

# Implementation of a Host-Protein Test (MMBV) Into Routine Care for Children Hospitalized with Symptoms of Lower Respiratory Tract Infection.

Vered Nir, M.D.<sup>1,2</sup>, Vered Schichter Konfino, M.D.<sup>1,2</sup>, Naama Kuchinski Cohen, M.D.<sup>1,2</sup>, Esther Levy, Ph.D.<sup>1</sup>, Ma’anit Shapira, Ph.D.<sup>1,2</sup>, Michal Stein, M.D.<sup>3,4</sup> and Adi Klein, M.D.<sup>1,2</sup>

<sup>1</sup> Hillel Yaffe Medical Center, Hadera, Israel; <sup>2</sup> Technion Institute of Technology, Haifa, Israel; <sup>3</sup> Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Tel-Hashomer, Israel; <sup>4</sup> Tel Aviv University, Tel Aviv, Israel

**Background:** Infectious etiology is often unclear in children hospitalized with symptoms of lower respiratory tract infection (LRTI), driving antibiotic misuse. A host-protein test (MMBV) exhibits high diagnostic accuracy for differentiating bacterial from viral etiology, with early real-world data signaling the potential for guiding appropriate antibiotic use. However, no evidence is available on how MMBV complements existing pathogen-based diagnostic tests. Here we assessed the combined use of the host-response MMBV test and rapid pathogen testing on antibiotic use in children hospitalized with LRTI symptoms.

**Methods:** Retrospective pragmatic study of MMBV implementation (intervention) at Hillel Yaffe medical center. Children 3 months to 6 years old hospitalized with LRTI symptoms were included. The study design is illustrated in Figure 1. MMBV test informed routine care only in the post-intervention period. Pathogen-based testing informed routine care in both pre- and post-intervention periods. Patients were subdivided in 4 subgroups based on pathogen and MMBV test results, namely: no viral detection, viral detection, viral MMBV (score < 35) and viral detection & viral MMBV.

**Results:** Age, sex and MMBV results were similar across arms (table 1). Antibiotic use during the post-intervention period was lowest for patients with both viral pathogen and viral MMBV results discharged with an RTI (42.6%) or LRTI (46.5%)(Figure 2). A viral MMBV result significantly reduced antibiotic use in patients discharged with an RTI, irrespective of the detection of a pathogen (p = 0.001) or not (p = 0.015). When comparing the pre- and post-intervention antibiotic use for patients with a viral detection and viral MMBV, a significant reduction was observed for patients with any (p = 0.039), RTI (p = 0.01), or LRTI (p = 0.018) discharge diagnosis.

Figure 1: Study flow for the pre- and post-MMBV intervention design.

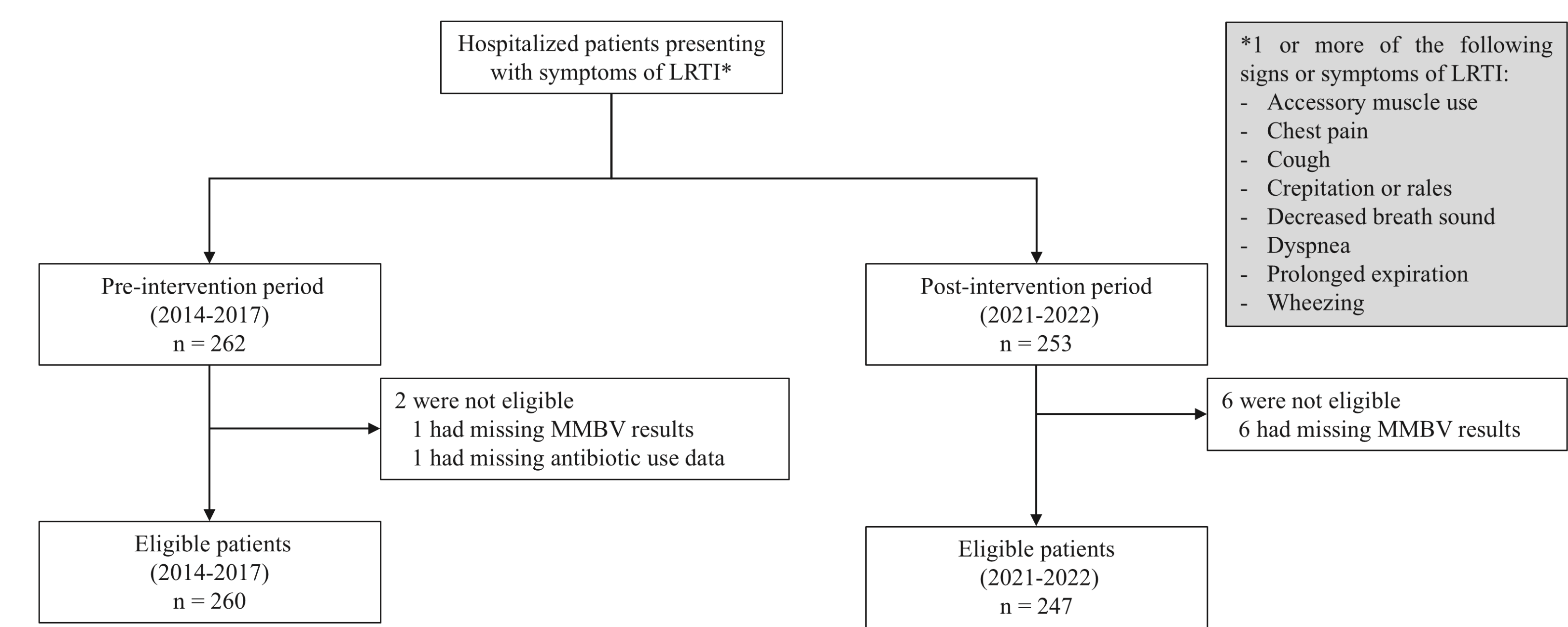


Table 1. Patient demographics and clinical characteristics of the pre- and post-intervention cohorts.

	Pre-intervention (n = 260)	Post-intervention (n = 247)
Sex, m; n (%)	124 (47.9%)	109 (44.1%)
Age, y; median (IQR)	1.3 (0.8-2.2)	1.3 (0.8-2.1)
3m – 3y	233 (89.6%)	208 (84.2%)
3y – 6y	27 (10.4%)	39 (15.8%)
Time from symptoms onset, median (IQR)	3.0 (1.0-4.0)	3.0 (2.0-5.0)
Length of stay, d; median (IQR)	3.0 (2.0-4.0)	3.0 (2.0-4.0)
Temperature, °C; median (IQR)	39.6 (39.0-40.0)	38.5 (37.9-39.4)
Main symptoms, n (%)		
Accessory muscle use	32 (12.3%)	51 (20.6%)
Cough	136 (52.3%)	205 (83.0%)
Decreased breath sounds	42 (16.2%)	42 (17.0%)
Dyspnea	77 (29.6%)	64 (25.9%)
Prolonged expiration	25 (9.6%)	25 (10.1%)
Wheezing	42 (16.2%)	45 (18.2%)
Rhinorrhea	178 (68.5%)	68 (27.5%)
Rales/crepitations	142 (54.6%)	139 (56.3%)
Blood work		
CRP, mg/l; median (IQR)	36.6 (11.9-74.1)	42.9 (16.5-80.0)
WBC, x 10^9/l; median (IQR)	14.1 (9.8-19.9)	13.9 (11.2-18.9)
ANC, x 10^9/l; median (IQR)	7.8 (4.8-13.0)	7.5 (5.0-11.5)
MMBV; n (%)		
Viral	157 (60.4%)	142 (57.5%)
Bacterial	61 (23.5%)	76 (30.8%)
Equivocal	42 (16.2%)	29 (11.7%)
Respiratory infection; n (%)		
RTI	124 (47.7%)	140 (56.7%)
LRTI	99 (38.1%)	121 (49.0%)
URTI	25 (9.6%)	19 (7.7%)
Non-RTI	136 (52.3%)	107 (43.3%)
Chest x-ray; n (%)	170 (65.4%)	187 (75.7%)

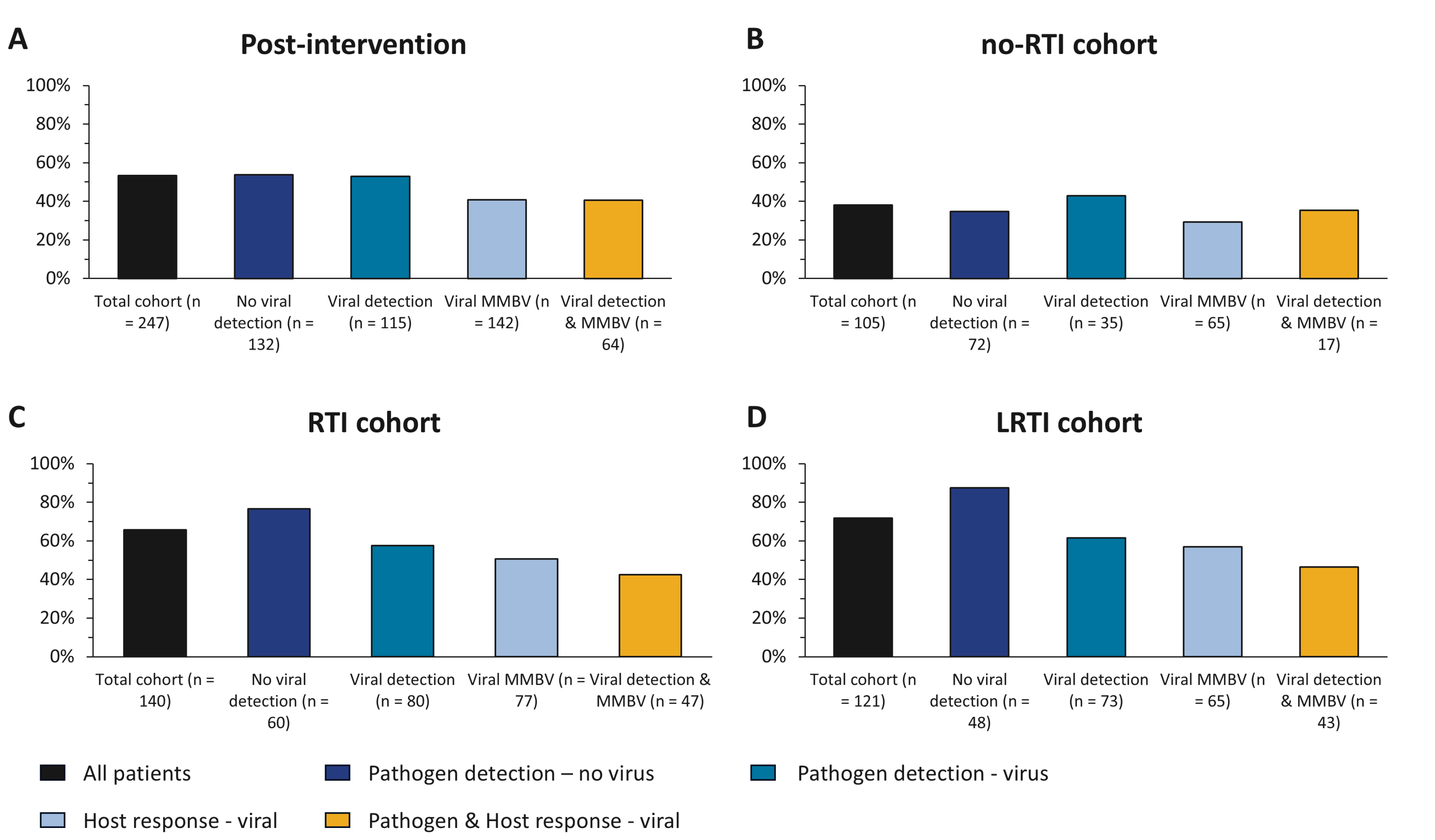


Figure 2: Antibiotic use in the post-intervention period for patients with different discharge diagnoses. Discharge diagnoses plotted were broken down in any discharge diagnosis (A), patients with a non-respiratory (B), respiratory (C), or a Lower respiratory tract infection.

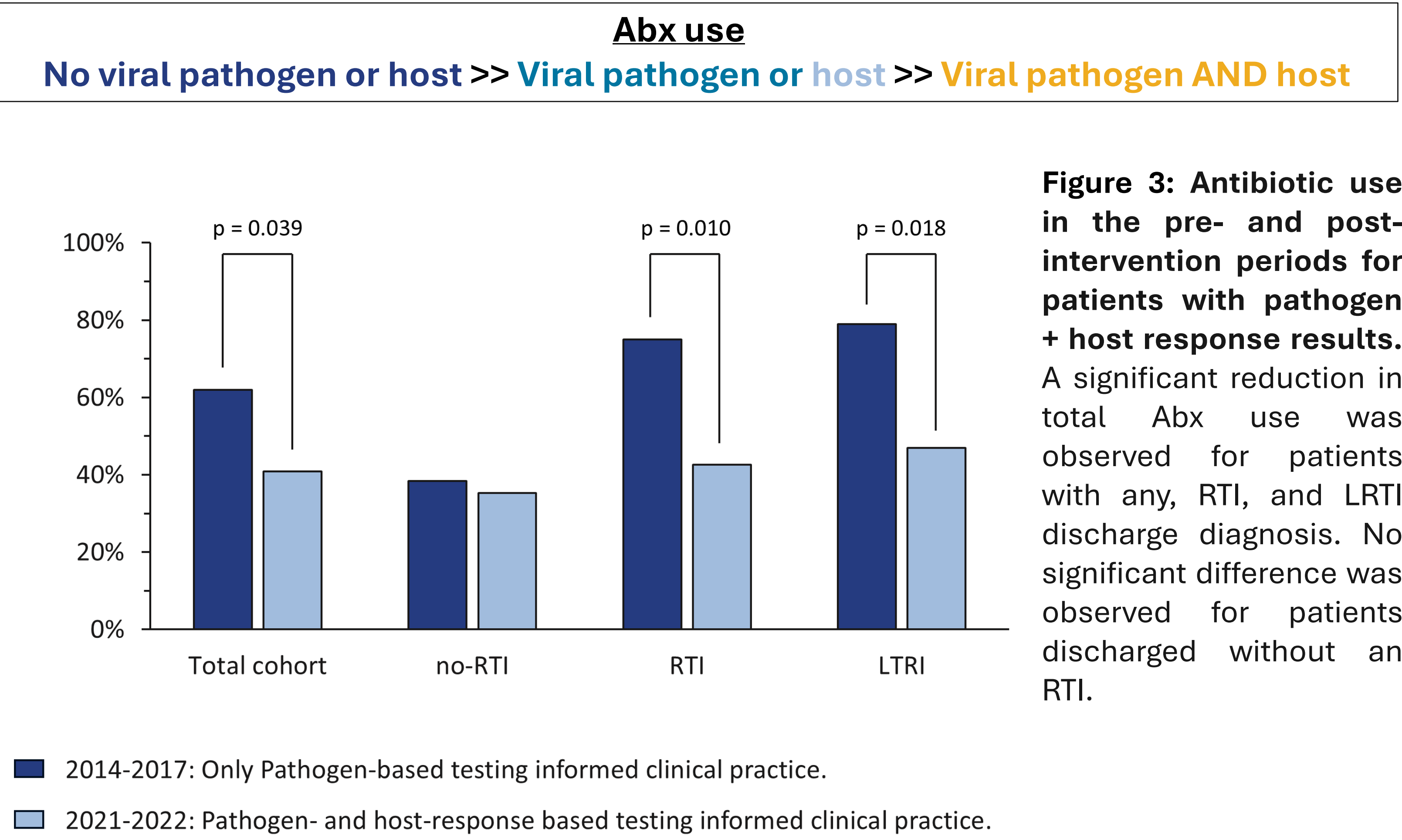


Figure 3: Antibiotic use in the pre- and post-intervention periods for patients with pathogen + host response results. A significant reduction in total Abx use was observed for patients with any, RTI, and LRTI discharge diagnosis. No significant difference was observed for patients discharged without an RTI.

## Conclusion:

- Pathogen- and host-response based test may work in synergy to improve antibiotic use in patients with respiratory infections.
- Compared to the control, MMBV improved antibiotic use irrespective of the available pathogen detection test result.
- Additional studies are need to further investigate the value of MMBV in combination with pathogen-detection tests.