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



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**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.

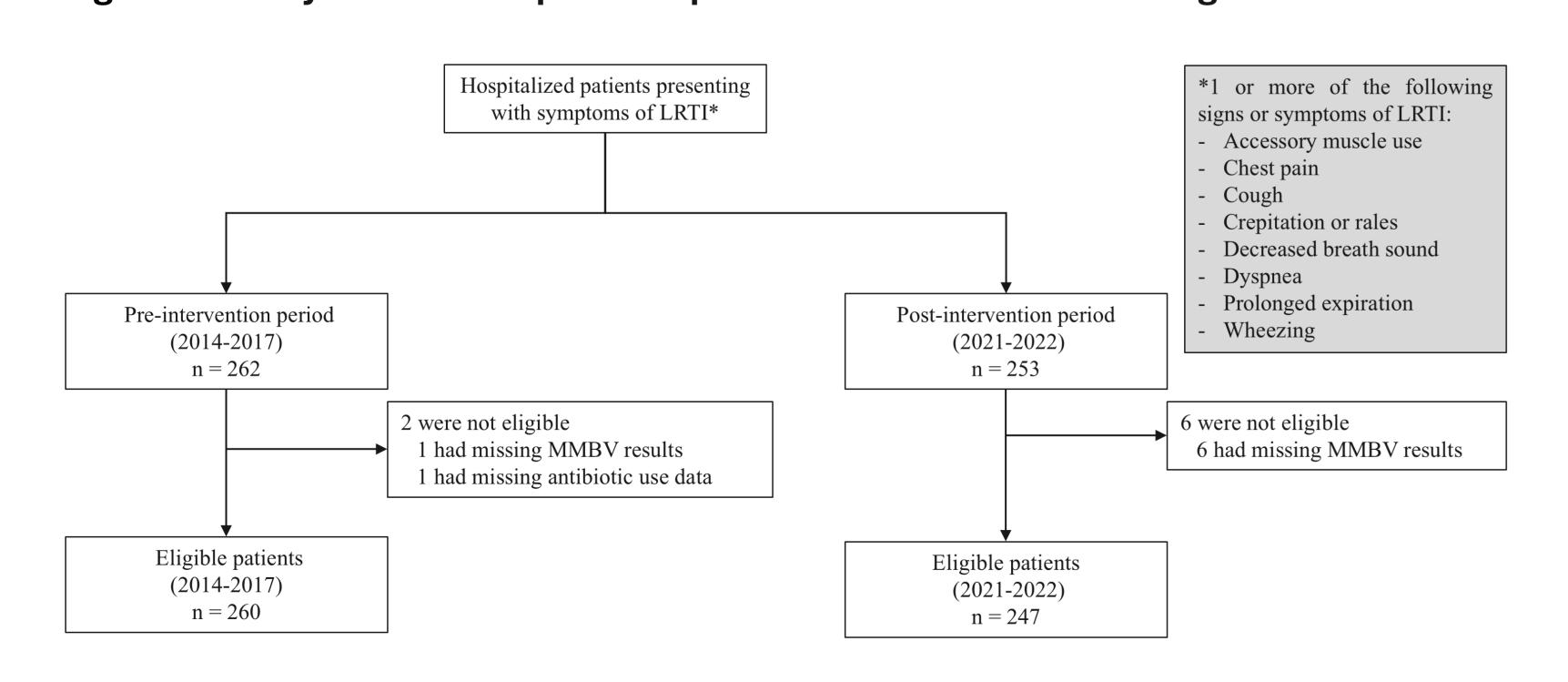


Table 1. Patient demographics and clinical characteristics of the pre- and post-intervention cohorts.

Age, y; median (IQR)  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) 3.0 (2.0-4.0) 3.0 (2.0-4.0) 3.0 (2.0-4.0) 3.0 (2.0-4.0) 3.0 (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%)  Prolonged expiration 25 (9.6%) 25 (10.1%)  Wheezing Ahinorrhea 178 (68.5%) 68 (27.5%)  Rales/crepitations 142 (54.6%) 139 (56.3%)  MBD, x 10^9/L; median (IQR) 36.6 (11.9-74.1) 42.9 (16.5-80.0) 45 (30.8%)  WBC, 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%) 140 (56.7%) 140 (56.7%)  Respiratory infection; n (%)  RII 124 (47.7%) 140 (56.7%) 19 (7.7%) 19 (7.7%) 107 (43.3%)		Pre-intervention (n = 260)	Post-intervention (n = 247)
3m - 3y   233 (89.6%)   208 (84.2%)   3y - 6y   27 (10.4%)   39 (15.8%)   3y - 6y   27 (10.4%)   39 (15.8%)   3.0 (1.0-4.0)   3.0 (2.0-5.0)   3.0 (2.0-5.0)   3.0 (2.0-4.0)   3.0 (2.0-4.0)   3.0 (2.0-4.0)   3.0 (2.0-4.0)   3.0 (2.0-4.0)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   39.6 (39.0-40.0)   38.5 (37.9-39.4)   39.5 (83.0%)   39	Sex, m; n (%)	124 (47.9%)	109 (44.1%)
3y - 6y   27 (10.4%)   39 (15.8%)	Age, y; median (IQR)	1.3 (0.8-2.2)	1.3 (0.8-2.1)
Time from symptoms onset, median (IQR)  Length of stay, d; median (IQR)  Remperature, °C; median (IQR)  Accessory muscle use  Cough  Accessory muscle use  Cough  Decreased breath sounds  Prolonged expiration  Wheezing  Rales/crepitations  CORP, mg/I; median (IQR)  ANC, x 10^9/I; median (IQR)  Respiratory infection; n (%)  RIII  25 (9.6%)  20 (1.0-4.0)  3.0 (2.0-4.0)  42 (16.2%)  42	3m – 3y	233 (89.6%)	208 (84.2%)
Length of stay, d; median (IQR) 3.0 (2.0-4.0) 3.0 (2.0-4.0) 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%)  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) 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%)	3y – 6y	27 (10.4%)	39 (15.8%)
Temperature, °C; median (IQR)  Main symptoms, n (%)  Accessory muscle use  Cough  136 (52.3%)  Decreased breath sounds  Dyspnea  77 (29.6%)  Prolonged expiration  Wheezing  42 (16.2%)  Rhinorrhea  178 (68.5%)  Rales/crepitations  Blood work  CRP, mg/l; median (IQR)  ANC, x 10^9/l; median (IQR)  ANC, x 10^9/l; median (IQR)  Bacterial  CHARTI  Bacterial  61 (23.5%)  Respiratory infection; n (%)  RII 124 (47.7%)  LRTI 99 (38.1%)  LRTI 99 (38.1%)  LRTI 99 (38.3%)  38.5 (37.9-39.4)  42 (16.2%)  42 (17.0%)  42 (17.0%)  42 (16.2%)  7.5 (5.0-11.5)  AND (1.2 (1.2 (1.2 (1.2 (1.2 (1.2 (1.2 (1.2	Time from symptoms onset, median (IQR)	3.0 (1.0-4.0)	3.0 (2.0-5.0)
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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)   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%)	Temperature, °C; median (IQR)	39.6 (39.0-40.0)	38.5 (37.9-39.4)
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%)	Main symptoms, n (%)		
Decreased breath sounds   42 (16.2%)   42 (17.0%)	Accessory muscle use	32 (12.3%)	51 (20.6%)
Dyspnea   77 (29.6%)   64 (25.9%)   Prolonged expiration   25 (9.6%)   25 (10.1%)   Wheezing   42 (16.2%)   45 (18.2%)   45 (18.2%)   Rhinorrhea   178 (68.5%)   68 (27.5%)   139 (56.3%)   142 (54.6%)   139 (56.3%)   142 (54.6%)   139 (56.3%)   142 (54.6%)   139 (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%)	Cough	136 (52.3%)	205 (83.0%)
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%)	Decreased breath sounds	42 (16.2%)	42 (17.0%)
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URTI 25 (9.6%) 19 (7.7%)  Non-RTI 136 (52.3%) 107 (43.3%)	RTI	124 (47.7%)	140 (56.7%)
Non-RTI 136 (52.3%) 107 (43.3%)	LRTI	99 (38.1%)	121 (49.0%)
	URTI	25 (9.6%)	19 (7.7%)
Chaot v. rove p (0/)	Non-RTI	136 (52.3%)	107 (43.3%)
I/U (65.4%) 18/ (75.7%)	Chest x-ray; n (%)	170 (65.4%)	187 (75.7%)

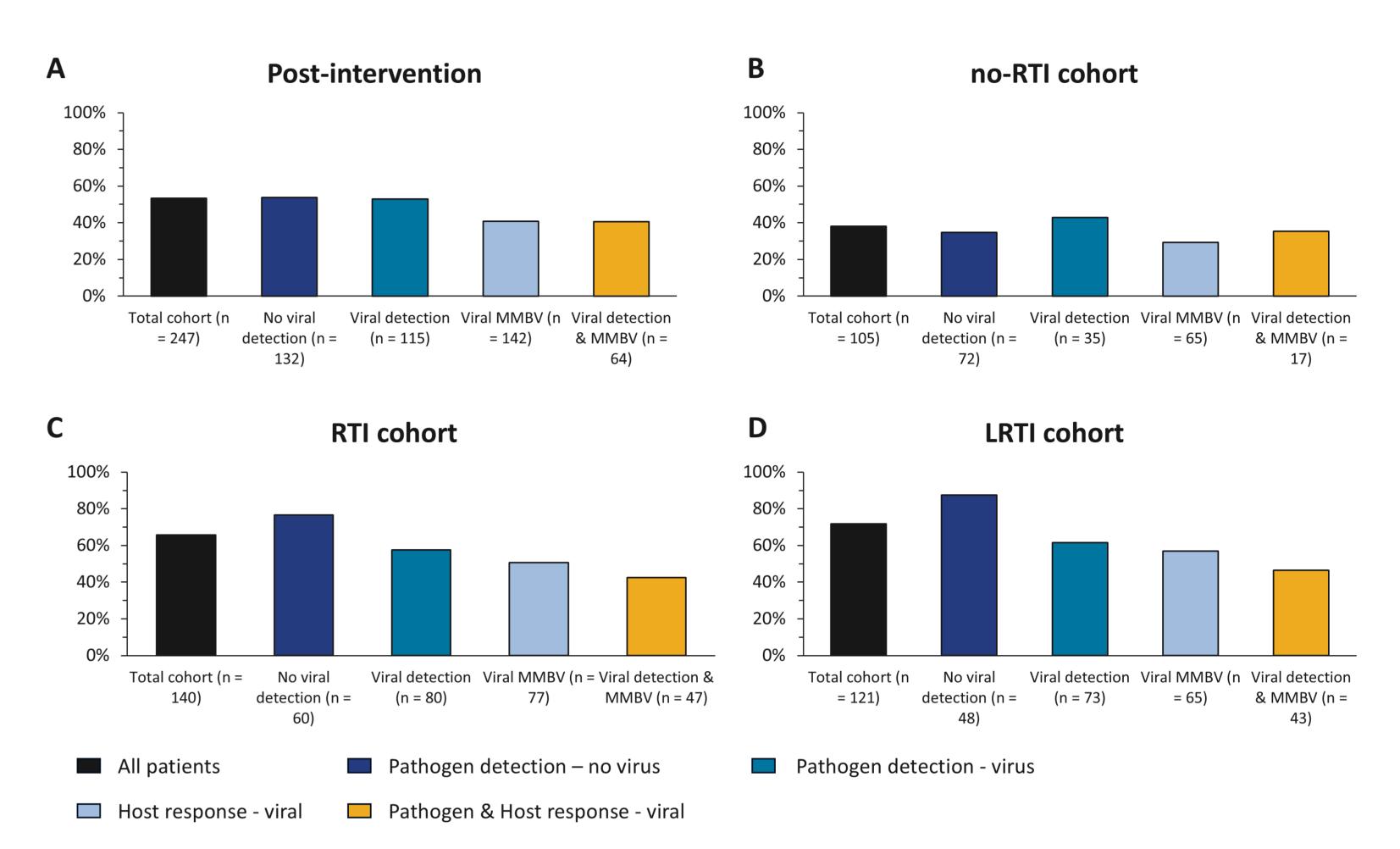
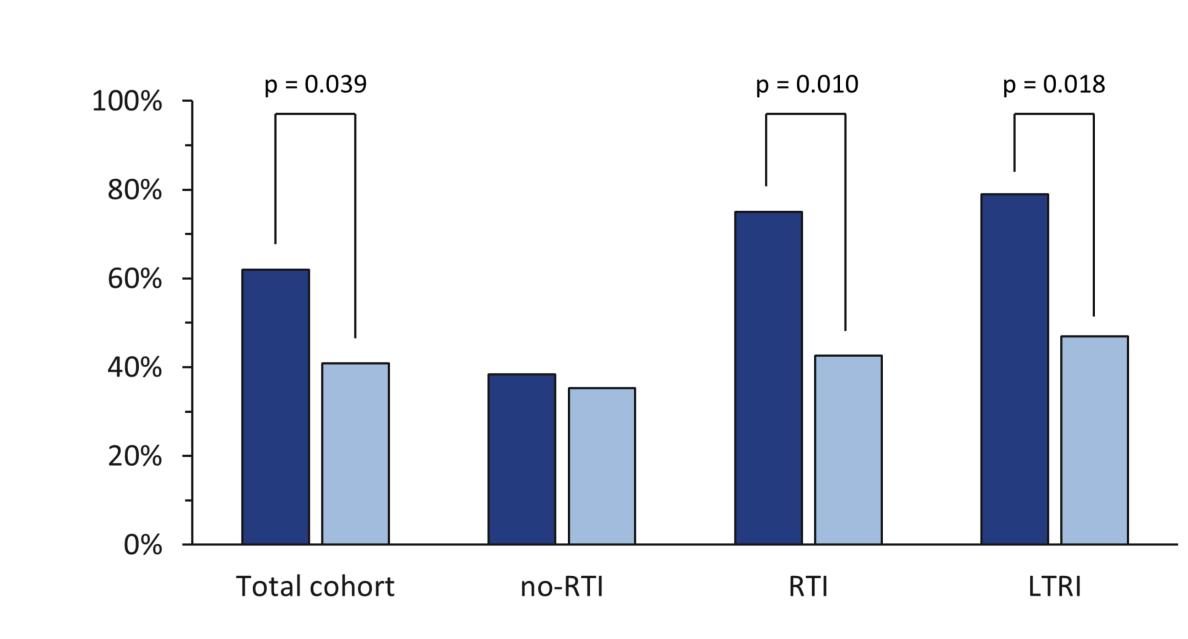


Figure 2: Antibiotic use in the post-intervention period for patients with different discharge diagnoses. Discharge diagnoses plotted were broken down in any discharge diagnosis (A), patients with a non-respiratory (B), respiratory (C), or a Lower respiratory tract infection.





in the pre- and postintervention 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.

- 2014-2017: Only Pathogen-based testing informed clinical practice.
- 2021-2022: Pathogen- and host-response based testing informed clinical practice.

## 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.