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Emmanuel Novy, Antoine Goury, Carine Thivilier, Thomas Guillard,
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1 **Title:** Algorithm for rational use of FilmArray Pneumonia Panel in bacterial coinfections of
2 critically ill ventilated COVID-19 patients

3 **Authors list:** Emmanuel Novy, MD^{1,2}, Antoine Goury, MD³, Carine Thivilier, MD⁴, Thomas
4 Guillard, PharmD.PhD^{5,6}, Corentine Alauzet, PharmD.PhD^{2,7*}

5 **Affiliations:**

6 1. Department of Anesthesiology, critical care and peri-operative medicine, University
7 Hospital of Nancy, Vandœuvre-Lès-Nancy F-54511, France; University of Lorraine, F-
8 54000 Nancy, France.

9 2. Université de Lorraine, SIMPA, Stress Immunity Pathogens unit, EA 7300, F-54000
10 Nancy, France.

11 3. Medical Intensive Care Unit, University hospital of Reims, France.

12 4. Medical Intensive Care Unit, University Hospital of Nancy, Brabois Hospital, F-54000
13 Nancy, France.

14 5. Laboratoire de Bactériologie-Virologie-Hygiène Hospitalière-Parasitologie-Mycologie,
15 CHU Reims, Hôpital Robert Debré, Reims, France.

16 6. Université de Reims-Champagne-Ardenne, SFR CAP-Santé, Inserm UMR-S 1250 P3Cell,
17 51097, Reims, France.

18 7. CHRU-Nancy, Service de Microbiologie, F-54000 Nancy, France

19

20 ***Corresponding author:**

21 Dr Corentine ALAUZET, PharmD, PhD

22 CHRU-Nancy, Service de Microbiologie, F-54000 Nancy, France

23 Université de Lorraine, SIMPA, Stress Immunity Pathogens unit, EA 7300, F-54000 Nancy,

24 France.

25 E-mail: c.alauzet@chru-nancy.fr; corentine.alauzet@univ-lorraine.fr

26 Phone: + 33 3 83 15 39 38

27 Fax: + 33 3 83 15 43 76

28

29 **Abstract**

30 The FilmArray® Pneumonia Panel has proven to be an effective tool for rapid detection of
31 main respiratory pathogens. However, its rational use needs appropriate knowledge and
32 formation regarding its indication and interpretation. Herein, we provide some advices to help
33 with success of its daily routine use, particularly in critically ill ventilated COVID-19
34 patients.

35

36

37 **Clinical Trial registration number:** NCT04453540.

38

39 **Keywords:** Covid-19 / bacterial coinfection / antimicrobial stewardship / pneumonia /
40 critically ill / molecular diagnosis

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43 Since the start of the pandemic Covid-19 outbreak, molecular respiratory panel such as
44 FilmArray® Pneumonia Panel (FAPP; bioMérieux, France) has been widely used in critically
45 ill patients for bacterial coinfections management. Regarding its performance for pathogens
46 and antimicrobial resistance detection (Suppl. **Table 1**), all authors highlighted FAPP interest
47 for antimicrobial stewardship, especially antibiotic sparing [1-6]. However, FAPP
48 interpretation could be challenging [4,5]. Indeed, as evoked by Maataoui *et al.*, one of the
49 reasons of a non-optimal use of FAPP was the “lack of knowledge and confidence in the test”
50 [4]. The present study reports the lessons from the implementation of FAPP during the first
51 COVID-19 outbreak, when a training on “how to use FAPP” could not be performed due to
52 the work overload.

53 This is a multicenter retrospective analysis (clinicalTrial.gov NCT04453540) of all critically
54 ill patients who were admitted to the Nancy and Reims University Hospitals (six ICUs) from
55 March to May 2020, with COVID-19 and respiratory failure requiring invasive mechanical
56 ventilation (IMV). The local institutional ethics committee approved this study (Comité
57 d'éthique du CHRU de Nancy, N°CO-20). Informed consent was obtained from all
58 participants and/or their legal guardians. Presence of SARS-CoV-2 was diagnosed using RT-
59 PCR. All patients with suspicion of bacterial pneumonia were eligible. The decision to
60 prescribe FAPP was at the discretion of the clinician. Only patients with concomitant FAPP,
61 conventional culture (CC) and Gram stain were included. Samples were endotracheal
62 aspirates (ETA) and bronchoalveolar lavages (BAL). Results of the FAPP and Gram stain
63 were available for the intensivists within four hours. A first result of the CC was available
64 after one day with a definitive result within five days. For quantitative culture, only the
65 bacteria above the following threshold were considered: 10^4 CFU/mL for BAL and 10^5
66 CFU/mL for ETA. Phenotypic drug susceptibility testing was performed according to the

67 recommendations of the antibiogram committee of the French Society for Microbiology (CA-
68 SFM)/European Committee for Antibiotic Susceptibility Testing (EU-CAST). A
69 multidisciplinary expert committee (MEC) composed of intensivists, infectious disease
70 specialists and microbiologists from both centers analyzed retrospectively the contribution of
71 FAPP compared to CC in the treatment decision of pneumonia according to criteria from
72 Weiss *et al.* [7]. Antibiotics used to treat any concomitant infection were not considered by
73 the MEC. Early bacterial coinfections, represented by community-acquired pneumonia
74 (CAP), were defined as infections occurring during the first 48h of ICU admission. The
75 ventilator-associated pneumonia (VAP) were defined as infections occurring after 48h of
76 IMV. Multiple tests from the same patient were considered independent when performed
77 during distinct infectious episodes. Categorical data were analyzed using chi-square test or
78 Fisher's exact test. Statistical analyses were performed by an independent statistician using
79 SAS 9.4 software (SAS Institute, Inc, Cary, N.C.).

80 Overall, 344 patients with a positive SARS-CoV-2 RT-PCR were admitted in the
81 participating ICUs of whom 90 fulfilled eligibility criteria. Samples were 74 ETA and 45
82 BAL. Characteristics and ICU data are presented in **Table 1**. Bacteriological results were
83 presented in **Tables 2** and **3**. The rate of clinically confirmed CAP and VAP were 5.0% and
84 40.3%, respectively. Bacterial pathogens were detected by FAPP (45.4%) and/or by CC
85 (38.7%) in 41 and 34 ETA and in 13 and 12 BAL, respectively. The adequacy between FAPP
86 and CC in pathogen detection was better ($p=0.017$) for BAL (95.6%) than for ETA (79.7%).
87 *Staphylococcus aureus* and *Pseudomonas aeruginosa* were the most prevalent pathogens.
88 Two cases of negative FAPP (no detection of *Morganella morganii*) have led to inappropriate
89 discontinuation of empirical antibiotic therapy. Two Extended-Spectrum β -lactamase ESBL
90 (not-CTX-M)-producing *Enterobacter cloacae* and one 3GC-resistant *P. aeruginosa* were

91 isolated by CC without detection of resistance gene by FAPP. Regarding the six samples with
92 methicillin-resistance of *S. aureus* (MRSA) detected in FAPP, only three have a *S. aureus*-
93 positive culture and all where methicillin-susceptible (MSSA). According to MEC analysis,
94 FAPP-based therapeutic decision was concordant with CC-based therapeutic decision in 91%
95 for BAL compared with 69% for ETA ($p=0.009$). The most contribution of FAPP regarding
96 antibiotic prescription was antibiotic spare (**Table 2**). However, we observed that intensivists
97 considered FAPP for treatment only in 42.0% (50/119) of cases.

98 These results confirmed the usefulness of FAPP to rapidly diagnose bacterial coinfection.
99 However, there is a room for improvement of its use and interpretation. Herein, we suggest
100 four tips for a tailored use of FAPP in critically ill ventilated patients:

101 **1. Training for mastering FAPP by the intensivists is required for successful utilization**
102 **in the daily routine practice.** We believe that an appropriate knowledge about FAPP
103 performance and results interpretation should led to a better antibiotic use. Therefore, a
104 collaboration between microbiologists and intensivists is mandatory.

105 **2. FAPP should be performed on BAL to avoid over-diagnosis of bacterial coinfection.**
106 Lower relevance of FAPP results from ETA compared to BAL for treatment could be
107 explained by detection of not significant bacteria from the tracheobronchial colonization.
108 However, if BAL could not be performed, ETA could be used with cautious interpretation
109 of FAPP results.

110 **3. Conventional culture should be systematically performed in parallel.** To detect
111 bacteria not included in the FAPP [5] and to confirm resistance gene detection. For Gram-
112 negative bacilli, FAPP detects only CTX-M ESBL. Moreover, as previously described [8],
113 FAPP led to over-detection of MRSA that could lead to an overuse of anti-MRSA
114 antibiotics, especially in case of local ecology with low prevalence of MRSA. Indeed,

115 among the 6 samples with MRSA detected in FAPP (5 ETA and 1 BAL), only three (2
116 ETA and 1 BAL) had a *S. aureus*-positive culture and all where MSSA. Such discordance
117 could be explained either by the co-occurrence of a *S. aureus* with an empty *SCCmec*
118 cassette and methicillin-resistant negative coagulase staphylococci, or by a mixed
119 specimen of MSSA and MRSA, respectively above and below the threshold of culture
120 detection.

121 **4. Therapeutic decision must be re-evaluated with the result of 2-days conventional**
122 **culture.** The delay of 2 days for definitive CC interpretation should cover slowing
123 growing bacteria (low bacterial load or prior antimicrobial treatment) as well as drug
124 susceptibility testing results. Moreover, of 65 negative-FAPP, 62 (95.4%) showed 5-days
125 negative culture and 3 (4.6%) were positive (for outside-panel bacteria) but within 2 days
126 of culture. Consequently, in absence of i) severity criteria, namely septic shock or severe
127 ARDS (according to Berlin criteria), and of ii) Gram-negative bacilli at Gram stain,
128 empirical antibiotic therapy could be stopped based on a negative-FAPP result.

129 In the present study, a FAPP use based on these tips would allow 65.6% of antibiotic spare in
130 bacterial coinfection and a better adequacy of empirical antibiotic treatment. Regarding VAP,
131 FAPP should consider local ecology for optimal interpretation, especially for resistance
132 detection (i.e. *P. aeruginosa* with non-enzymatic resistance). Based on our results, we
133 propose an algorithm to improve the use of FAPP for antibiotic stewardship at the bedside
134 (**Figure 1**). Further studies are now warranted to demonstrate that rational use of FAPP will
135 also improve patient outcome.

136

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138 this study.

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146 Eliane Albuisson

147

148

149 **References**

- 150 1. Caméléna F, Moy A-C, Dudoignon E, Poncin T, Deniau B, Guillemet L, et al. Performance of
151 a multiplex polymerase chain reaction panel for identifying bacterial pathogens causing
152 pneumonia in critically ill patients with COVID-19. *Diagn Microbiol Infect Dis*
153 2020;99:115183. <https://doi.org/10.1016/j.diagmicrobio.2020.115183>.
154
- 155 2. Ginocchio CC, Garcia-Mondragon C, Mauerhofer B, Rindlisbacher C, and the EME
156 Evaluation Program Collaborative. Multinational evaluation of the BioFire® FilmArray®
157 Pneumonia plus Panel as compared to standard of care testing. *Eur J Clin Microbiol Infect Dis*
158 2021. Epub ahead of print. <https://doi.org/10.1007/s10096-021-04195-5>.
159
- 160 3. Furukawa D, Kim B, Jeng A. Real-life utilization of BioFire® Filmarray® pneumonia panel
161 as an antibiotic stewardship tool. *Infect Dis (Lond)*. 2021;53:308-13.
162 <https://doi.org/10.1080/23744235.2020.1866774>.
163
- 164 4. Maataoui N, Chemali L, Patrier J, Tran Dinh A, Le Fèvre L, Lortat-Jacob B, et al. Impact of
165 rapid multiplex PCR on management of antibiotic therapy in COVID-19-positive patients
166 hospitalized in intensive care unit. *Eur J Clin Microbiol Infect Dis* 2021. Epub ahead of print.
167 <https://doi.org/10.1007/s10096-021-04213-6>.
168
- 169 5. Mitton B, Rule R, Said M. Laboratory evaluation of the BioFire FilmArray Pneumonia plus
170 panel compared to conventional methods for the identification of bacteria in lower respiratory
171 tract specimens: a prospective cross-sectional study from South Africa. *Diagn Microbiol*
172 *Infect Dis*. 2021;99:115236. <https://doi.org/10.1016/j.diagmicrobio.2020.115236>.
173
- 174 6. Zacharioudakis IM, Zervou FN, Dubrovskaya Y, Inglima K, See B, Agüero-Rosenfeld M.
175 Evaluation of a Multiplex PCR Panel for the Microbiological Diagnosis of Pneumonia in
176 Hospitalized Patients: Experience from an Academic Medical Center. *Int J Infect Dis*
177 2021;104:354–60. <https://doi.org/10.1016/j.ijid.2021.01.004>.
178
- 179 7. Weiss E, Zahar J-R, Lesprit P, Ruppe E, Leone M, Chastre J, et al. Elaboration of a
180 consensual definition of de-escalation allowing a ranking of β -lactams. *Clin Microbiol Infect*
181 2015;21:649.e1-10. <https://doi.org/10.1016/j.cmi.2015.03.013>.
182
- 183 8. Webber DM, Wallace MA, Burnham CA, Anderson NW. Evaluation of the BioFire
184 FilmArray Pneumonia Panel for Detection of Viral and Bacterial Pathogens in Lower
185 Respiratory Tract Specimens in the Setting of a Tertiary Care Academic Medical Center. *J*
186 *Clin Microbiol* 2020;58:e00343-20. <https://doi.org/10.1128/JCM.00343-20>.
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190

191 **Figure legend.**

192 **Fig. 1.** Clinical algorithm for initiating antibiotics using FAPP in bacterial coinfection of
193 critically ill COVID-19 patients. IMV, invasive mechanical ventilation; BAL,
194 bronchoalveolar lavage; FAPP, FilmArray® Pneumonia Panel; ATB, antibiotics; GNB,
195 Gram-negative bacilli.

196 ^a Endotracheal aspirate samples could be used but need cautious interpretation regarding the
197 risk of over-diagnosis due to tracheobronchial colonization

198 ^b Septic shock (according to SEPSIS-3) or severe ARDS (according to Berlin criteria)

199

200 **Ethics consideration**

201 The institutional ethics committee approved this study (Comité d'éthique du CHRU de
202 Nancy, N°CO-20). All experiments were performed in accordance with guidelines and
203 regulations. Informed consent was obtained from all participants and/or their legal guardians.

204

205 **Authors' contributions:** EN and CA participated equally in this work. EN, CA and TG
206 contributed substantially to the study design and the writing of the manuscript. EN, CA, TG,
207 CT, AG contributed to the acquisition, analysis and interpretation of data. CT and AG made
208 critical revision of the manuscript.

209

210 **Table 1.** Clinical characteristics of patients

Variables	Patients N=90
Male Sex	72 (80.0)
Age (years)	65 [58.3-70.0]
Obesity (BMI >40 kg/m²)	6 (6.6)
Comorbidities:	
Hypertension	50 (55.5)
Diabetes	27 (30.0)
Immune deficiency	18 (20)
Chronic respiratory failure	10 (11.0)
Chronic hemodialysis	1 (1.0)
Cirrhosis	1 (1.0)
ICU data:	
SAPS 2 score	44 [36-61]
ICU LOS (days)	23 [14-37]
IMV duration (days)	17 [11-27]
ECMO	10 (11)
ICU mortality	25 (28)

211 Data are presented as: n (%) – median [IQR]

212 Immune deficiency: diabetes, neoplasia, transplant, neutropenia/aplasia, immunosuppressive
 213 therapy / SAPS 2 score: Simplified Acute Physiology Score II / LOS: Length of stay / IMV:
 214 invasive mechanical ventilation.

215

216

217 **Table 2.** Bacteriological results according to the type of pneumonia and contribution of the
 218 panel FAPP on antibiotic prescription

	Samples N=119	
	CAP	VAP
Type of suspected pneumonia	27 (22.7)	92 (77.3)
Confirmed diagnostic of pneumonia	6	48
(% among suspected / % among total)	(22.2 / 5.0)	(52.2 / 40.3)
Type of samples:		
ETA	15	59
BAL	12	33
Antibiotics 48h prior to samples	15 (55.6)	40 (43.5)
Bacterial copathogens:	FAPP / CC	FAPP / CC
<i>Staphylococcus aureus</i>	0 / 0	17 / 12
<i>Pseudomonas aeruginosa</i>	0 / 0	11 / 11
<i>Haemophilus influenzae</i>	4 / 0	6 / 3
<i>Escherichia coli</i>	0 / 0	9 / 5
<i>Klebsiella pneumoniae</i>	1 / 1	6 / 6
<i>Enterobacter cloacae</i>	0 / 0	5 / 5
<i>Klebsiella aerogenes</i>	0 / 0	4 / 2
<i>Proteus spp.</i>	0 / 0	4 / 3
<i>Serratia marcescens</i>	0 / 0	3 / 3
<i>Streptococcus agalactiae</i>	0 / 0	3 / 1
<i>Moraxella catarrhalis</i>	1 / 0	1 / 1
<i>Mycoplasma pneumoniae</i>	1 / NA	0 / NA

<i>Morganella morganii</i>	NA / 0	NA / 2
<i>Hafnia alvei</i>	NA / 0	NA / 1 ^a
<i>Providencia stuartii</i>	NA / 0	NA / 1 ^a
Resistance detection:	FAPP / AST	FAPP / AST
MRSA	0 / 0	6 / 0
3GC-R Gram-negative bacilli	0 / 0	5 / 6 ^b
Type of pneumonia	CAP	VAP
Contribution of FAPP at first intensivist decision^c		
No modification of empirical antibiotics	0	3 (7.5)
Speeded-up adequate antibiotic	2 (20.0)	9 (22.5)
Antibiotic spare ^d	8 (80.0)	20 (50.0)
Inappropriate antibiotic treatment	0	7 (17.5)
Inappropriate stopped antibiotic	0	1 (2.5)
Contribution of FAPP based on MEC analysis^e		
No modification of empirical antibiotics	1 (3.7)	11 (12.0)
Speeded-up adequate antibiotic	4 (14.8)	13 (14.1)
Antibiotic spare ^d	22 (81.5)	56 (60.9)
Inappropriate antibiotic treatment	0	10 (10.9)
Inappropriate stopped antibiotic	0	2 (2.2)

219 Data are presented as: n (%)

220 ETA: endotracheal aspirate / BAL: bronchoalveolar lavage / CAP: community-acquired
221 pneumonia (defined as infections occurring during the first 48h of ICU admission) / VAP:
222 ventilator-associated pneumonia / FAPP: FilmArray® Pneumonia Panel / CC: conventional
223 culture / AST: antimicrobial susceptibility testing / MRSA: methicillino-resistant
224 *Staphylococcus aureus* / 3GC-R: third generation cephalosporins resistance / NA: not
225 applicable (species not detected either by the FAPP or by the CC) / MEC: multidisciplinary
226 expert committee.

227 ^a The isolation of *H. alvei* and *P. stuartii* in CC had no impact on antibiotic therapy as they
228 were covered by the antibiotics administered following the detection of other pathogens
229 detected by FAPP.

230 ^b Among 3GC-resistant Gram-negative bacilli, 3 CTX-M were detected by both FAPP and
231 CC, 2 CTX-M were detected only by FAPP, 2 ESBL not belonging to CTX-M as well as one
232 3GC-resistant *P. aeruginosa* were detected only by CC.

233 ^c A contribution of FAPP at first intensivist decision was noted in 50 samples (42.0%).

234 ^d Decrease unnecessary antibiotic use (interruption or de-escalation).

235 ^e Theoretical contribution of FAPP after MEC analysis of the 119 samples (100.0%).

236

237 **Table 3.** Bacteriological results according to the type of respiratory samples

238

Samples N=119		
	ETA (n=74)	BAL (n=45)
Type of pneumonia		
CAP : suspected/confirmed	15 / 5	12 / 1
VAP : suspected/confirmed	59 / 34	33 / 14
Antibiotics 48h prior to samples (n=55)	32 (58)	23 (42)
Positive direct examination		
Presence of Gram +	6 (15)	3 (21)
Presence of Gram –	9 (23)	1 (7)
Polymicrobial	24 (62)	10 (72)
Infection polymicrobial		
FAPP (n=18)	14 (77)	4 (23)
Mean number of bacteria detected	2.2	2.25
CC (n=8)	5 (62)	3 (38)
Mean number of bacteria detected	2.2	2
Bacterial copathogens:		
	FAPP / CC	FAPP / CC
<i>Staphylococcus aureus</i>	12 / 6	5 / 6
<i>Pseudomonas aeruginosa</i>	10 / 10	1 / 1
<i>Haemophilus influenzae</i>	7 / 2	3 / 1
<i>Escherichia coli</i>	7 / 4	2 / 1
<i>Klebsiella pneumoniae</i>	6 / 6	1 / 1
<i>Enterobacter cloacae</i>	3 / 3	2 / 2
<i>Klebsiella aerogenes</i>	3 / 1	1 / 1
<i>Proteus spp.</i>	4 / 3	0 / 0
<i>Serratia marcescens</i>	2 / 2	1 / 1
<i>Streptococcus agalactiae</i>	2 / 1	1 / 0
<i>Moraxella catarrhalis</i>	2 / 1	0 / 0
<i>Mycoplasma pneumoniae</i>	1 / NA	0 / NA
<i>Morganella morganii</i>	NA / 1	NA / 1
<i>Hafnia alvei</i>	NA / 1 ^a	NA / 0
<i>Providencia stuartii</i>	NA / 1 ^a	NA / 0
Resistance detection:		
	FAPP / AST	FAPP / AST
MRSA	5 / 0	1 / 0
3GC-R Gram-negative bacilli ^b	4 / 3	1 / 3

239 Data are presented as: n (%)

240 ETA: endotracheal aspirate / BAL: bronchoalveolar lavage / CAP: community-acquired
241 pneumonia (defined as infections occurring during the first 48h of ICU admission) / VAP:
242 ventilator-associated pneumonia / FAPP: FilmArray® Pneumonia Panel / CC: conventional
243 culture / AST: antimicrobial susceptibility testing / MRSA: methicillino-resistant
244 *Staphylococcus aureus* / 3GC-R: third generation cephalosporins resistance / NA: not
245 applicable (species not detected either by the FAPP or by the CC).

246 ^a The isolation of *H. alvei* and *P. stuartii* in CC had no impact on antibiotic therapy as they
247 were covered by the antibiotics administered following the detection of other pathogens
248 detected by FAPP.

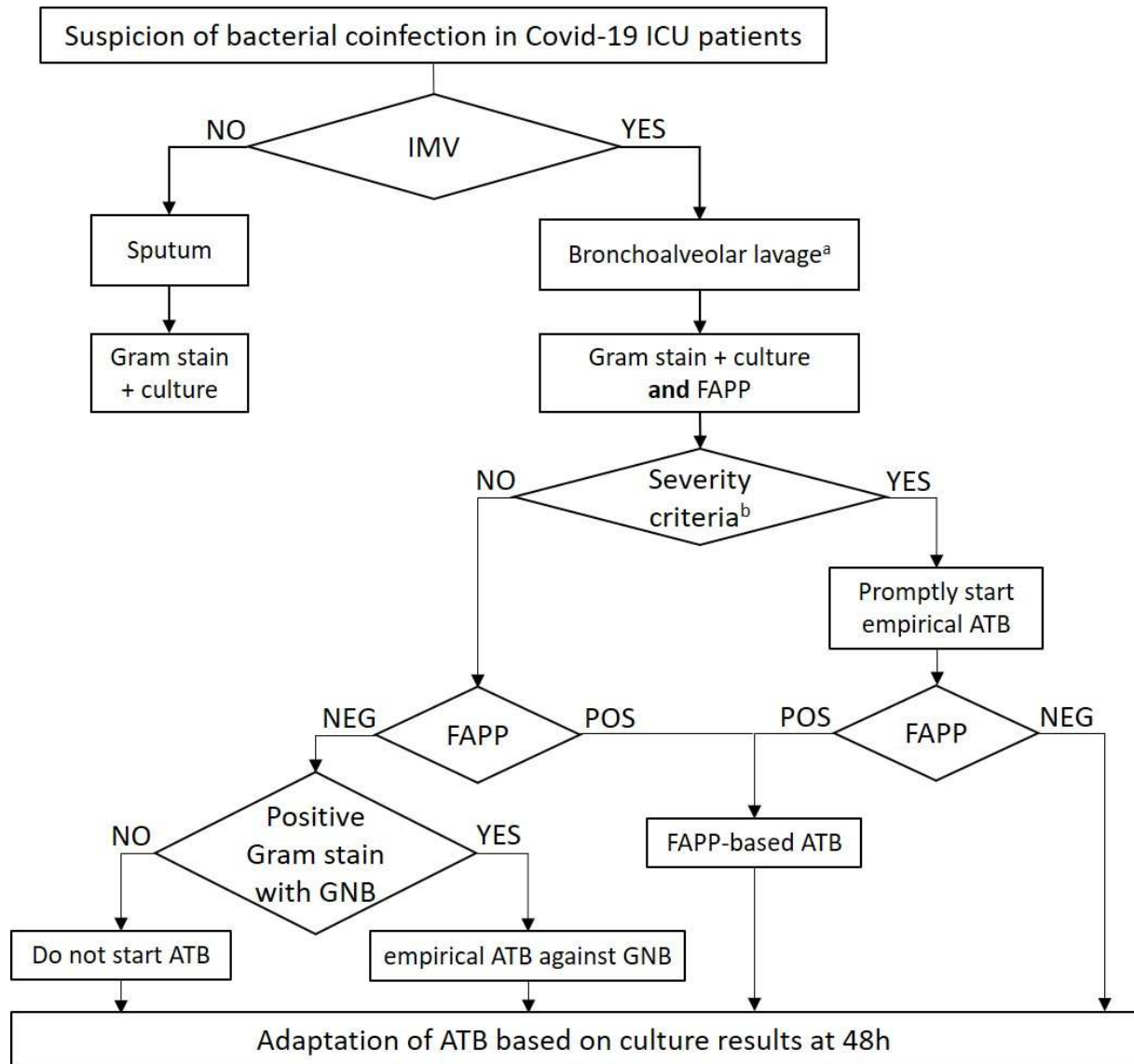
249 ^b Among 3GC-resistant Gram-negative bacilli, 3 CTX-M were detected by both FAPP and
250 CC, 2 CTX-M were detected only by FAPP, 2 ESBL not belonging to CTX-M as well as one
251 3GC-resistant *P. aeruginosa* were detected only by CC.

252

253

254 **Figure 1.** Clinical algorithm for initiating antibiotics using FAPP in bacterial coinfection of

255 critically ill COVID-19 patients.



256

257 IMV, invasive mechanical ventilation; BAL, bronchoalveolar lavage; FAPP, FilmArray®
258 Pneumonia Panel; ATB, antibiotics; GNB, Gram-negative bacilli.

259 ^a Endotracheal aspirate samples could be used but need cautious interpretation regarding the
260 risk of over-diagnosis due to tracheobronchial colonization

261 ^b Septic shock (according to SEPSIS-3) or severe ARDS (according to Berlin criteria)

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264

265 **Supplementary Table 1.** Targets identified by the FAPP assay

Category	Result type	Targets
Viruses	qualitative	Adenovirus, coronavirus, human metapneumovirus, human rhinovirus/enterovirus, influenza A virus, influenza B virus, parainfluenza virus, respiratory syncytial virus
Atypical bacteria	qualitative	<i>Chlamydophila pneumoniae</i> , <i>Legionella pneumophila</i> , <i>Mycoplasma pneumoniae</i>
Bacteria	semi-quantitative*	<i>Acinetobacter calcoaceticus</i> - <i>Acinetobacter baumannii</i> complex, <i>Enterobacter cloacae</i> complex, <i>Escherichia coli</i> , <i>Haemophilus influenzae</i> , <i>Klebsiella aerogenes</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumoniae</i> , <i>Moraxella catarrhalis</i> , <i>Proteus</i> spp., <i>Pseudomonas aeruginosa</i> , <i>Serratia marcescens</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus agalactiae</i> , <i>Streptococcus pneumoniae</i> , <i>Streptococcus pyogenes</i>
Antimicrobial resistance markers	qualitative	CTX-M, KPC, NDM, IMP, VIM, OXA-48 like <i>mecA/mecC</i> and MREJ

266 * Reported as 10⁴, 10⁵, 10⁶, or ≥10⁷ copies/mL.

267

268