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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**

4 Maïa Simon¹, Nathalie Thilly^{1,2}, Ouarda Pereira³, Céline Pulcini^{1,4}

5

6 ¹ Université de Lorraine, APEMAC, Nancy, France

7 ² Université de Lorraine, CHRU-Nancy, Département Méthodologie, Promotion, Investigation, Nancy,
8 France

9 ³ Direction Régionale du Service Médical (DRSM) Grand Est, Strasbourg, France

10 ⁴ Université de Lorraine, CHRU-Nancy, Département de maladies infectieuses, Nancy, France

11

12 **Corresponding author:** Professor Céline PULCINI, MD PhD. Centre Hospitalier Régional Universitaire
13 de Nancy, Service de Maladies Infectieuses et Tropicales, Hôpitaux de Brabois, allée du Morvan,
14 54511 Vandoeuvre-Lès-Nancy, France. Tel: + 33 (0) 3 83 15 40 97, Fax: + 33 (0) 3 83 15 70 27, e-mail:
15 celine.pulcini@univ-lorraine.fr

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 ± 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

284 **REFERENCES**

285 [1] World Health Organization (WHO). Antibiotic resistance. Available at: [https://www.who.int/news-](https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance)
286 [room/fact-sheets/detail/antibiotic-resistance](https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance).

287 [2] Santé publique France. Résistance aux antibiotiques. Available at:
288 [https://www.santepubliquefrance.fr/maladies-et-traumatismes/infections-associees-aux-soins-](https://www.santepubliquefrance.fr/maladies-et-traumatismes/infections-associees-aux-soins-et-resistance-aux-antibiotiques/resistance-aux-antibiotiques)
289 [et-resistance-aux-antibiotiques/resistance-aux-antibiotiques](https://www.santepubliquefrance.fr/maladies-et-traumatismes/infections-associees-aux-soins-et-resistance-aux-antibiotiques/resistance-aux-antibiotiques).

290 [3] Santé publique France. Consommation d'antibiotiques et antibiorésistance en France en 2019.
291 Available at: [https://www.santepubliquefrance.fr/les-actualites/2020/consommation-d-](https://www.santepubliquefrance.fr/les-actualites/2020/consommation-d-antibiotiques-et-antibioresistance-en-france-en-2019)
292 [antibiotiques-et-antibioresistance-en-france-en-2019](https://www.santepubliquefrance.fr/les-actualites/2020/consommation-d-antibiotiques-et-antibioresistance-en-france-en-2019).

293 [4] Dyar OJ, Huttner B, Schouten J, Pulcini C, ESGAP (ESCMID Study Group for Antimicrobial
294 stewardship). What is antimicrobial stewardship? *Clin Microbiol Infect Off Publ Eur Soc Clin*
295 *Microbiol Infect Dis*. 2017;23(11):793-8.

296 [5] Howard P, Huttner B, Beovic B, Beraud G, Kofteridis DP, Pano Pardo J, et al. ESGAP inventory of
297 target indicators assessing antibiotic prescriptions: a cross-sectional survey. *J Antimicrob*
298 *Chemother*. 2017;72(10):2910-4.

299 [6] Thilly N, Pereira O, Schouten J, Hulscher ME, Pulcini C. Proxy indicators to estimate
300 appropriateness of antibiotic prescriptions by general practitioners: a proof-of-concept cross-
301 sectional study based on reimbursement data, north-eastern France 2017. *Eurosurveillance*.
302 2020;25(27):1900468.

303 [7] Cadieux G, Tamblyn R, Dauphinee D, Libman M. Predictors of inappropriate antibiotic prescribing
304 among primary care physicians. *CMAJ Can Med Assoc J*. 2007;177(8):877-83.

- 305 [8] Pulcini C, Lions C, Ventelou B, Verger P. Approaching the quality of antibiotic prescriptions in
306 primary care using reimbursement data. *Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin*
307 *Microbiol.* 2013;32(3):325-32.
- 308 [9] Nowakowska M, van Staa T, Mölter A, Ashcroft DM, Tsang JY, White A, et al. Antibiotic choice in
309 UK general practice: rates and drivers of potentially inappropriate antibiotic prescribing. *J*
310 *Antimicrob Chemother.* 2019;74(11):3371-8.
- 311 [10] Degnan KO, Cluzet V, David MZ, Dutcher L, Cressman L, Lautenbach E, et al. Development and
312 validation of antibiotic stewardship metrics for outpatient respiratory tract diagnoses and
313 association of provider characteristics with inappropriate prescribing. *Infect Control Hosp*
314 *Epidemiol.* 2021;1-8.
- 315 [11] Institut national de la statistique et des études économiques (Insee). Statistiques. Available at:
316 <https://www.insee.fr/fr/statistiques>.
- 317 [12] Le Maréchal M, Tebano G, Monnier AA, Adriaenssens N, Gyssens IC, Huttner B, et al. Quality
318 indicators assessing antibiotic use in the outpatient setting: a systematic review followed by an
319 international multidisciplinary consensus procedure. *J Antimicrob Chemother.*
320 2018;73(suppl_6):vi40-9.
- 321 [13] Masson P. La prescription des médecins généralistes : conflits entre la profession médicale et
322 l'Assurance maladie. *Soc Contemp.* 2011;n°83(3):33-57.
- 323 [14] Paraponaris A, Ventelou B, Verger P, Desprès P, Aubry C, Colin C, et al. La médecine générale vue
324 par les médecins généralistes libéraux. *Rev Francaise Aff Soc.* 16 déc 2011;(2):29-47.
- 325 [15] Silverman M, Povitz M, Sontrop JM, Li L, Richard L, Cejic S, et al. Antibiotic Prescribing for
326 Nonbacterial Acute Upper Respiratory Infections in Elderly Persons. *Ann Intern Med.*
327 2017;166(11):765-74.

- 328 [16] Choudhry NK, Fletcher RH, Soumerai SB. Systematic review: the relationship between clinical
329 experience and quality of health care. *Ann Intern Med.* 2005;142(4):260-73.
- 330 [17] Aabenhus R, Siersma V, Sandholdt H, Køster-Rasmussen R, Hansen MP, Bjerrum L. Identifying
331 practice-related factors for high-volume prescribers of antibiotics in Danish general practice. *J*
332 *Antimicrob Chemother.* 2017;72(8):2385-91.
- 333 [18] Gjelstad S, Straand J, Dalen I, Fetveit A, Strøm H, Lindbæk M. Do general practitioners'
334 consultation rates influence their prescribing patterns of antibiotics for acute respiratory tract
335 infections? *J Antimicrob Chemother.* 2011;66(10):2425-33.
- 336 [19] Hayward GN, Moore A, Mckelvie S, Lasserson DS, Croxson C. Antibiotic prescribing for the older
337 adult: beliefs and practices in primary care. *J Antimicrob Chemother.* 2019;74(3):791-7.
- 338 [20] Kitano T, Langford BJ, Brown KA, Pang A, Chen B, Garber G, et al. The Association Between High
339 and Unnecessary Antibiotic Prescribing: A Cohort Study Using Family Physician Electronic
340 Medical Records. *Clin Infect Dis Off Publ Infect Dis Soc Am.* 2021;72(9):e345-51.

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 st quartile ; 3 rd 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).

		Cluster 1 “Better than average practices” N = 709 GPs (14.7%) Appropriateness score ^a : 71.4 (70.0 ; 80.0)	Cluster 2 “Average practices” N = 1,574 GPs (32.7%) Appropriateness score ^a : 55.6 (50.0 ; 60.0)	Cluster 3 “Worse than average practices” N = 2,536 GPs (52.6%) Appropriateness score ^a : 30.0 (30.0 ; 40.0)
Proxy indicator (PI) [6]	Target value	Performances (% of GPs who reached the target)		
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

^a The appropriateness score is expressed as a percentage, displayed using medians (1st quartile ; 3rd 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
GPs' characteristics					
Geographic area %	08 Ardennes	13.3	37.8	48.9	< 0.0001
	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	
GP's gender %	Male	11.7	28.6	59.7	< 0.0001
	Female	19.9	39.3	40.9	
Particular medical practice %	Yes	32.2	32.6	35.3	< 0.0001
	No	13.7	32.7	53.6	
Practice setting %	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	

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

Patients' characteristics

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

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)	0.010
	10 Aube	2.52 (1.45 ; 4.38)	0.001	3.80 (2.17 ; 6.66)	< 0.0001
	51 Marne	1 (reference)	-	1 (reference)	-
	52 Haute-Marne	1.60 (0.76 ; 3.35)	0.216	5.18 (2.58 ; 10.40)	< 0.0001
	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)	0.033
	57 Moselle	1.24 (0.89 ; 1.73)	0.213	2.17 (1.55 ; 3.05)	< 0.0001
	67 Bas-Rhin	1.75 (1.28 ; 2.38)	0.0004	3.45 (2.51 ; 4.73)	< 0.0001
	68 Haut-Rhin	1.74 (1.22 ; 2.48)	0.002	2.99 (2.08 ; 4.30)	< 0.0001
	88 Vosges	1.54 (1.01 ; 2.35)	0.043	2.02 (1.32 ; 3.11)	0.001
GP's gender	Male	0.92 (0.76 ; 1.12)	0.411	1.23 (1.01 ; 1.49)	0.040
	Female	1 (reference)	-	1 (reference)	-
Particular medical practice	Yes	1 (reference)	-	1 (reference)	-
	No	2.20 (1.57 ; 3.08)	< 0.0001	4.30 (3.00 ; 6.18)	< 0.0001
Number of years of practice (2019 - installation date) ^a		1.03 (1.02 ; 1.03)	< 0.0001	1.05 (1.04 ; 1.06)	< 0.0001
Number of consultations per month ^b		1.003 (1.002 ; 1.003)	< 0.0001	1.004 (1.003 ; 1.005)	< 0.0001

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

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

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

3 P4P: pay-for-performance

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