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1 Effectiveness of a multimodal intervention to Improve Blood Culture
2 Collection in an Adult Emergency Department

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19 **Abstract**
20

21 We investigated the impact of a multimodal intervention to improve the compliance of BC
22 collections as a composite outcome, taking into account both blood volume collected and
23 absence of solitary BC. We performed a quasi-experimental study using a before-after design
24 (5 months for pre and post intervention evaluation) in an adult emergency department at a
25 tertiary care hospital that showed that a multimodal intervention was associated with a dramatic
26 increase in the proportion of blood cultures that were collected as recommended per national
27 guidelines, from 17.3% (328/1896), to 68.9% (744/1080), $P < 0.0001$. The implementation of
28 such intervention in other settings could improve the diagnosis of bloodstream infections and
29 reduce irrelevant costs.

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35 INTRODUCTION

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37 Sepsis is a life-threatening multiorgan dysfunction affecting up to 49 million patients/year
38 worldwide, with in-hospital mortality rates around 20% [1]. Identification of the pathogen
39 involved through blood cultures (BC), combined with drug-susceptibility testing, are
40 paramount to get the right diagnosis [2], optimize antimicrobial treatment [3] and reduced
41 mortality [4].

42 Current sepsis guidelines recommend to obtain at least two sets with 35-40 mL of blood,
43 directly inoculated on aerobic and anaerobic bottles, ensuring > 90% sensitivity [5,6]. However,
44 despite the importance of blood volume collected to reliably detect pathogens, recent studies
45 have shown that 20-97 % of BC bottles contain less than the recommended volume, and that
46 for 10-33 % of patients only one pair of BC is collected during the first 24-hour period, this
47 detrimental situation being referred to as ‘solitary BC’ [7].

48 Although several studies reported a positive impact of educational interventions to optimize the
49 volume of blood collected for BC [8–10], and reduce the proportion of solitary BC [7,11], no
50 study has investigated the simultaneous impact of interventions on these outcomes, which is
51 key to attain the recommended target of 35-40 mL blood collected.

52 Here, we aim to investigate the impact of a multimodal intervention to improve the compliance
53 of BC collections as a composite outcome, taking into account both blood volume collected in
54 each bottle, and absence of solitary BC.

55 METHODS

56 Study population

57 We conducted a quasi-experimental study using a before-after design in the adult emergency
58 department (AED) of the Rennes University Hospital, a 1,500-bed tertiary care center in
59 western France. We selected this department for the intervention as a baseline assessment of
60 BC use in our hospital revealed that AED was the largest user of BC, with the highest proportion
61 of non-compliance with guidelines.

62 The pre-intervention evaluation was carried out from April 1st to August 31st 2020, before any
63 educational intervention focused on appropriate use of BC in the hospital. The intervention was
64 implemented from March 1st to March 31st 2021. The post-intervention evaluation was
65 conducted from April 1st to August 31st 2021.

66 **Intervention**

67 The intervention relied on a new local protocol based on the concept of a BC train (BCT),
68 defined by the concomitant collection of 35-40 mL blood through two pairs of BC obtained on
69 a single venipuncture with the following sequence: i) aerobic bottle; ii) anaerobic bottle; iii)
70 aerobic bottle; iv) anaerobic bottle. The protocol was designed according to the medical
71 literature [12], by a local multidisciplinary committee including infectious diseases physicians,
72 intensivist, microbiologist, and methodologist.

73 This protocol consisted of two educational tools. The first one targeted nurses (Supplemental
74 Material I), who are in charge of BC sampling in France, specifying optimal procedures to
75 collect BCT. The second one targeted BC prescribers (physicians) (Supplemental Material II)
76 explaining the concept of BCT with a medical decision support listing the indications, and non-
77 indications, of ordering BC.

78 During the intervention period, we conducted 15 to 30-minute training sessions involving
79 nurses and physicians. During each session, one voluntary nurse and one physician from the
80 AED who received a specific training instructed other members of the team. These trainings
81 included oral presentation of the new BCT protocol, an educative video of BC collection that
82 remained available at any time on the AED computers, and a questions/answers session
83 (Supplemental Material III and IV). A pocket memo was provided to each physician. Briefings
84 and feedbacks were scheduled before and after each session. The AED medical files and
85 prescription software (Résurgence® Berger-Levrault) were adapted to facilitate the application
86 of the BCT protocol, and cancel pre-existing systematic rules for BC collection by nurses
87 without medical prescription (eg, collect BC when patients present with body temperature
88 >38.5 °C).

89 **Pertinence of BC prescription**

90 For a random sample of 50 patients admitted during the pre-intervention period, and a random
91 sample of 50 patients admitted during the post-intervention period, the pertinence of BC
92 prescription was evaluated by a physician (AM), through retrospective review of medical
93 records.

94 **Data collected for BC**

95 All BCs sampled in the AED are carried to the microbiology laboratory within 2 hours of
96 collection, 24/7. Bottles are placed in an automated BC system (Bactec FX 480, Becton
97 Dickinson), at 37°C, that detects microorganism growth by fluorescence. When a signal is
98 detected by the automated system, a laboratory technician performs microscopic examination

99 after Gram staining, and a BC sample is inoculated on aerobic and anaerobic Agar plates for
100 culture.

101 During the study period, the number of BC received and the volume of blood collected in each
102 bottle assessed by visual inspection were routinely recorded in the TD Synergy (nexlabs
103 technidata) software.

104 **Statistical analysis**

105 Comparisons of categorical variables were made using the chi-square test or Fisher's exact test
106 according to the usual conditions of validity. Comparisons of means were made using the
107 Student's t test or Wilcoxon tests if the conditions of validity were not met. Knowledge of
108 physicians and nurses before and after the training session was compared. The primary outcome
109 criteria was compliance to BC sampling guidelines, defined as blood volume collected ≥ 8 mL
110 per bottle, with at least two sets (4 bottles) collected within the first 24 h. Secondary outcome
111 criteria included: i) knowledge of training participants, evaluated through a short questionnaire
112 on the concept of BCT, indications for BC sampling, optimal sampling rules (ie, number of
113 bottles and volume), and risk factors for contamination; ii) pertinence of BC prescription.
114 Primary and secondary outcomes were compared before and after the intervention. We
115 conducted two sensitivity analysis with different pre-intervention period to take into account
116 potential effect of COVID-19 waves : one before the COVID-19 pandemic (April 1st to August
117 31st 2019) and one just before the intervention (January 1st to February 30st 2021). A value
118 of $P < 0.005$ was considered as significant. SAS 9.5 software was used to perform the statistical
119 analyses.

120

121 **RESULTS**

122 We found a dramatic increase in the proportion of appropriate BC sampling, defined as
123 appropriate volume for each bottle and no solitary BC, from 17.3% (328/1896) before the
124 intervention, to 68.9% (744/1080) after the intervention ($P < 0.0001$). The proportion of AED
125 patients with BC sampling decreased from 8.7% (1896/21771) to 4.2% (1080/25977),
126 $P < 0.0001$ (Table 1). Sensitivity analysis conducted with two different pre-intervention period
127 found similar results on the primary outcome (Supplemental Material V and VI).

128 During the intervention period, 48 nurses (67.6% of all AED nurses), and 28 physicians (50.9%
129 of all AED physicians) participated jointly to training sessions. Pertaining to BCs sampling,
130 training sessions led to a significant improvement of nurses knowledge on the BCT concept
131 (67.4% before vs 95.8% after, $P = 0.0004$), BC qualitative criteria (55.8% to 79.2% $P = 0.02$),

132 contamination factors (23.3% to 87.5% $P<0.0001$) and material required for sampling (48.8%
133 to 91.7% $P<0.0001$). Pertaining to BCs prescription training sessions increased physicians
134 knowledge about non-indications of prescription (55.6% to 89.3%, $P=0.005$), the BCT rules
135 (40.7% to 96.4%, $P<0.0001$), and variables that improve BC sensitivity (11.1% to 67.8%,
136 $P<0.0001$). Physicians knowledge about BC indications did not significantly improve (60.7%
137 to 67.6%, $P=0.51$).

138 The analysis of BC prescription on two random samples of 50 medical records before and after
139 the intervention found a trend towards increased proportion of compliance to guidelines, from
140 44.0% to 60.0% ($P=0.07$).

141

142 **DISCUSSION**

143 This quasi-experimental study showed that a multimodal educational intervention improved the
144 knowledge of nurses and physicians on good practices for BC prescription and sampling. This
145 intervention was followed by better compliance in terms of BC sampling and decreased
146 proportion of stays with BC sampling.

147 These results are in line with previous studies [7,9–11,13] : Three of them [8–10] reported a
148 positive impact of educational programs, followed by significant improvement in the volume
149 of blood collected in each BC bottle. Two others [7,11,13] reported educational programs that
150 were followed by decreased proportion of solitary BC. To our knowledge, our study is the first
151 that observed an improvement in both outcomes, using a composite criterion to define
152 appropriate BC sampling, in terms of volume collected in each bottle, and number of bottles
153 sampled (ie, no solitary BC). In addition, our study is the first to document that a multimodal
154 educational intervention focusing on physicians and nurses was followed by a reduction in the
155 proportion of AED patients with BC sampling. This reduction of BC collection was not
156 unexpected, given that the educational program included a special focus on appropriate
157 prescription of BCs by physicians, and emphasized that nurses should not collect BC in the
158 absence of medical prescription.

159 Our study carries limitations. First, as a quasi-experimental study the improvement of practices
160 for BC sampling after the intervention may be due to other factors. This is especially relevant
161 given that the study took place during the first 2 years of the Covid-19 pandemic, which had a
162 dramatic impact on health care in general. However, additional sensitivity analysis with another
163 pre-intervention period before Covid-19 showed similar results . Second, as the intervention
164 was multimodal, we are unable to analyze the separate effects of each intervention. Finally, the

165 evaluation occurred within the first 6 months following the intervention, so that we cannot
166 extrapolate on its long-term impact. Strengths of the study were its location in an AED, where
167 the early management of most sepsis cases occur [14], the sample size, and the standardization
168 of data collection during the study period.

169 This study demonstrates that a multimodal educational intervention on BC in an AED was
170 followed by significant improvement in BC compliance. The implementation of such
171 intervention in other settings could improve the diagnosis of bloodstream infections and reduce
172 irrelevant costs.

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176 **Table 1.** Patient characteristics and appropriateness of blood cultures before and after the
 177 intervention
 178

	Pre-intervention period	Post-intervention period	P-value
Number of AED patients	21 771	25 977	
Sex			
- Male	1011 (53.3%)	624 (57.8%)	0.02
- Female	885 (46.7%)	456 (42.2%)	
Age, years	61.8 (± 22.6)	61.1 (± 2.9)	0.42
Number of AED patients with at least one pair of blood cultures sampled	1 896 (8.7%)	1 080 (4.2%)	<0.0001
Appropriateness of blood cultures sampling per hospital stay			
Solitary blood culture *	1431 (75.5%)	102 (9.4%)	<0.0001
Appropriate volume for each bottle §	1906 (79.0%)	1718 (82.4%)	0.004

179

180 * only one pair of blood cultures collected during the first 24-hour period

181 § 8-10 mL per blood cultures bottle

182 Qualitative variables are reported as numbers (%), quantitative variables as mean ± standard
 183 deviation

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241 **Declaration of interest**

242 The authors reported no potential conflict of interest.

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244 of individuals who participated in the study, the data underlying this article cannot be shared.

245 **Code availability** : Not available.

246 **Ethics approval Ethical committee**: Validated by the local ethical committee.

247 **Author contribution statement**

248 RG and YM designed the study. YM, PT, CP, VC, AB were in charge of the implementation
249 of the local protocol. AM, DB, LS were in charge of the staff training and of data collection.
250 CP and VC were in charge of microbiological data collection. RG analysed the data. AB, AM,
251 DB, RG, PT and YM wrote the initial manuscript. All authors contributed to the revision of the
252 manuscript and approved the final version.

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