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1 **ORIGINAL ARTICLE**

2 **Factors associated with the appropriateness of antibiotics prescribed in French general**  
3 **practice: a cross-sectional study using reimbursement databases**

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16 **ABSTRACT**

17 **Objectives** – Identifying characteristics associated with the appropriateness of antibiotic  
18 prescriptions is useful to guide antibiotic stewardship interventions. Proxy indicators estimating the  
19 appropriateness of antibiotic prescriptions at the general practitioner (GP) level have recently been  
20 validated. Our objectives were to identify (i) clusters of GPs according to their appropriateness score  
21 based on these proxy indicators results, and (ii) GPs', patients' and practices' characteristics  
22 associated with inappropriate prescriptions.

23 **Methods** – We conducted a cross-sectional observational study analysing antibiotics prescribed by  
24 GPs in one large French region in 2019, using the Health Insurance databases. We identified clusters  
25 of GPs according to their appropriateness score calculated from 10 proxy indicators' results. We then  
26 analysed the association between the clusters with more inappropriate practices as compared to the  
27 one with less inappropriate practices, and GPs', patients', and practices' characteristics. We  
28 performed bivariate and multivariable analyses using logistic polytomous regressions.

29 **Results** – We included 4,819 GPs who were grouped into three clusters. GPs who belong to the  
30 clusters with more inappropriate practices were more likely to practice in certain geographical area,  
31 to be male, not to have a particular medical practice, to be practicing for longer, to have more  
32 patients and consultations, to have a higher proportion of elderly patients, and to prescribe more  
33 drugs, more antibiotics and a higher proportion of broad-spectrum antibiotics.

34 **Conclusion** – We identified clusters of practice as well as factors associated with the appropriateness  
35 of antibiotic prescriptions, using routinely collected data. This might help guide antibiotic  
36 stewardship interventions.

37

38 **Keywords:** antimicrobial stewardship; general practitioners; antibiotic prescriptions; clusters;  
39 appropriateness; characteristics; quality of care.

40

41 **INTRODUCTION**

42 Antimicrobial resistance is a rising threat to global health, and is accelerated by the misuse  
43 and overuse of antibiotics in humans and animals.[1] In France, around 125,000 persons are infected  
44 by multidrug-resistant bacteria each year, causing 5,500 deaths.[2] Seventy-eight percent of  
45 antibiotics are prescribed in primary care in France, with 70% of those being prescribed by general  
46 practitioners (GPs).[3]

47 Antimicrobial stewardship (AMS) has been defined as a “coherent set of actions which  
48 promote using antimicrobials responsibly”.[4] Metrics are important AMS tools to set targets for  
49 improvement and give a feedback to professionals and stakeholders. Indications/diagnoses are  
50 required to calculate quality indicators, but computerized national systems linking drug prescriptions  
51 to indications/diagnoses are rarely available.[5] In this context, we recently developed 10 proxy  
52 indicators (PIs) calculable from routine databases, estimating the appropriateness of antibiotic  
53 prescriptions at GP level without requiring indications/diagnoses.[6]

54 Identifying factors associated with the appropriateness of antibiotic prescriptions is useful to  
55 guide AMS interventions. However, in the literature, few studies aimed at identifying such factors in  
56 general practice.[7–10] **Supplementary Table S1** summarises the four identified studies, all  
57 conducted more than five years ago.

58 Our objectives were to identify, based on routinely collected data (i) clusters of GPs  
59 according to their appropriateness score based on PIs results, and (ii) GPs’, patients’ and practices’  
60 characteristics associated with inappropriate prescriptions (by comparing clusters with more  
61 inappropriate practices with the one with less inappropriate practices).

## 62 **METHODS**

### 63 ***Study setting and population***

64 GPs were selected from the Health Insurance databases. We included GPs practicing in the  
65 Grand Est region of France (66,524,000 inhabitants in France and 5,550,000 inhabitants in the Grand  
66 Est region, according to the 2017 census[11]), who took care of at least 100 different patients in 2019  
67 and prescribed at least 10 antibiotic treatments during the year. We excluded GPs who had an  
68 exclusive particular medical practice during the year (e.g. homeopathy, acupuncture).

69

### 70 ***Study design***

71 We conducted a retrospective cross-sectional observational study analysing antibiotics  
72 prescribed by eligible GPs and dispensed by a community pharmacy in 2019.

73

### 74 ***Data source***

75 In France, all antibiotics are prescribed and reimbursed. The Health Insurance databases link  
76 the prescriber and the patient identification numbers to the antibiotics dispensed by community  
77 pharmacies, the prescriber specialty and his/her main characteristics and the patients' characteristics  
78 (e.g. age, gender, chronic diseases, low income). Dispensing was used as a proxy for prescription as  
79 information on prescriptions is not available. The term "antibiotic prescription" refers here to an  
80 antibiotic course, whatever the duration of treatment. When two different antibiotics were  
81 prescribed by a GP and dispensed on the same day, they were counted separately. As mentioned  
82 previously, indications/diagnoses related to a prescription are not available in these databases.

83

### 84 ***Proxy indicators (PIs)***

85 To overcome the absence of indications/diagnoses in the Health Insurance databases, Thilly  
86 *et al.* developed 10 PIs estimating the appropriateness of antibiotic prescriptions at GP level,

87 calculable from routine Health Insurance databases.[6] These PIs were based on a literature review  
88 and used national guidelines as a reference.[12]

89 Each PI was associated with targets set to reflect the appropriateness of antibiotic  
90 prescriptions: the optimal target aims at 100% compliance with national guidelines, while the  
91 acceptable target is less restrictive and takes into account that guidelines are not applicable to all  
92 patients. These targets were used to calculate the performance for each PI, which is the percentage  
93 of GPs who reach the defined target.

94 **Supplementary Table S2** presents these 10 PIs, their definition and targets.

95

### 96 ***Cluster analysis***

97 For each GP, an appropriateness score expressed as a percentage was calculated as followed:  
98  $[(\text{number of PIs applicable for the GP and for whom the acceptable target is reached}) / (\text{number of}$   
99  $\text{PIs applicable for the GP})] \times 100$ . A PI was considered applicable if it was based on at least 10 clinical  
100 situations per year for the GP. A cluster analysis was conducted to group GPs according to their  
101 appropriateness score, reflecting the appropriateness of their antibiotic prescribing practices. The  
102 Ward method was used, linking clusters according to the degree of similarity between observations  
103 in the same cluster.

104

### 105 ***Statistical analyses***

106 GPs' and patients' characteristics, as well as GPs' practices, explored for their potential  
107 association with inappropriate practices are presented in **Supplementary File S3**.

108 PIs' results were first calculated for each GP and presented as medians with the interquartile  
109 range (IQR: lower quartile; upper quartile). Performances were calculated for each PI and presented  
110 as percentages. The cluster analysis was then conducted using a hierarchical clustering method to  
111 identify clusters of GPs according to their practices' appropriateness, estimated from their

112 appropriateness score. For each cluster, the median appropriateness score with the IQR and the  
113 performances for each PI were presented.

114 Comparisons of GPs' and patients' characteristics between the previously identified clusters  
115 were performed using Chi-square tests for categorical variables (expressed as percentages) and  
116 Kruskal-Wallis tests for continuous variables (expressed as medians and IQR). Characteristics  
117 identified with p value < 0.10 in bivariate analyses were then introduced in a multivariable  
118 polytomous logistic regression model to identify characteristics significantly associated with the  
119 clusters having more inappropriate practices as compared with the one with less inappropriate  
120 practices (used as the reference), taking into account other characteristics. When two identified  
121 characteristics were highly collinear, we excluded from the model the one with the higher p-value in  
122 the bivariate analysis.

123 Comparisons of practices' characteristics between clusters was restricted to bivariate  
124 analyses (as described for GPs and patients' characteristics), because of high collinearity between the  
125 six considered variables.

126 For all final analyses, a p-value < 0.05 for two-sided tests was considered significant. Analyses  
127 were performed with SAS Enterprise Guide version 7.15 (SAS Institute Inc., Cary, N.C., USA).

128

### 129 ***Ethical statement***

130 This is a retrospective observational study which did not modify the medical care of patients.  
131 Anonymity was preserved for both patients and prescribers. According to the French law, ethical  
132 approval was therefore not required.

## 133 RESULTS

### 134 *Characteristics of GPs and their patients*

135 Of the 6,041 GPs practicing in the Grand Est region, 1,187 GPs took care of less than 100  
136 different patients in 2019 or prescribed less than 10 antibiotics during the year, and 35 GPs had an  
137 exclusive particular medical practice. We therefore included in this study 4,819 GPs who met the  
138 inclusion criteria. Their mean age was  $53 \pm 11.6$  years and 63% were male. They took care, on  
139 average, of  $1,471 \pm 736$  different patients in 2019, with  $4,957 \pm 2,521$  consultations. The 4,819  
140 included GPs prescribed in 2019 a total of 2,950,425 antibiotic treatments that were dispensed to  
141 1,962,654 different patients. Regarding the characteristics of these patients, 45% were male, 20%  
142 were aged < 16 years and 19% > 65 years, 0.8% lived in a nursing home, 14% had a chronic disease  
143 and 10% were in the low-income category.

144

### 145 *Appropriateness of antibiotic prescriptions*

146 Results about the 10 PIs are presented in **Table 1**. The performance results were not optimal,  
147 varying between 15.3% (PI 4) and 88.5% (PI 2). Substantial variations in prescribing were noticed  
148 (large IQR).

149

### 150 *Cluster analysis*

151 Three clusters of GPs were identified. **Table 2** presents the description of the three clusters  
152 and their performances for each PI.

153

### 154 *GPs' and patients' characteristics*

155 **Table 3** presents GPs' and patients' characteristics for each of the three clusters and their  
156 comparisons in bivariate analyses. All GPs' characteristics were significantly associated with the  
157 clusters, except for the practice setting. All patients' characteristics were significantly associated with  
158 the clusters, except for the percentage of patients with low income.



159           **Table 4** presents results of the multivariable analysis evaluating the association between GPs'  
160 and patients' characteristics and inappropriate practices (cluster 2 and cluster 3 versus cluster 1). All  
161 GPs' characteristics included in the model were significantly associated with the clusters with a  
162 gradient in the associations (OR in cluster 3 > OR in cluster 2 > OR in cluster 1 (= 1), except for  
163 gender).

#### 164 ***GPs' practices***

165           **Table 5** describes GPs' practices for each of the three clusters and their comparisons in  
166 bivariate analyses. All the investigated characteristics were significantly associated with  
167 inappropriate practices, with a gradient in the associations except for the attainment of the target for  
168 the variable "number of antibiotic prescriptions per 100 patients aged 16 to 65 years old without a  
169 chronic disease per year".

170 **DISCUSSION**

171

172 ***Summary of the main findings***

173 We identified three clusters of GPs reflecting the appropriateness of their antibiotic  
174 prescriptions: 15% of GPs with better than average practices, 33% with average practices and 52%  
175 with worse than average practices. Almost all GPs' and patients' characteristics were associated with  
176 the appropriateness of practices. Several quantity metrics reflecting the volume of drugs and  
177 antibiotics prescribed by GPs were also associated with these clusters.

178

179 We identified several GPs' characteristics strongly associated with the appropriateness of  
180 prescriptions. We showed significant differences of practices across the geographic areas, that might  
181 be explained by different factors to be investigated, for example different medical density.[13]  
182 Female GPs were more likely to belong to the cluster with better than average practices. It has been  
183 shown that male GPs participate less in postgraduate training in France.[14] GPs with a particular  
184 medical practice were more likely to belong to the cluster with better practices. They may use more  
185 alternatives to drugs for self-limiting infections, and thus prescribe less antibiotics.

186 GPs who had been in practice longer were more likely to prescribe inappropriately as it has  
187 been shown previously.[7,15] Physicians who had been in practice longer may be less likely to adhere  
188 to standards of appropriate therapy [16], whereas younger GPs may be more aware and educated on  
189 antimicrobial resistance and stewardship.

190 We also found an association between a higher number of consultations per month and a  
191 higher risk of inappropriateness of antibiotic prescriptions. As it has been shown in the literature, a  
192 high number of consultations could reflect short consultation durations.[7,17] In this case, it might be  
193 too time-consuming for GPs to educate patients and to explain to them why they do not need an  
194 antibiotic.[17,18] Shorter consultation duration or higher workload could also lead to less exhaustive

195 clinical examination and thus contribute to diagnostic uncertainty, with GPs prescribing more  
196 antibiotics and notably more broad-spectrum agents to avoid risks.[18]

197

198 Overall, patients' characteristics were associated with the appropriateness of practices,  
199 except for the percentage of patients with low income. The National Health Insurance usually  
200 reimburses 65% of the cost of antibiotics in France, with 100% of the costs covered in case of low  
201 income and almost all other patients having a complementary insurance covering the remaining  
202 costs.

203 The percentage of patients < 16 years old and the percentage of patients > 65 years old were  
204 highly collinear ( $r = -0.64$ ): the more patients < 16 years old the GP had, the less patients > 65 years  
205 old s/he had and *vice-versa*. Both variables were significantly associated with the appropriateness of  
206 prescriptions when they were selected individually in the multivariable model. Results show a global  
207 effect of patients' age with a gradient: practices are more inappropriate for older patients.

208 The percentage of patients with chronic diseases and the percentage of patients > 65 years  
209 old were also highly collinear ( $r = 0.79$ ): patients aged 65 and more are indeed more likely to have  
210 chronic diseases. When we removed the percentage of patients < 16 years old and percentage of  
211 patients > 65 years old variables from the multivariable model, the percentage of patients with  
212 chronic diseases was significantly associated with the appropriateness of prescriptions.

213 Older patients are more likely to have chronic diseases. Among other potential contributing  
214 factors, GPs might be more likely to prescribe antibiotics to prevent potential bacterial  
215 superinfections.[19]

216

217 We also looked at the association between the appropriateness of antibiotic prescribing and  
218 quantity metrics commonly used in France to describe the volume of drugs and antibiotics prescribed  
219 by GPs. GPs were more likely to belong to the clusters with average or worse than average practices  
220 when they prescribed more drugs, more antibiotics, and a higher proportion of broad-spectrum

221 antibiotics. More appropriate antibiotic prescribing practices seem therefore associated with more  
222 prudent use of drugs in general. Our results also suggest that targeting GPs with high total antibiotic  
223 use, when other more refined screening methods are not available, seems acceptable. These results  
224 are in line with the literature.[20]

225

### 226 ***Comparison with existing literature***

227         The few published studies aiming at identifying factors associated with the appropriateness  
228 of antibiotic prescriptions in general practice are summarised in **Supplementary Table S1**. [7–10] In  
229 three of the four studies, clinical indications were needed to define the appropriateness of antibiotic  
230 prescriptions. Some of the characteristics we identified as associated with the appropriateness of  
231 antibiotic prescriptions were also identified in at least one of these studies: number of years of  
232 practice, number of patients, patients' age.

233

### 234 ***Strengths and limitations***

235         This work brings innovative findings. We believe that the method we used to identify clusters  
236 and explore characteristics associated with the estimated appropriateness of antibiotic prescriptions  
237 might be replicated in other countries, by adapting the PIs and their targets to the national  
238 prescribing guidelines. However, we acknowledge that our study has several limitations. First, the PIs  
239 cannot directly assess the appropriateness of each antibiotic prescription, i.e. the adherence to  
240 antibiotic prescribing guidelines per indication, as they are calculated without data on  
241 indications/diagnoses. Second, while content and clinimetric validities have been assessed [6], a  
242 structured consensus procedure is currently ongoing in France, piloted by health authorities, to  
243 confirm the face validity of our 10 PIs by a large group of stakeholders. So, the relevance and the  
244 understanding of each PI (definition and target) are not yet definitively validated. Third, the present  
245 investigation allowed us to identify associations between GPs', patients' and practices' characteristics  
246 and the appropriateness of antibiotic prescriptions but we cannot exclude that the associations we

247 found might be due to other unexplored factors. For example, the association between gender and  
248 appropriateness might be the consequence of a higher participation in postgraduate training among  
249 female GPs in France.

250

### 251 ***Implications***

252         Such a cluster analysis may be used to guide AMS interventions. For example, the “worse  
253 than average” cluster might benefit from high-intensity AMS interventions and the situations  
254 covered by the different proxy indicators might help design tailored messages as already suggested  
255 previously (e.g. reducing durations of antibiotic prescriptions according to national guidelines for PI  
256 8).[6] In addition, identifying the GPs and practices’ characteristics associated with the  
257 appropriateness of antibiotic prescriptions can help to select GPs to target in priority for AMS  
258 interventions. For example, in our sample of GPs from the Grand Est region of France, GPs who need  
259 to improve their antibiotic prescriptions the most are male who have been in practice longer, in  
260 certain geographical areas, who do not have a particular medical practice and who had a higher  
261 number of consultations per month.

262

263         In conclusion, several characteristics related to GPs, their patients, and their practices were  
264 associated with the estimated appropriateness of their antibiotic prescriptions. Identifying such  
265 characteristics as well as clusters of GPs was easily done based on routine reimbursement data and  
266 might help guide antibiotic stewardship interventions, with the overall objectives of improving the  
267 quality of care and reducing antibiotic resistance.

268 **TRANSPARENCY DECLARATION**

269 All authors: no conflicts of interest to declare.

270

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274

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277

278 **CONTRIBUTION**

279 Conceptualization: CP

280 Methodology: CP, NT, OP, MS

281 Software and formal analysis: OP

282 Writing – Original draft: MS

283 Writing – Review and Editing: CP, NT, OP

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**Table 1. Results for the 10 proxy indicators estimating the appropriateness of antibiotic prescriptions by general practitioners (GPs) of the Grand Est region in north-eastern France in 2019 (n = 4,819 GPs).**

Proxy indicator (PI) [6]	Median	IQR (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	Acceptable target value	Performance (% of GPs who reached the target)
PI 1 Antibiotic prescriptions against urinary tract infections in men (ratio)	0	0.0 ; 0.3	< 0.5	82.5
PI 2 Antibiotic prescriptions against urinary tract infections in women (ratio)	3.8	2.0 ; 7.0	> 1	88.5
PI 3 Repeated prescription of quinolones (%)	13.0	5.0 ; 21.1	< 10%	38.5
PI 4 Seasonal variation of total antibiotic prescriptions (%)	45.0	29.2 ; 62.5	< 20%	15.3
PI 5 Seasonal variation of quinolone prescriptions (%)	28.6	-9.1 ; 80.0	< 10%	38.0
PI 6 Amoxicillin / second-line antibiotics prescriptions (ratio)	0.9	0.5 ; 1.3	> 1	40.0
PI 7 Prescriptions of not indicated antibiotics (%)	1.1	0.4 ; 2.2	< 0.5%	29.7
PI 8 Estimated duration of antibiotic prescriptions > 8 days (%)	3.9	2.1 ; 6.9	< 10%	86.5
PI 9 Co-prescription of antibiotic and systemic non-steroidal anti-inflammatory drugs (%)	9.9	5.3 ; 16.6	< 5%	23.2
PI 10 Co-prescription of antibiotic and systemic corticosteroids (%)	12.3	6.8 ; 20.3	< 5%	15.9

**Table 2. Description of the three clusters reflecting the appropriateness of antibiotic practices and their performances for the 10 proxy indicators (n = 4,819 GPs).**

		<b>Cluster 1</b> <b>“Better than average practices”</b> N = 709 GPs (14.7%)	<b>Cluster 2</b> <b>“Average practices”</b> N = 1,574 GPs (32.7%)	<b>Cluster 3</b> <b>“Worse than average practices”</b> N = 2,536 GPs (52.6%)
		Appropriateness score <sup>a</sup> : 71.4 (70.0 ; 80.0)	Appropriateness score <sup>a</sup> : 55.6 (50.0 ; 60.0)	Appropriateness score <sup>a</sup> : 30.0 (30.0 ; 40.0)
<b>Proxy indicator (PI) [6]</b>	<b>Target value</b>	<b>Performances (% of GPs who reached the target)</b>		
PI 1 Antibiotic prescriptions against urinary tract infections in men	< 0.5	97.8	94.9	70.5
PI 2 Antibiotic prescriptions against urinary tract infections in women	> 1	95.9	96.1	82.0
PI 3 Repeated prescription of quinolones	< 10%	76.0	53.5	19.5
PI 4 Seasonal variation of total antibiotic prescriptions	< 20%	43.2	18.3	6.0
PI 5 Seasonal variation of quinolone prescriptions	< 10%	64.2	51.7	23.4
PI 6 Amoxicillin / second-line antibiotics prescriptions	> 1	75.2	58.3	18.8
PI 7 Prescriptions of not indicated antibiotics	< 0.5%	76.9	39.6	10.3
PI 8 Estimated duration of antibiotic prescriptions > 8 days	< 10%	91.3	91.4	82.2
PI 9 Co-prescription of antibiotic and systemic non-steroidal anti-inflammatory drugs	< 5%	69.1	28.6	6.9
PI 10 Co-prescription of antibiotic and systemic corticosteroids	< 5%	44.6	18.3	6.3

<sup>a</sup> The appropriateness score is expressed as a percentage, displayed using medians (1<sup>st</sup> quartile ; 3<sup>rd</sup> quartile) and calculated as [(number of PIs applicable for each GP and for whom the acceptable target is reached) / (number of PIs applicable for each GP)] x 100.

**Table 3. Description of GPs' and patients' characteristics for the three identified clusters – Bivariate analyses (n = 4,819 GPs).**

Bold indicates a p-value < 0.05.

Characteristics		Cluster 1 "Better than average practices" N = 709 GPs (14.7%)	Cluster 2 "Average practices" N = 1,574 GPs (32.7%)	Cluster 3 "Worse than average practices" N = 2,536 GPs (52.6%)	p-value
<b>GPs' characteristics</b>					
<b>Geographic area</b> %	08 Ardennes	13.3	37.8	48.9	<b>&lt; 0.0001</b>
	10 Aube	9.6	36.8	53.6	
	51 Marne	25.1	39.0	35.9	
	52 Haute-Marne	8.3	22.6	69.2	
	54 Meurthe-et-Moselle	20.3	35.5	44.2	
	55 Meuse	13.8	34.8	51.5	
	57 Moselle	12.6	28.7	58.7	
	67 Bas-Rhin	11.3	29.8	59.0	
	68 Haut-Rhin	13.3	32.2	54.5	
	88 Vosges	15.1	35.6	49.4	
<b>GP's gender</b> %	Male	11.7	28.6	59.7	<b>&lt; 0.0001</b>
	Female	19.9	39.3	40.9	
<b>Particular medical practice</b> %	Yes	32.2	32.6	35.3	<b>&lt; 0.0001</b>
	No	13.7	32.7	53.6	
<b>Practice setting</b> %	Rural (< 5,000 inhabitants)	14.5	32.3	53.3	0.108
	Suburban (5,000 – 20,000 inhabitants)	14.0	31.2	54.8	
	Urban (> 20,000 inhabitants)	15.8	34.5	49.8	

<b>Number of years of practice (2019 - installation date)</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	8 (2 ; 25)	15 (5 ; 28)	24.5 (13 ; 32)	< <b>0.0001</b>
<b>Number of patients (in 2019)</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	1257 (871 ; 1709)	1397 (1029 ; 1815)	1399 (1039.5 ; 1847.5)	< <b>0.0001</b>
<b>Number of consultations per month</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	310.3 (219.8 ; 420.0)	376.2 (282.1 ; 497.4)	427.6 (315.4 ; 565.4)	< <b>0.0001</b>

#### Patients' characteristics

<b>% of patients with chronic diseases</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	13.2 (10.6 ; 16.0)	13.1 (10.9 ; 15.8)	13.8 (11.5 ; 16.8)	< <b>0.0001</b>
<b>% of patients with low income</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	6.5 (3.3 ; 13.1)	6.5 (3.5 ; 12.6)	6.6 (3.3 ; 12.5)	0.815
<b>% of patients &lt; 16 years old</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	21.0 (16.1 ; 25.4)	19.8 (15.4 ; 23.9)	17.8 (13.8 ; 21.6)	< <b>0.0001</b>
<b>% of patients &gt; 65 years old</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)	18.5 (13.1 ; 24.7)	18.7 (13.7 ; 24.5)	19.8 (14.9 ; 25.5)	< <b>0.0001</b>

**Table 4. Association between the GPs' and patients' characteristics and the identified clusters – Multivariable polytomous logistic analysis (n = 4,819 GPs).**

The following variables were not included since they were highly collinear with included variables: number of patients (collinear with the number of consultations per month,  $r = 0.71$ ); and percentage of patients > 65 years old (collinear with the percentage of patients with chronic diseases,  $r = 0.79$ ). The variable percentage of patients with chronic diseases was removed from the model because of its non-significance ( $p = 0.131$ ). The reference class is Cluster 1 “better than average practices”. Bold indicates a  $p$ -value < 0.05.

For example, cluster 3 (“worse than average practices”) included 23% more men than cluster 1 (“better than average practices”). The variables percentage of patients < 16 years old, percentage of patients > 65 years old and percentage of patients with chronic disease were moderately to highly collinear (percentage of patients < 16 years old and percentage of patients with chronic disease ( $r = - 0.53$ ); percentage of patients < 16 years old and percentage of patients > 65 years old ( $r = - 0.64$ ); and percentage of patients > 65 years old and percentage of patients with chronic disease ( $r = 0.79$ )). However, when we selected only one of these three variables in the model at a time, they were all significantly associated with inappropriate practices.

Characteristics		MULTIVARIABLE ANALYSIS			
		Cluster 2 “average practices” VS Cluster 1 “better than average practices”		Cluster 3 “worse than average practices” VS Cluster 1 “better than average practices”	
		Odd Ratio (95% confidence interval)	p-value	Odd Ratio (95% confidence interval)	p-value
Geographic area	08 Ardennes	1.58 (0.98 ; 2.55)	0.063	1.92 (1.17 ; 3.15)	<b>0.010</b>
	10 Aube	2.52 (1.45 ; 4.38)	<b>0.001</b>	3.80 (2.17 ; 6.66)	<b>&lt; 0.0001</b>
	51 Marne	1 (reference)	-	1 (reference)	-
	52 Haute-Marne	1.60 (0.76 ; 3.35)	0.216	5.18 (2.58 ; 10.40)	<b>&lt; 0.0001</b>
	54 Meurthe-et-Moselle	1.19 (0.87 ; 1.64)	0.280	1.35 (0.97 ; 1.89)	0.075
	55 Meuse	1.43 (0.79 ; 2.57)	0.238	1.91 (1.05 ; 3.45)	<b>0.033</b>
	57 Moselle	1.24 (0.89 ; 1.73)	0.213	2.17 (1.55 ; 3.05)	<b>&lt; 0.0001</b>
	67 Bas-Rhin	1.75 (1.28 ; 2.38)	<b>0.0004</b>	3.45 (2.51 ; 4.73)	<b>&lt; 0.0001</b>
	68 Haut-Rhin	1.74 (1.22 ; 2.48)	<b>0.002</b>	2.99 (2.08 ; 4.30)	<b>&lt; 0.0001</b>
	88 Vosges	1.54 (1.01 ; 2.35)	<b>0.043</b>	2.02 (1.32 ; 3.11)	<b>0.001</b>
GP's gender	Male	0.92 (0.76 ; 1.12)	0.411	1.23 (1.01 ; 1.49)	<b>0.040</b>
	Female	1 (reference)	-	1 (reference)	-
Particular medical practice	Yes	1 (reference)	-	1 (reference)	-
	No	2.20 (1.57 ; 3.08)	<b>&lt; 0.0001</b>	4.30 (3.00 ; 6.18)	<b>&lt; 0.0001</b>
Number of years of practice (2019 - installation date) <sup>a</sup>		1.03 (1.02 ; 1.03)	<b>&lt; 0.0001</b>	1.05 (1.04 ; 1.06)	<b>&lt; 0.0001</b>
Number of consultations per month <sup>b</sup>		1.003 (1.002 ; 1.003)	<b>&lt; 0.0001</b>	1.004 (1.003 ; 1.005)	<b>&lt; 0.0001</b>

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<b>% of patients &lt; 16 years old</b> <sup>c</sup>	0.99 (0.98 ; 1.00)	0.126	0.95 (0.94 ; 0.97)	<b>&lt; 0.0001</b>
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<sup>a</sup> increased risk of being in cluster 2 or 3 (as compared to cluster 1) per additional year of practice.

<sup>b</sup> increased risk of being in cluster 2 or 3 (as compared to cluster 1) per additional consultation per month.

<sup>c</sup> increased risk of being in cluster 2 or 3 (as compared to cluster 1) per 1% more patients.



1 **Table 5. Description of GPs' practices according to the identified clusters – Bivariate analyses (n = 4,819 GPs).**

2 Bold indicates a p-value < 0.05.

Variables		Cluster 1 "Better than average practices" N = 709 GPs (14.7%)	Cluster 2 "Average practices" N = 1,574 GPs (32.7%)	Cluster 3 "Worse than average practices" N = 2,536 GPs (52.6%)	p-value
<b>Number of units of all drugs per patient per month</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)		4.5 (3.9 ; 5.3)	4.8 (4.2 ; 5.6)	5.3 (4.6 ; 6.1)	<b>&lt; 0.0001</b>
<b>Number of antibiotic prescriptions per 1000 patients per year</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)		236.1 (156.7 ; 334.7)	335.9 (242.7 ; 447.6)	455.1 (322.8 ; 618.2)	<b>&lt; 0.0001</b>
<b>Number of antibiotic prescriptions per 100 patients aged 16 to 65 years old without a chronic disease per year</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)		20.7 (14.3 ; 31.9)	28.6 (19.5 ; 39.2)	36.5 (25.5 ; 52.6)	<b>&lt; 0.0001</b>
<b>% of patients treated by broad-spectrum antibiotics (amoxicillin-clavulanate, 3rd and 4th generation cephalosporins and fluoroquinolones) per year</b> Median (1 <sup>st</sup> quartile ; 3 <sup>rd</sup> quartile)		25.3 (19.0 ; 31.5)	27.4 (21.5 ; 34.4)	34.2 (26.2 ; 44.8)	<b>&lt; 0.0001</b>
<b>Target reached (≤ 20%) for the P4P indicator 'number of antibiotic prescriptions per 100 patients from 16 to 65 years old without a chronic disease'</b> %	Yes	25.7	38.7	35.6	<b>&lt; 0.0001</b>
	No	8.4	30.5	61.1	
<b>Target reached (≤ 32%) for the P4P indicator 'percentage of patients treated by broad-spectrum antibiotics (amoxicillin-clavulanate, 3rd and 4th generation cephalosporins and fluoroquinolones)'</b> %	Yes	16.4	40.1	43.5	<b>&lt; 0.0001</b>
	No	6.3	22.8	70.9	

3 P4P: pay-for-performance

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