

# THE LANCET

## Respiratory Medicine

### Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Brendish NJ, Malachira AK, Armstrong L, et al. Routine molecular point-of-care testing for respiratory viruses in adults presenting to hospital with acute respiratory illness (ResPOC): a pragmatic, open-label, randomised controlled trial. *Lancet Respir Med* 2017; published online April 5. [http://dx.doi.org/10.1016/2213-2600\(17\)30120-0](http://dx.doi.org/10.1016/2213-2600(17)30120-0).

**Table S1: List of final clinical diagnoses in ‘Other’ category**

	<b>POCT (n=47)</b>	<b>Control (n=47)</b>
Congestive cardiac failure	10	9
Exacerbation of other lung diseases*	9	12
Tonsillopharyngitis	6	1
Pulmonary embolism	3	6
Pleural effusion	3	0
Urinary sepsis	3	2
Gastroenteritis	3	0
Musculoskeletal chest pain	2	1
Empyema	1	1
Anaemia	1	0
Infected spinal metal work	1	0
Infectious mononucleosis	1	1
Lymphoma	1	0
Pericarditis	1	0
Atrial fibrillation	1	0
Pyogenic liver abscess	1	0
Sepsis/bacteraemia of unknown source	0	4
Viral meningitis	0	2
Sinusitis	0	1
Tuberculosis	0	1
Acute cholecystitis	0	1
Haemarthrosis	0	1
Inflammatory bowel disease	0	1
Lobar collapse unclear aetiology	0	1
Transverse myelitis	0	1
Diabetic ketoacidosis	0	1

POCT=point-of-care test group.

\*Includes bronchiectasis and interstitial lung diseases

**Table S2: Percentage positive and negative agreement between FilmArray respiratory panel (POCT) and Laboratory PCR results for all patients in the intervention group who received both tests (n=110)**

	Number detected by FilmArray/ Laboratory PCR*				Positive % agreement [a/(a+c)] (95%CI)	Negative % agreement [d/(b+d)] (95%CI)
	+ /+ (a)	+ / - (b)	- / + (c)	- / - (d)		
Influenza A	19	2	2	87	90% (70 to 99)	98 (92 to 100)
Influenza B	11	1	1	97	92% (61 to 100)	99 (94 to 100)
RSV	2	0	0	108	100 (16 to 100)	100 (97 to 100)
Parainfluenza 3	2	0	0	108	100 (16 to 100)	100 (97 to 100)
hMPV	3	0	0	107	100 (30 to 100)	100 (97 to 100)
Adenovirus	1	0	0	109	100 (30 to 100)	100 (97 to 100)
Rhino/enterovirus	NA	12	NA	NA	-	-
Coronavirus	NA	5	NA	NA	-	-
Total	38	3	3	66	93 (80 to 98)	96 (88 to 99)

PCR=polymerase chain reaction. 95%CI=95% confidence interval. RSV=respiratory syncytial virus. hMPV=human metapneumovirus. NA=not applicable; rhino/enterovirus and coronavirus were not targets on the laboratory PCR panel.

\*Includes all viruses detected by laboratory PCR with Ct value of  $\leq 38$  of 45 cycles.

**Table S3: Multivariable analysis for the primary outcome, receipt of any antibiotics**

Variable	Odds ratio (95% CI)	p value
Point-of-care test	0.99 (0.57 to 1.70)	0.957
Age, years	1.03 (1.01 to 1.05)	0.001
Duration of symptoms prior to admission, days	0.96 (0.83 to 1.11)	0.579
Temperature, °C	1.34 (0.97 to 1.84)	0.073
Sex: male	0.71 (0.40 to 1.25)	0.235
Antibiotics <14 days prior*	1.54 (0.79 to 3.01)	0.204
Cardiovascular disease*	0.58 (0.27 to 1.23)	0.158
Respiratory disease*	2.25 (0.97 to 5.20)	0.059
Other comorbidity*	2.70 (1.17 to 6.25)	0.059
Current smoker*	1.11 (0.57 to 2.19)	0.755
Influenza vaccine*†	0.79 (0.42 to 1.48)	0.468
CRP, mg/L	1.02 (1.01 to 1.02)	<0.001
Diagnosis**		
Asthma	0.15 (0.04 to 0.54)	0.004
IECOPD	0.31 (0.08 to 1.25)	0.101
ILI/NPLRTI	0.16 (0.05 to 0.49)	0.001
Other	0.20 (0.06 to 0.70)	0.012

All continuous variables are mean-centred.

95% CI=95% confidence interval. CRP=C-reactive protein.

IECOPD=infective exacerbation of COPD.

ILI=influenza-like illness.

NPLRTI=non-pneumonic lower respiratory tract infection

\*Reference category: no.

\*\*Reference category: pneumonia.

†For the current influenza season

**Table S4: Multivariable analysis for the duration of antibiotics**

<b>Variable</b>	<b>Incidence rate ratio (95% CI)</b>	<b>p value</b>
Point-of-care test	0.92 (0.83 to 1.02)	0.119
Age, years	1.00 (1.00 to 1.00)	0.979
Duration of symptoms prior to admission, days	1.00 (0.97 to 1.030)	0.980
Temperature, °C	0.99 (0.94 to 1.04)	0.683
Sex: male	1.02 (0.92 to 1.13)	0.737
Antibiotics <14 days prior*	1.05 (0.93 to 1.19)	0.413
Cardiovascular disease*	0.97 (0.85 to 1.10)	0.614
Respiratory disease*	1.04 (0.92 to 1.19)	0.497
Other comorbidity*	1.03 (0.91 to 1.16)	0.674
Current smoker*	0.96 (0.85 to 1.09)	0.523
Influenza vaccine*†	1.00 (0.89 to 1.13)	0.952
CPR, mg/L	1.00 (1.00 to 1.00)	<0.001
Diagnosis**		
Asthma	0.52 (0.42 to 0.64)	<0.001
IECOPD	0.83 (0.71 to 0.98)	0.025
ILI/NPLRTI	0.69 (0.59 to 0.81)	<0.001
Other	0.99 (0.84 to 1.16)	0.873

All continuous variables are mean-centred.  
95% CI=95% confidence interval. CRP=C-reactive protein.  
IECOPD=infective exacerbation of COPD.  
ILI=influenza-like illness.  
NPLRTI=non-pneumonic lower respiratory tract infection  
\*Reference category: no.  
\*\*Reference category: pneumonia.  
†For the current influenza season

**Table S5: Post-hoc analysis showing baseline characteristics in patients not prescribed antibiotics prior to randomisation and POCT result availability**

	<b>POCT (n=120)</b>	<b>Control (n=167)</b>	<b>p value</b>
Age, years	54 (33-71)	57 (40-70)	0.48
Female sex	68 (57%)	82 (49%)	0.23
<b>Co-morbidity</b>			
CVD	36 (30%)	52 (31%)	0.90
Respiratory disease	72 (60%)	93 (56%)	0.47
Renal disease	3 (3%)	6 (4%)	0.74
Liver disease	4 (3%)	2 (1%)	0.24
Diabetes	17 (14%)	20 (12%)	0.60
Cancer	8 (7%)	9 (5%)	0.80
<b>Observations</b>			
Temperature, °C	36.8 (36.2-37.3)	36.6 (36.3-37.3)	0.65
CRP, mg/L	23 (4-76)	28 (8-86)	0.38
<b>Final diagnosis</b>			
Asthma	31 (26%)	32 (19%)	0.20
IECOPD	22 (18%)	40 (24%)	0.31
Pneumonia	20 (17%)	31 (19%)	0.76
ILI/NPLRTI	31 (26%)	37 (22%)	0.49
Other	16 (13%)	27 (16%)	0.62

All data are given as number (%), or median (IQR).

POCT=Point-of-care test group. CVD=cardiovascular disease.

CRP=C-reactive protein. IECOPD=infective exacerbation of COPD.

ILI=influenza-like illness. NPLRTI=non pneumonic lower respiratory tract infection.

**Table S6: Post-hoc analysis showing antibiotic use in patients not prescribed antibiotics prior to randomisation and POCT result availability.**

	<b>POCT (n=120)</b>	<b>Control (n=167)</b>	<b>Difference (95% CI)</b>	<b>Odds ratio (95% CI)</b>	<b>NNT (95% CI)</b>	<b>p value</b>
Any antibiotic prescribed	61/120 (51%)	107/167 (64%)	-13.2% (-24.8 to -1.7)	0.58 (0.36 to 0.93)	8 (4 to 59)	0.0289
Single dose only	2/61 (3)	0/107 (0)	3.3% (-1.8 to 12.4)	9.0 (0.4 to 191.4)	-	0.14
<48 hours in total	9/61 (15)	3/107 (3)	12.0% (3.5 to 23.0)	6.0 (1.6 to 23.1)	-	0.0092
<b>Duration, days</b>						
mean (SD)	8.0 (6.0)	8.7 (5.1)	-0.7 (-2.5 to 1.2)	-	-	0.48
median (IQR)	6.5 (5.5-9.8)	7.1 (5.9-9.8)	-0.5 (-1.5 to 0.4)	-	-	0.28

All data are given as number (%), n/n (%), mean (SD) or median (IQR). POCT=Point-of-care test group. 95% CI=95% confidence interval. NNT=number needed to test.

**Table S7. Post-hoc analysis showing antibiotic duration and length of hospital stay by POCT result**

	<b>POCT positive (n=158)</b>	<b>POCT negative (n=202)</b>	<b>Difference 95%CI</b>	<b>Odds ratio 95%CI</b>	<b>p value</b>
<b>Antibiotic use</b>					
Any antibiotic given	129 (80%)	172 (85%)	-5.4% (-13.3 to 2.5)	0.73 (0.41 to 1.27)	0.21
Duration, days					
mean (SD)	6.2 (4.8)	8.0 (5.3)	-1.7 (-2.9 to -0.6)	-	0.0033
median (IQR)	6.5 (2.1-8.2)	7.0 (5.7-9.2)	-0.5 (-1.8 to -0.2)	-	0.0010
<b>Length of stay</b>					
Hospitalised	142 (90%)	190 (94%)	-4.2 (-9.7 to 1.3)	0.56 (0.26 to 1.22)	0.17
Length of stay, days§					
mean (SD)	4.7 (4.6)	6.5 (7.2)	-1.7 (-3.0 to -0.4)	-	0.0085
median (IQR)	3.1 (1.3-6.7)	4.0 (1.9-7.1)	-0.9 (-1.3 to 0.1)	-	0.059

Data are given as number (%), mean (standard deviation) and median (interquartile range).

†POCT negative compared with control group

§Adjusted for in hospital mortality

**Table S8: Antibiotic use and length of stay for the clinical subgroups**

	<b>POCT (n=360)</b>	<b>Control (n=354)</b>	<b>Difference (95%CI)</b>	<b>Odds ratio (95%CI)</b>	<b>p value</b>
<b>Asthma</b>	62	57			
Antibiotics given	43 (69.4%)	36 (63.2%)	6.2% (-10.5 to 22.6)	1.32 (0.62 to 2.83)	0.56
Single dose only	14/43 (32.6%)	3/36 (8.3%)	24.2% (6.1 to 40.1)	5.31 (1.38 to 20.41)	0.0125
<48hrs given	18/43 (41.9%)	4/36 (11.1%)	30.8% (11.2 to 47.0)	5.76 (1.73 to 19.20)	0.0026
Duration of antibiotics, days					
mean (SD)	3.9 (3.4)	5.3 (2.3)	-1.4 (-2.7 to -0.1)	-	0.0382
median (IQR)	5.5 (0.1-6.7)	6.0 (5.0-6.7)	-0.5 (-2.5 to 0.1)	-	0.0492
Length of hospital stay, days					
mean (SD)	3.4 (3.3)	3.9 (3.5)	-0.5 (-1.8 to 0.9)	-	0.49
median (IQR)	2.4 (1.3-4.9)	2.8 (1.6-6.0)	-0.4 (-1.3 to 0.5)	-	0.51
<b>IECOPD</b>	81	83			
Antibiotics given	75 (92.6%)	75 (90.4%)	2.2% (-6.9 to 11.4)	1.33 (0.44 to 4.03)	0.78
Single dose only	7/75 (9.3%)	3/75 (4.0%)	5.3% (-3.2 to 14.4)	2.47 (0.61 to 9.95)	0.33
<48hrs given	11/75 (14.7%)	3/75 (4.0%)	10.7% (1.2 to 20.7)	4.13 (1.10 to 15.50)	0.0462
Duration of antibiotics, days					
mean (SD)	6.1 (3.2)	8.0 (5.0)	-1.9 (-3.2 to -0.5)	-	0.0078
median (IQR)	6.4 (5.3-7.6)	6.5 (5.5-8.9)	-0.1 (-1.6 to 0.1)	-	0.13
Length of hospital stay, days					
mean (SD)	4.5 (3.6)	6.3 (6.2)	-1.8 (-3.4 to -0.2)	-	0.0276
median (IQR)	3.7 (1.9-6.2)	4.2 (2.3-8.8)	-0.5 (-2.1 to 0.2)	-	0.0871
<b>Asthma + IECOPD combined</b>	143	140			
Antibiotics given	118 (82.5%)	111 (79.3%)	3.2% (-6.0 to 12.4)	1.23 (0.68 to 2.24)	0.54
Single dose only	21/118 (17.8%)	6/111 (5.4%)	12.4% (4.1 to 20.8)	3.79 (1.47 to 9.78)	0.0041
<48hrs given	29/118 (24.6%)	7/111 (6.3%)	18.3% (9.0 to 27.4)	4.84 (2.02 to 11.59)	0.0002
Duration of antibiotics, days					
mean (SD)	5.3 (3.4)	7.1 (4.5)	-1.8 (-2.8 to -0.8)	-	0.0008
median (IQR)	6.0 (2.2-7.1)	6.4 (5.5-7.4)	-0.4 (-1.4 to -0.1)	-	0.0352
Length of hospital stay, days					
mean (SD)	4.0 (3.5)	5.4 (5.5)	-1.4 (-2.5 to -0.2)	-	0.0186
median (IQR)	3.1 (1.6-5.4)	3.8 (2.0-7.2)	-0.7 (-1.4 to -0.1)	-	0.0468
<b>Pneumonia</b>	94	98			
Antibiotics given	92/94 (97.8%)	96/98 (98.0%)	-0.1% (-5.2 to 5.6)	0.96 (0.13 to 6.95)	1.00
Single dose only	3/92 (3.3%)	1/96 (1.0%)	2.2% (-2.9 to 8.2)	3.20 (0.33 to 31.37)	0.36
<48hrs given	5/92 (5.4%)	4/96 (4.2%)	1.3% (-5.5 to 8.4)	1.32 (0.34 to 5.08)	0.74
Duration of antibiotics, days					
mean (SD)	9.6 (5.4)	9.0 (5.3)	0.7 (-0.9 to 2.2)	-	0.41
median (IQR)	8.3 (6.6-11.6)	7.9 (6.3-10.6)	0.4 (-0.3 to 1.5)	-	0.23
Length of hospital stay, days					
mean (SD)	7.5 (6.5)	7.0 (6.4)	0.5 (-1.4 to 2.4)	-	0.58
median (IQR)	5.6 (3.1-9.6)	5.0 (3.0-8.5)	0.5 (-0.7 to 1.6)	-	0.43



*Table S8 continued*

	<b>POCT (n=360)</b>	<b>Control (n=354)</b>	<b>Difference (95%CI)</b>	<b>Odds ratio (95%CI)</b>	<b>p value</b>
<b>ILI/NPLRTI</b>	76	69			
Antibiotics given	53/76 (69.7%)	51/69 (73.9%)	-4.2% (-18.4 to 10.5)	0.81 (0.39 to 1.68)	0.59
Single dose only	6/53 (11.3%)	3/51 (5.9%)	5.4% (-6.3 to 17.4)	2.04 (0.48 to 8.65)	0.48
<48hrs given	11/53 (20.8%)	9/51 (17.7%)	3.1% (-12.2 to 18.2)	1.22 (0.46 to 3.26)	0.81
Duration of antibiotics, days					
mean (SD)	5.9 (4.5)	5.8 (3.2)	0.1 (-1.4 to 1.6)	-	0.84
median (IQR)	6.4 (4.4-7.4)	6.3 (4.4-7.3)	0.1 (-0.7 to 0.9)	-	0.88
Length of hospital stay, days				-	
mean (SD)	3.7 (4.1)	2.9 (4.3)	0.8 (-0.7 to 2.3)	-	0.30
median (IQR)	2.2 (1.0-4.4)	1.9 (0.9-3.1)	0.3 (-0.2 to 1.0)	-	0.23
<b>Other diagnoses</b>	47	47			
Antibiotics given	38/47 (80.9%)	36/47 (76.6%)	4.3% (-12.3 to 20.6)	1.29 (0.48 to 3.48)	0.80
Single dose only	1/38 (2.6%)	0/36 (0%)	2.6% (-7.3 to 13.5)	2.92 (0.12 to 74.1)	1.00
<48hrs given	5/38 (13.2%)	5/36 (13.9%)	-0.7% (-15.5 to 17.3)	0.94 (0.25 to 3.56)	1.00
Duration of antibiotics, days				-	
mean (SD)	9.2 (6.4)	8.4 (5.6)	0.8 (-2.0 to 3.6)	-	0.56
median (IQR)	8.1 (6.0-11.3)	7.3 (5.5-12.2)	0.8 (-1.5 to 2.6)	-	0.77
Length of hospital stay, days					
mean (SD)	7.0 (8.1)	7.4 (6.0)	-0.4 (-2.7 to 3.5)	-	0.79
median (IQR)	3.4 (1.3-7.5)	6.0 (2.2 to 10.0)	-2.6 (-3.3 to 0.6)	-	0.25

All data are given as number (%), n/n (%), mean (SD) or median (IQR). POCT=Point-of-care test group. 95%CI=95% confidence interval. IECOPD=infective exacerbation of COPD. ILI=influenza-like illness. NPLRTI=non-pneumonic lower respiratory tract infection.

**Table S9: Median (interquartile range) values for selected outcomes**

	<b>POCT (n=360)</b>	<b>Control (n=354)</b>	<b>Difference (95%CI)</b>	<b>p value</b>
Turnaround time of viral testing, hours*	1.6 (1.3-3.1)**	29.8 (24.7-45.8)†	-35.6 (-39.0 to -32.2)	<0.0001
Duration of NAI in influenza negative patients , doses‡	1.0 (1.0-2.0)	5.0 (3.0-10.0)	-4.0 (-7.0 to -2.0)	0.0003
Time to first dose of NAI, hours‡	6.5 (2.0-11.8)	8.5 (0.0-41.5)	-2.0 (-22.0 to 3.0)	0.35
Time to isolation, days‡	0.5 (0.0-1.0)	1.0 (1.0-2.0)	-0.5 (-1.0 to 0.0)	0.0149
Time to de-isolations, days‡	1.0 (1.0-1.0)	2.0 (1.0-5.0)	-1.0 (-4.0 to 0.0)	0.0025

POCT=point of care test group. 95%CI=95% confidence interval.

\*Refer to table 2 for full details

\*\*Assessed 356 patients

†Assessed in the 158 patients tested for viruses by laboratory PCR

‡Refer to table 6 for full details

Figure S1: Distribution of antibiotic duration in patients with asthma

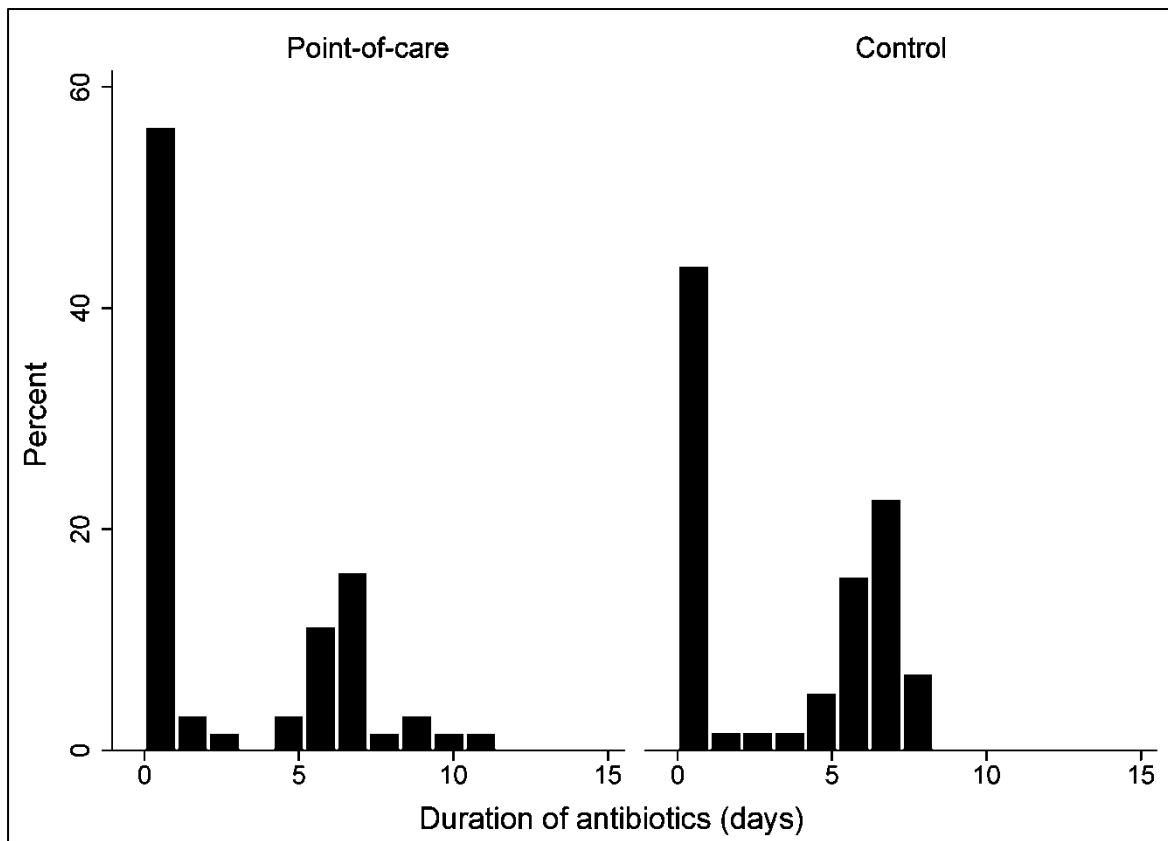


Figure S2: Distribution of antibiotic duration in patients with COPD

