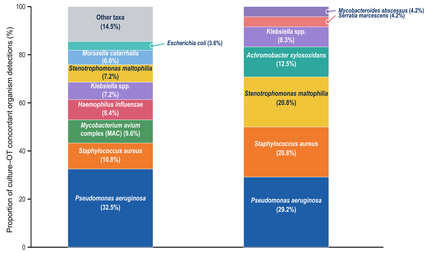
Cohort Demographics



Percentages represent proportions of the overall cohort (n = 360); ribbon widths reflect specimen counts

- Transplant recipients were more frequently male than non-transplant patients (71.5% vs 51.1%), with most transplant recipients aged 25–64 years (56.9%).

Species distribution of Culture-confirmed Organisms Detected by OT, Stratified by Transplant Status



Stacked bars show the relative species distribution of culture-positive organisms also detected by OT in transplant recipients (n = 24) and non-transplant patients (n = 83). Percentages are calculated using the total number of concordant organism detections within each group, rather than the number of patients. Multiple organisms may originate from the same BAL specimen, less frequent taxa are grouped as "Other taxa." .

- Among culture-confirmed organisms detected by ONETest, two opportunistic nonfermenting Gram-negative bacteria accounted for 33.3% of transplant versus 9.6% of non-transplant detections. Conversely, two common respiratory bacterial pathogens and MAC collectively accounted for 24.1% of non-transplant detections, compared with none in transplant recipients, suggesting distinct respiratory microbial profiles by transplant.

ONETest–Culture agreement by transplant status

Non-transplant (n = 223)

	Culture (+)	Culture (–)
ONETest (+)	71 (31.8%)	44 (19.7%)
ONETest (–)	14 (6.3%)	94 (42.2%)
	Sensitivity 83.5%	**Specificity 68.1%**	**Overall agreement 74.0%**

Transplant (n = 137)

	Culture (+)	Culture (–)
ONETest (+)	24 (17.5%)	32 (23.4%)
ONETest (–)	6 (4.4%)	75 (54.7%)
	Sensitivity 80.0%	**Specificity 70.1%**	**Overall agreement 72.3%**

Values BAL specimens, n (% within each group). Culture was used as the comparator for sample-level assay performance

- ONETest demonstrated comparable sensitivity relative to culture in transplant and non-transplant BAL specimens (80% vs 84%), despite lower culture positivity in transplant recipients (22% vs 38%).

Species-Level ONETest–Culture Agreement in Transplant Recipients

n = 137

Species	Culture (+)	Agreement	Specificity	Sensitivity	PPV	NPV
Pseudomonas aeruginosa	7	0.93	0.93	1.00	0.44	1.00
Staphylococcus aureus	7	0.96	0.98	0.71	0.62	0.98
Stenotrophomonas maltophilia	6	0.96	0.97	0.83	0.56	0.99
Achromobacter xylosoxidans	4	0.99	1.00	0.75	1.00	0.99
Klebsiella spp.	4	0.99	1.00	0.50	1.00	0.99
Rare taxa						
Chryseobacterium indologenes	1	0.99	1.00	0.00	NA	0.99
Mycobacterium avium complex (MAC)	1	0.99	0.99	0.00	0.00	0.99
Mycobacteroides abscessus	1	1.00	1.00	1.00	1.00	1.00
Serratia marcescens	1	0.99	0.99	1.00	0.33	1.00
Micro-average Recurrent taxa: cultured in ≥3 specimens within the transplant subgroup	—	**Agreement 96.8%**	**Specificity 97.6%**	**Sensitivity 78.6%**	**PPV 57.9%**	**NPV 99.1%**

Rare taxa were defined as species cultured in fewer than three specimens per subgroup. The individual performance estimates of rare taxa are reported for completeness but excluded from the recurrent-species micro-averaged analysis. Each taxon is counted once per specimen. Culture is the comparator, not a clinical-infection reference.

- Among transplant recipients, ONETest demonstrated 97% overall agreement with culture across recurrent species, with 97.6% specificity and variable sensitivity (78.6% overall). Species-specific sensitivity was highest for *P. aeruginosa* (100%, 7/7 culture-positive specimens) and *S. maltophilia* (83.3%, 5/6).

Species-Level ONETest–Culture Agreement in Non-Transplant Patients

n = 223

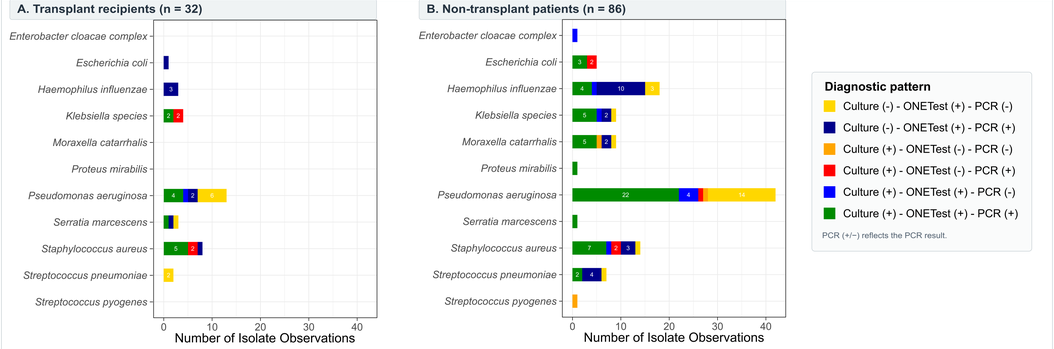
Species	Culture (+)	Agreement	Specificity	Sensitivity	PPV	NPV
Pseudomonas aeruginosa	30	0.92	0.93	0.90	0.66	0.98
Staphylococcus aureus	12	0.97	0.98	0.75	0.69	0.99
Mycobacterium avium complex (MAC)	11	0.98	1.00	0.64	1.00	0.98
Haemophilus influenzae	7	0.93	0.93	1.00	0.32	1.00
Klebsiella spp.	6	1.00	1.00	1.00	0.86	1.00
Moraxella catarrhalis	6	0.98	0.98	0.83	0.56	1.00
Stenotrophomonas maltophilia	6	0.98	0.98	1.00	0.60	1.00
Escherichia coli	5	0.99	1.00	0.60	1.00	0.99
Other rare taxa (pooled)	17	0.99	1.00	0.71	0.50	1.00
Micro-average Recurrent taxa: cultured in ≥3 specimens within the non-transplant subgroup	—	**Agreement 96.9%**	**Specificity 97.5%**	**Sensitivity 84.3%**	**PPV 62.5%**	**NPV 99.2%**

Other rare taxa pool 13 low-frequency taxa, this pooled row is descriptive and is excluded from the recurrent-species micro-average.Each taxon is counted once per specimen; culture is the comparator, not a clinical-infection reference

- Among non-transplant patients, ONETest achieved 96.9% agreement with culture, 97.5% specificity, and 84.3% sensitivity across recurrent species. Sensitivity was highest for *H. influenzae, Klebsiella* spp., and *S. maltophilia* (100%), but lower for MAC (64%).

Additional ONETest Detections and Culture–PCR Concordance Patterns by Transplant Status

PCR-tested BAL specimens n = 118, culture-recoverable species covered by the PCR panel (n=11)



Stacked bars represent organism-level detection patterns across culture, OT, and PCR in the BioFire FilmArray Pneumonia (PN) Panel-available subset, stratified by transplant status. Culture(−)/OT(+) indicates an additional organism not recovered by culture, including findings from BAL specimens culture-positive for other organisms. Panel sample sizes (n=32 and n=86) represent specimens, whereas bar segments represent organism observations. PCR support does not establish clinical infection.

- ONETest provided additional microbiologic findings beyond routine culture in both transplant and non-transplant patients. Among culture-negative BAL specimens, ONETest identified additional microbial findings in 32/107 transplant (30%) and 44/138 non-transplant (32%) specimens.
- In the PCR-available subset, OT identified 17 additional organism detections across 16/32 transplant specimens (50.0%) and 42 additional organism detections across 36/86 non-transplant specimens (41.9%) that were not recovered by culture. Of these additional detections, 8/17 (47.1%) and 21/42 (50.0%), respectively, were supported by orthogonal PCR.
- Among culture-negative transplant specimens, six had PCR-supported additional findings, representing an observed 5.6% additive microbiologic yield (6/107) beyond routine culture.

CONCLUSIONS

- Transplant recipients exhibited lower routine culture positivity than non-transplant patients (22% vs. 38%), potentially reflecting differences in BAL sampling indications or antimicrobial exposure, although these factors were not evaluated. Culture-confirmed organisms detected by ONETest showed greater representation of opportunistic nonfermenting Gram-negative bacteria in transplant recipients, whereas common respiratory pathogens and MAC were more prominent in non-transplant patients.
- ONETest maintained comparable sample-level sensitivity (80% vs. 84%) and identified 95 additional LRT-associated organism detections across 76 culture-negative BAL specimens, representing additional findings in 30% of culture-negative transplant and 32% of non-transplant specimens. Approximately half of additional detections in the PCR-tested subset received orthogonal support, including an observed 5.6% PCR-supported additive microbiologic yield among culture-negative transplant specimens.
- These findings support ONETest as a complementary BAL diagnostic approach, providing additional microbiologic information beyond culture while requiring appropriate clinical interpretation.

FUTURE DIRECTIONS

Future investigations should assess the influence of transplant status, prior antimicrobial exposure, and indications for BAL sampling, while evaluating the impact of ONETest findings on antimicrobial management and patient outcomes. Further studies should also refine detection and interpretation thresholds for challenging organisms, particularly nontuberculous mycobacteria and fungi.

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