

# Identifying General Practitioners' Antibiotic Prescribing Profiles Based on National Health Reimbursement Data

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**Background.** Antibiotic selection pressure in human medicine is a significant driver of antibiotic resistance in humans. The primary aspect of antibiotic consumption is associated with general practitioner (GP) prescriptions. We aimed to identify prescriber profiles for targeted antimicrobial stewardship programs using novel indicators.

**Methods.** A cross-sectional study was conducted in 2018 investigating GPs' antibiotic prescriptions in a French department, utilizing the reimbursement database of the national health service. Three antibiotic prescribing indicators were used. Specific targets were established for each indicator to identify the antibiotic prescribers most likely contributing to the emergence of resistance.

**Results.** Over 2018, we had 2,908,977 visits to 784 GPs, leading to 431,549 antibiotic prescriptions. Variations between GPs were shown by the 3 indicators. The median antibiotic prescription rate per visit was 13.6% (interquartile range [IQR], 9.8%–17.7%). Median ratios of the prescriptions of low-impact antibiotics to the prescriptions of high-impact antibiotics and of amoxicillin prescriptions to amoxicillin–clavulanic acid prescriptions were 2.5 (IQR, 1.7–3.7) and 2.94 (IQR, 1.7–5), respectively. We found 163 (21%) high prescribers of antibiotics with 3 distinct patterns: The first group overuses broad-spectrum antibiotics but without an overprescription rate per visit, the second group displays an overprescription rate but no excessive use of broad-spectrum antibiotics, and the third group shows both an overprescription rate and excessive use of broad-spectrum antibiotics.

**Conclusions.** Prescription-based indicators enable the identification of distinct profiles of antibiotic prescribers. This identification may allow for targeted implementation of stewardship programs focused on the specific prescribing patterns of each profile.

**Keywords.** antibiotic consumption; antibiotic stewardship; general practitioners; primary healthcare; quality indicators.

Antimicrobial resistance (AMR) poses a burgeoning global threat, with an estimated 1.27 million fatalities in 2019, as disclosed in a recent study [1]. It has been forecasted that, by 2050, AMR will be accountable for >10 million deaths per year [2, 3].

The development of antimicrobial resistance is a natural evolutionary response to antimicrobial exposure in all bacterial ecosystems at the human, animal, and environmental levels [4]. Certain antibiotics in human medicine have a higher

propensity to encourage antibiotic resistance, irrespective of their importance to treat specific pathogens or their spectrum [4–6]. Other important factors to consider include pharmacological properties, concentration reaching the microbiota, and bacterial species sensitivity [7–10]. To slow the emergence of antibiotic resistance, it is crucial to restrict the usage of antibiotics with a high AMR impact, or “ecological impact,” as recommended by Ruppé et al [11].

By 2022, 92% of antibiotics in France are projected to be dispensed in ambulatory care, with the remaining 8% in health-care facilities. General practitioners (GPs) are responsible for 76% of the total consumption of antibiotics in ambulatory care [12–14]. Therefore, a comprehensive global antibiotic stewardship program must encompass antibiotic consumption surveillance in ambulatory care.

There are multiple indicators available to evaluate and monitor the trends in antibiotic consumption. These indicators employ quantitative measures like the defined daily dose (DDD) [15] and the count of packs or prescriptions, with discrepancies in trends depending on the specific indicator used [16–18].

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A systematic review and global consensus procedure carried out by the Driving Reinvestment in Research and Development and Responsible Antibiotic Use (DRIVE-AB) consortium has suggested that a combination of metrics may be the best approach, given that all metrics have limitations [19]. Other studies have also reported differences between the rates of antibiotic usage expressed in DDD and AMR, with some countries demonstrating a low rate of AMR despite high use of antibiotics [20, 21]. For instance, although the consumption rate of aminopenicillins is 2 times lower in the outpatient setting in France, the incidence of *Escherichia coli* resistant to this class is equally high in France and Germany (54% and 48%, respectively, in 2020) [12, 22, 23]. This highlights the need for a supplementary approach to DDDs to measure the AMR impact of antibiotics, and for adaptations to be made to reflect the AMR context and prescribing practices within the relevant setting.

We aimed to identify prescriber profiles using novel indicators for targeted antimicrobial stewardship programs (ASPs) in general practice.

## METHODS

### Data Source and Study Design

We conducted a cross-sectional analysis of antibiotic prescriptions (APs) by GPs during 2018. The database provided AP data, categorized by antibiotic classes using the J01 Anatomical Therapeutic Chemical Classification system [24], and the number of visits stratified by patient age group (<6, 6–16, 16–36, 36–66, and >66 years) for each GP practicing in the county that year.

### Inclusion and Exclusion Criteria

We included all GPs practicing in Seine-et-Marne, the largest county in the Île-de-France region. GPs with a limited practice activity (less than 10 visits/year and/or 10 antibiotic prescriptions per year and/or 1 amoxicillin prescription/year) were excluded, as we considered their impact on AMR in an outpatient setting to be minimal.

In France, national health insurance reimburses nearly all (88%) of the population for medical appointments with GPs and antibiotic prescriptions [25]. This system enables the collection of annual data on the number of visits and the antibiotics prescribed by GPs and provided to outpatients through community pharmacies.

### Patient Consent Statement

Databases are subject to full anonymization at both the GP and patient levels. The use of these data is authorized for the purposes of this study in accordance with French legislation, and patient consent is waived.

### AMR Impact Indicators

We have devised 3 sets of indicators. One indicator is related to the overall APs per visit, and the other 2 are related to the relative frequency of the types of antibiotics prescribed. The categorization of an antibiotic as either first-line or critical was according to the French health authorities' classification [26]. We analyzed the most frequently prescribed antibiotic classes in French outpatient settings: amoxicillin (AMX), amoxicillin–clavulanic acid (AMC), second- and third-generation cephalosporins (2GCs and 3GCs, respectively), macrolides, fluoroquinolones (FQs), fosfomycin and nitrofurantoin (FOS-NIT), and sulfonamides and trimethoprim (SXT) [13, 27].

### Indicators Associated With an Increased Prescription Rate per Visit

As the AMR impact is influenced by the overall pressure of antibiotic use, we used the quantitative measure suggested by the DRIVE-AB project [28], which reports the ratio of the number of antibiotic prescriptions per year to the number of visits per year (AP/V). We then further analyzed this ratio according to patient age groups. An indicator value exceeding the 90th percentile was deemed to reflect excessive initiation of APs.

### Indicators Associated With an Increased Prescription of High-Impact Antibiotics

As our aim was to identify the propensity to favor the AMR impact of GPs' APs, we adjusted the drug-specific quality indicators "narrow over broad-spectrum antibiotics" proposed by the European Surveillance of Antibiotic Consumption Project for monitoring outpatient antibiotic use [29]. We replaced the DDD with the number of APs and included molecules according to national recommendations.

Since the French National Medicine Safety Agency (ANSM) classified AMC, 3GCs, and FQs as critical antibiotics in community medicine for their propensity to select resistant microorganisms, we have included them in the high-AMR-impact antibiotic (HIA) group [26]. While macrolides are usually recommended as second-line drugs in most French guidelines for the treatment of pneumonia and upper respiratory tract infections, they are not included in the critical antibiotics group by ANSM [28]); thus, we have grouped them with AMX, SXT, and FOS-NIT as low-AMR-impact antibiotics (LIAs). The drug-specific quality indicator was evaluated using the ratio of LIA prescriptions to HIA prescriptions (LIA/HIA). As AMX and AMC constitute the most significant portion of antibiotic consumption in France, we also investigated the ratio of AMX prescriptions to AMC prescriptions (AMX/AMC).

Given that LIAs are preferable to HIAs, a cut-off value of 1 was established for these 2 indicators to signal excessive use of antibiotics with high AMR impact.

## Analyses and Statistics

The set of the 3 indicators (LIA/HIA, AMX/AMC, and AP/V) was calculated for each GP to describe antibiotic consumption at the county level (median and interquartile range [IQR]). GPs above the threshold for at least 1 of the 3 indicators were classified as high-risk prescribers (HRPs). Comparison of antibiotic use patterns and age distribution of the patient base between GPs identified as HRPs and the reference group of GPs who did not reach the target for any of the indicators and identified as low-risk prescribers (LRPs) was performed using  $\chi^2$  or Wilcoxon test, depending on the variable. Analysis was performed using Epi Info 7.2.

## RESULTS

### Prescription Practices

In 2018, GPs' prescriptions accounted for 85.6% of the DDDs delivered in Seine-et-Marne County, despite GPs representing only 823 of 1453 (57%) physicians. Among them, 784 (95.3%) met inclusion criteria. They treated 1 171 004 patients through 2 908 977 visits, which resulted in 431 549 APs, equating to a rate of 13.6 (9.8–17.7) APs per 100 visits for any condition (Table 1). Maximum initiation rate was observed in children aged <6 years at 22.7 (14.6–33.4), while minimum rate was observed in patients aged >66 years at 11.2 (8.5–14.5).

Around one-third (31.7%) of APs were for high-impact antibiotics. The ratio of HIAs to LIAs and of AMX to AMC use displayed significant variation (large IQR) among GPs. When considering the total number of APs by age group, penicillin was found to be the most prescribed class across all age groups, with cephalosporin being the second most prescribed antibiotic class for children aged <16 years and macrolides for adults. In contrast, fluoroquinolones were predominantly prescribed for elderly patients (Table 2).

### Identification of HRPs

Among the 784 GPs, 163 (21%) met the threshold for 1 or more indicators. One hundred four (13.3%) exceeded the threshold for at least 1 of the 2 drug-specific AMR impact indicators AMX/AMC and LIA/HIA. Of those, 43 GPs (41.3%) overused only AMC, and 61 (58.7%) overused all HIAs. Among the 61 GPs who exceeded the HIA/LIA threshold, 42 (68.9%) also exceeded the AMX/AMC threshold. Of the 77 GPs who prescribed antibiotics at a rate in the 90th percentile for any condition, 18 (24%) were also above the threshold for 1 or both of the drug-specific AMR indicators, while 59 (76%) fell below the threshold. Those above the threshold for LIA/HIA showed a tendency to overuse antibiotics per visit (odds ratio, 3.86 [95% confidence interval, 1.9–7.4];  $P < .001$ ).

**Table 1. Descriptive Data of Antibiotic Prescriptions by Antibiotic Class**

Antibiotic Class	Total, No. (%)	Median (IQR) (per GP)
All classes	431 549	462 (291–704)
Penicillin	221 395 (51.5)	53 (42–62)
Amoxicillin	158 210 (36.8)	37.3 (30–46)
Amoxicillin–clavulanic acid	59 065 (13.7)	12.5 (8.3–17.6)
Cephalosporin	62 114 (14.4)	9.6 (5.3–16.1)
1GC/2GC	9030 (2.1)	3.4 (1.9–4.9)
3GC	53 084 (12.3)	8.3 (4.4–14.2)
Oral 3GC	50 880 (11.8)	7.8 (3.9–13.6)
Parenteral 3GC	2204 (0.5)	0.2 (0–0.7)
Sulfonamides and trimethoprim	4843 (1.1)	0.6 (0.1–1.4)
Macrolides, lincosamides, streptogramins	73 832 (17.2)	14.8 (10–21.7)
Quinolone	24 879 (5.8)	5.1 (3.2–7.9)
Other antibacterial	28 837 (6.7)	7.2 (4.6–11)
FOS-NIT	26 713 (6.2)	6.7 (4–10)
Other classes	15 649 (3.6)	3.4 (1.9–4.9)
Broad-spectrum antibiotics	137 028 (32)	28.5 (21.6–38)
Narrow-spectrum/broad-spectrum	...	2.5 (1.67–3.7)
Amoxicillin/amoxicillin–clavulanic acid	...	2.94 (1.67–5)

Abbreviations: 1GC, first-generation cephalosporin; 2GC, second-generation cephalosporin; 3GC, third-generation cephalosporin; FOS-NIT, fosfomycin-nitrofurantoin; GP, general practitioner; IQR, interquartile range.

### HRP Profiles

We have identified 3 profiles of HRPs based on the type of indicator that exceeds the threshold (Figure 1). The first profile, high-impact overprescribers (HIOPs), comprises prescribers who excessively use HIAs, as indicated by the LIA/HIA and AMX/AMC ratios. This profile encompasses almost 53% of all HRPs (86/163) who show a preference for HIA prescriptions. GPs who predominantly cater to pediatric patients have a higher tendency to prescribe more antibiotics, specifically oral 3GCs, in contrast to those who mainly treat geriatric patients and who commonly prescribe AMC. The low-impact overprescribers (LIOPs) form the second profile, accounting for 36% of the HRPs (59/163), and can be identified by their escalated AP/V rate. Such GPs have a reputation for excessively prescribing LIAs. The antibiotic overprescribers (AOPs) form the third group, which includes 11% of the HRPs (18/163), with GPs in this group exceeding the threshold in both indicator categories.

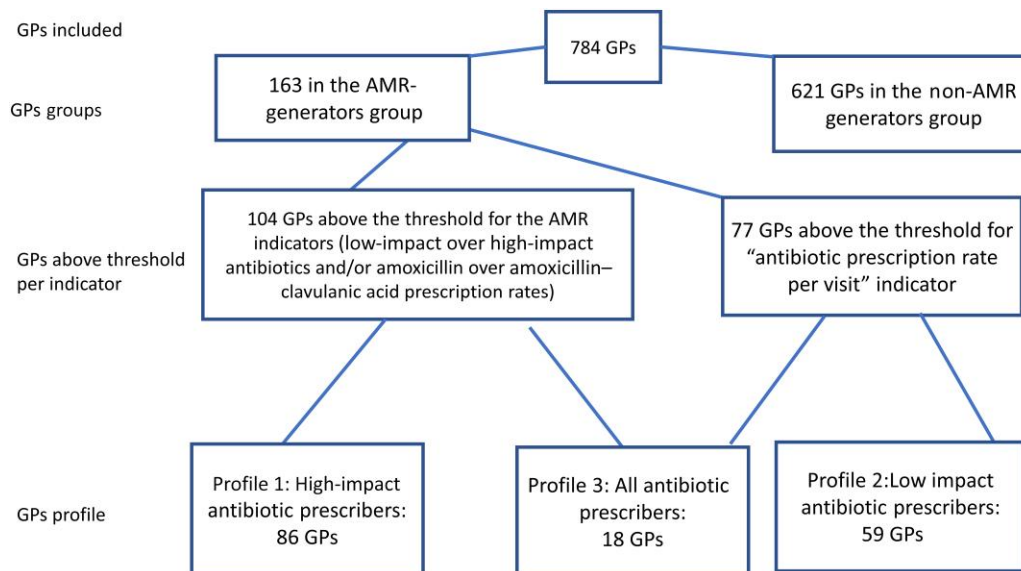
### Profile Characteristics of HRPs

Compared to the LRP group, HIOPs have treated a higher number of patients in the age ranges <6 years and 6–16 years (Table 3). Moreover, they have prescribed more antibiotics per consultation for the age categories <6 years and 36–66 years. Initiation rates did not differ between age categories for the LRP and the HIOP groups. However, they did not initiate more antibiotics per visit than the LRP group overall,

**Table 2. General Practitioners' Antibiotic Prescription Rates by Antibiotic Class and Age Group**

Age Group, y	% Penicillin		% Cephalosporin		% MLS		% Quinolones		% Other Classes	
	Total No. (%)	Median (IQR)	Total No. (%)	Median (IQR)	Total No. (%)	Median (IQR)	Total No. (%)	Median (IQR)	Total No. (%)	Median (IQR)
<6	43 811 (66.7)	74 (54–88)	15 143 (23)	15 (5–32)	5808 (8.8)	4.5 (1.2–10)	7 (0)	0	873 (1.3)	0 (0–1.3)
6–16	27758 (65.8)	71 (55–82)	7104 (16.8)	10 (4–21)	4894 (11.6)	7 (3–14)	95 (0)	0	2261 (5)	4.4 (0–9)
16–36	41 011 (49)	50 (39–60)	10 124 (12)	6.8 (3–14)	15 526 (18.5)	16 (10–24)	4443 (5)	4 (2–7)	12 518 (15)	15.2 (10–23)
36–66	80 267 (46.6)	48 (37–58)	20 727 (12)	7.4 (3–14)	35 025 (0.20)	18 (12–26)	13 269 (7.6)	7 (4–10)	23 075 (13.4)	13.6 (9–19)
>66	28 548 (42.1)	45 (35–56)	9016 (13)	9 (4–16)	12 579 (18.5)	17 (10–24)	7065 (10.4)	9 (5–14)	10 602 (15.6)	14 (8–21)

Abbreviations: IQR, interquartile range; MLS, macrolides, lincosamides, streptogramins.



**Figure 1.** General practitioners above the threshold for each set of indicators and their repartition by type of profile. Abbreviations: AMR, antimicrobial resistance; GP, general practitioner.

either in terms of number of prescriptions or in terms of DDD, but they prescribed more AMC and 3CGs and fewer LIAs than the LRP group. The differences in the ratio of AMC/total antibiotics (24.6% vs 11.5%,  $P < .001$ ), 3GCs/total antibiotics (13.8% vs 7.5%,  $P < .001$ ), and AMX/total antibiotics (14.2% vs 39%,  $P < .001$ ) were found to be significant.

LIOPs had fewer consultations but prescribed more antibiotics per consultation than the LRPs (27.7% vs 12.2%,  $P < .001$ ). They prescribed almost twice as much antibiotics as the LRPs in terms of DDD per GP with a median of 5805 (IQR, 3656–8539) vs 10 720 DDDs (IQR, 7289–14 831) ( $P < .001$ ). They treated a higher proportion of children and young adults than the LRPs (age groups <6, 6–16, and 16–36 years). Compared to the LRPs, LIOPs proportionally prescribed more amoxicillin (50% vs 39%,  $P < .001$ ) and fewer AMC, macrolides, and FQs.

Antibiotic overprescribers treated as many patients as the LRPs but prescribed twice as many antibiotics both in terms of

number of prescription and DDD. The age distribution of patients was comparable to that of the LRP group. Antibiotics were excessively prescribed across all age groups. Notably, 3GCs (36%) were the most commonly prescribed antibiotic. When compared to the LRP group, healthcare providers prescribed less AMX (11.5% vs 39%,  $P < .001$ ) and more AMC (17.5% vs 11.5%,  $P < .001$ ) and 3GCs (36% vs 7.5%,  $P < .001$ ). Only the prescription rate of FQs did not differ significantly.

## DISCUSSION

### Principal Findings

Antibiotic prescribing indicators were applied to individual prescriptions from a cohort of GPs rather than the aggregated consumption of the entire group. This investigation was facilitated by reimbursement data obtained from the health insurance databases of each doctor. Other studies have employed

**Table 3. Comparison Between the 3 High-Risk Prescriber Profiles and the Reference Group of Low-Risk Prescribers According to Their Median Rate of Antibiotic Class Use and Their Patients' Population Regarding Age Group Composition**

Characteristic	LRP (n = 621) (Reference Group)	HIOP <sup>a</sup> (n = 86)	P Value	AOP <sup>b</sup> (n = 18)	P Value	LIOP <sup>c</sup> (n = 59)	P Value
Total No. of DDDs	5805 (3656–8539)	5367 (3656–8539)	.25	11 296 (7300–17 001)	<.001	10 720 (7289–14 831)	<.001
Total APs	436 (289–647)	422 (213–703)	.51	966 (574–1520)	<.001	852 (585–1253)	<.001
Total No. of visits	3569 (2624–4716)	2897 (2036–4927)	.03	3363 (2624–4716)	.49	2693 (2006–3851)	<.001
AP/V (%)	12.6 (9.4–15.8)	13.47 (9.4–17.1)	.34	26.2 (24.7–30.4)	<.001	27.7 (25.5–35.24)	<.001
AMX/AP	39 (30–46.6)	14.2 (8.3–20.5)	<.001	11.5 (6.3–24.7)	<.001	50 (41–59.4)	<.001
MLS/AP	5.1 (3.2–5.1)	6.7 (8–1.3)	.001	6.2 (4.3–9.5)	.09	3.7 (2.5–6.1)	.001
FOS-NIT/AP	7.6 (5–11)	5.2 (2.8–7.6)	<.001	1.9 (0.3–3.1)	<.001	3 (1.7–4.5)	<.001
1GC-2GC/AP	0.24 (0–1.5)	0 (0–0.9)	.02	0.03 (0.02–1.4)	.053	0.17 (0–1.4)	.92
Sulfonamides/AP	0.64 (0.2–1.5)	0.39 (0–12)	.038	0.54 (0.00–0.02)	.77	0.17 (0–0.76)	.003
Others/AP	3.6 (2.2–5.2)	2.9 (1.4–4.5)	.009	2.5 (1.7–3.1)	.01	1.2 (0.5–3)	<.001
AMC/AP	11.5 (7.5–15.8)	24.6 (16.5–35.7)	<.001	14.6 (12–29.6)	.003	13.8 (8.8–19.6)	.025
FQ/AP	15.4 (10.5–21.3)	15.7 (10.7–21.3)	.1	17.5 (11.4–24.6)	.5	10.5 (7.4–13.9)	<.001
3GC/AP	7.5 (4–12.5)	13.8 (5.8–25.7)	<.001	36 (17–52)	<.001	8.6 (6–15)	.038
HIA/AP	26.5 (20–33)	50.5 (41.9–59.3)	<.001	57.4 (51.4–71)	<.001	29 (24–35)	.055
Drug-specific ecological impact indicators							
AMX/AMC	3.3 (2.17–5)	0.56 (0.38–0.83)	<.001	0.88 (0.51–1.36)	<.001	3.3 (1.42–2.5)	.5
LIA/HIA	2.77 (2–3.84)	0.98 (0.69–1.39)	<.001	0.74 (0.41–0.95)	<.001	2.5 (2–3.33)	.06
Proportion of visits by age group (y) %							
<6	7.8 (5.5–10.5)	5.5 (2.4–7.6)	<.001	8.7 (5.4–23.2)	.34	26 (9–30)	<.001
6–16	8.8 (7–10)	7.8 (5.3–10.4)	.02	9.4 (6.3–12.2)	.4	12 (9–14)	<.001
16–36	17 (14–21)	16.2 (12.1–22.6)	.13	16.5 (14.8–20.5)	.83	22 (19–25)	<.001
36–66	44 (41–51)	13.3 (8.8–16.4)	.33	44 (30–50)	.75	29 (26–42)	<.001
>66	19.7 (13–27)	11.1 (8.1–13.3)	.77	17 (11–26)	.49	8 (7–15)	<.001
AP/V by age group (y), %							
<6	20 (14–30)	27.2 (13.7–40)	<.001	46.3 (43–55.5)	<.001	40 (33–53)	<.001
6–16	12 (8–18)	15 (10–20.2)	.09	36.9 (32–44)	<.001	35 (27–41)	<.001
16–36	13 (0.1–0.17)	15 (10.4–20.2)	.09	28.3 (25.9–34.9)	<.001	28 (24–33)	<.001
36–66	12 (9–15)	13.3 (8.9–15.2)	.02	25.4 (21.9–38.1)	<.001	27 (24–34)	<.001
>66	10 (8–13)	11.5 (8.1–13.3)	.77	20.6 (16.4–27.5)	<.001	25 (19–31)	<.001

Data are presented as median (interquartile range) unless otherwise indicated. High-risk prescribers are defined by reaching the overuse threshold for at least 1 of the 3 ecological indicators (LIA/HIA, AMX/AMC, and AP/V). Conversely, LRPs are characterized by not reaching the overuse threshold for any of the 3 ecological indicators.

Abbreviations: 1GC, first-generation cephalosporin; 2GC, second-generation cephalosporin; 3GC, third-generation cephalosporin; AMC, amoxicillin-clavulanic acid; AMX, amoxicillin; AOP, antibiotic overprescriber; AP, antibiotic prescription; AP/V, ratio of the number of antibiotic prescriptions per year to the number of visits per year; DDD, defined daily dose; FOS-NIT, fosfomycin-nitrofurantoin; FQ, fluoroquinolone; HIA, high-impact antibiotic; HIOP, high-impact antibiotic overprescriber; LIA, low-impact antibiotic; LIOP, low-impact antibiotic overprescriber; LRP, low-risk prescriber; MLS, macrolides, lincosamides, streptogramins.

<sup>a</sup>HIOP profile is defined by an LIA/HIA and/or an AMX/AMC ratio <1 but an initiation of antibiotic prescription rate (AP/V) below the 90th percentile.

<sup>b</sup>AOP profile is defined by both an overinitiation of antibiotic prescriptions (AP/V rate >90th percentile) and an overuse of HIAs (LIA/HIA and/or AMX/AMC ratio <1).

<sup>c</sup>LIOP profile is defined by an overinitiation of antibiotic prescriptions (AP/V rate >90th percentile) but an LIA/HIA and AMX/AMC ratio >1.

“proxy indicators” that integrate indicators of poor practice or misuse, such as the combination of APs with anti-inflammatory drugs and indicators of overall good antibiotic use, such as seasonal variations in FQ prescriptions [30]. We have chosen indicators that are not linked to the gross number of prescriptions, the direct and indirect costs linked to AP, nor willful misuse of antibiotics. Instead, as physicians have an ethical obligation to promote antimicrobial stewardship and limit the propagation of resistance [31], we have opted for indicators that show a tendency to influence AMR, regardless of the fact that some broad-spectrum antibiotic prescriptions are justified. Our reasoning is based on the premise that the use of certain types of antibiotics is more likely to contribute to the development of AMR than others. The calculation of 3

indicators evaluating the global rate of use of antibiotic per visit and the relative use of HIAs over LIAs for each GP of the county allowed us to identify 3 different profiles of HRP. The HIOP profile includes prescribers who overuse HIAs. They are identified by the LIA/HIA and the AMX/AMC ratios. Those GPs preferentially use HIAs and had a propensity to initiate more APs per visit regardless of patients' age. GPs with a predominantly pediatric practice prescribe more antibiotics, particularly oral 3GCs, whereas those with a predominantly geriatric practice mostly prescribe AMC. The second profile is identified by a high AP/V. These GPs usually overprescribe LIAs. The third profile includes the minority of physicians who are above the threshold in both categories of indicators.

These findings confirmed the DRIVE-AB consortium's recommendations [28] of the need to combine different metrics to optimize the interpretation of antibiotic use as each of the single metrics had some limitations.

Our study also allows a more detailed analysis of the prescribing practices of GPs by analyzing the use of each class of molecule in relation to the total number of APs within each age group. For example, FQs are mostly prescribed in the age group 36–66 years, but the rate of FQ initiation in relation to the total number of APs is highest in the >66 years age group.

#### Comparison With Existing Data

Several studies showed the relationship between antibiotic usage and development of resistance. In a meta-analysis, Costelloe et al found that APs in primary care are associated with an increased resistance to such antibiotics and an increased usage of second-line antibiotics [32]. More recently, a Japanese study found that increased antimicrobial usage of quinolones and 3GCs is associated with an increased resistance to both groups of antimicrobials [33]. These studies provide the basis for establishing an ASP in outpatient settings.

In Belgium, the AMX prescription ratio over AMC is applied to supervise the community's antibiotic consumption and has a target of 4:1, which is more stringent than our set goal of 1:1 [34]. Our study revealed a median ratio of AMX to AMC prescriptions of 3:1. This more restrictive objective will require a change in the prescribing behavior of GPs in France. Recently, Thilly et al [30] suggested using proxy indicators based on primary care reimbursement data to estimate automated appropriateness of antibiotic use in ASPs. One of the proposed proxy indicators is the AMX/second-line antibiotic ratio with a target of >1 (with AMC, FQ, all cephalosporins, and macrolides as second-line antibiotics).

Our ecological impact indicators could be utilized as proxy indicators to target antibiotic resistance in ASPs. What sets our indicators apart is our use of more restrictive denominators. As a result, we identify fewer GPs with "poor prescribing practices" than other indicators that group more antibiotic classes. This approach allows us to target a more specific population and develop tailored ASPs. Hence, selecting appropriate indicators is essential and ought to be adjusted to the regional resistance epidemiology.

#### Limitations

Public databases on antibiotic consumption currently do not enable the linkage of a drug prescription to its indication for the assessment of the appropriateness of the prescribed drug and the justification of the use of an HIA. Nevertheless, the use of a relative indicator, such as HIAs versus LIAs, permits an approximate evaluation of the prescription quality. Choosing an LIA rather than an HIA may be a useful strategy

for controlling AMR and improving antibiotic use in individual patients, regardless of indication or patient population. However, 1 limitation of this study is the inability to correlate antimicrobial prescriptions with microbiology results, which would have aided in identifying whether some prescriptions for HIAs were justified. It is uncertain if the AP trends in Seine-et-Marne are reflective of those in other parts of France without mentioning the rest of the world. We could not evaluate the appropriateness of any individual prescription. We have not been able to assess whether having specific patient types has influenced some GPs' antibiotic prescriptions. We also have not been able to assess patients' requests and preferences on AP. Furthermore, when using a metric-based evaluation, it is important to remember that no indicator is without flaws, that using multiple metrics amplifies each one's flaws, and that our conclusions are only as good as the quality of our metrics and cannot replace a thorough evaluation of individual prescriptions.

The database we used did not furnish us with data regarding prescriber characteristics, such as their age, location, or experience, which would be useful in assessing differences in prescribing practices among various profiles of prescribers [13, 35, 36].

#### Implication for Policy and Future Research

Our research indicates that the 3 indicators we proposed are mutually reinforcing in tracking the impact of antibiotic use and can be applied to create tailored ASPs for GPs. Specifically, these indicators help to identify a range of patterns where antibiotics are being misused, so it is essential that ASPs adjust their messaging accordingly.

To further enhance prescriber profiles, the physician's knowledge and cognitive-behavioral factors should be studied to devise specific interventions tailored to individual practicing profiles.

Prescribers who exhibit a low initiation rate but prescribe only molecules with a high impact on antibiotic resistance may hold a particular perception regarding the "ecological" risk of their prescribing: "I prescribe few antibiotics but when it is truly necessary, it does not matter what the ecological impact is." Prescribers who frequently prescribe antibiotics but only with low-impact molecules may consider their behavior as not problematic as they prescribe mostly LIAs. It is crucial to consider such perceptions when developing interventions to promote appropriate antibiotic use. Furthermore, GPs often consider AMR as a national but not a local problem, therefore justifying their continuous use of antibiotics [37].

In France, the national health insurance yearly sends customized profiles of antibiotic consumption to GPs. By incorporating these indicators into the GPs' profiles, they could be calculated at an individual level and enable a comparison between different GPs. An accompanying note on the results of

individual indicators and the AMR impact effects of different antibiotic classes would enhance the educational value of this feedback, while also increasing awareness of antibiotic resistance among GPs. Physicians are likely to prioritize ecological indicators that highlight the impact on their patients' health and the preservation of antibiotic effectiveness over raw volumetric indicators, which may be viewed as administrative performance indicators and not reflective of their practice.

Furthermore, these profiles enable GPs to compare their personal prescribing patterns with those of their peers within the department. The outcomes may be adapted dependent on the patient population profile of the GP, to enable comparison with peers of comparable practices. This comparative analysis could motivate GPs to improve the quality of their APs, especially if specific targets are included.

Our indicators are not relevant for adaptation for all countries; they must inspire each country to develop its own set of indicators to identify the profile of GPs who may benefit from a targeted ASP. The effectiveness of such programs must be assessed by evaluating the association between prescription rates and antimicrobial resistance.

To establish the soundness of this concept, further studies must be conducted. Antibiotic resistance data are now available throughout the county, enabling the identification of any association between prescribing patterns and resistance rates in the community, particularly in areas with low medical density. Further studies are necessary to determine which profiles have the greatest impact on the emergence of antibiotic resistance. Our research will continue to identify the psychobehavioral factors associated with these profiles. This analysis will enable the development of specific ASPs for each profile.

## CONCLUSIONS

Indicators based on prescribing enable the identification of 3 distinct profiles of antibiotic prescribers. There are 2 opposing profiles: 1 made up of prescribers with a high rate of prescribing but using only narrow-spectrum molecules, and the other with a moderate rate of initiation but using mainly broad-spectrum molecules. This identification may allow for targeted implementation of stewardship programs focused on the specific prescribing patterns of each profile.

## Notes

**Author contributions.** P. A. drafted the manuscript. M. M. revised the manuscript and wrote the final version. A. S. revised the manuscript. C. L. M. participated in data acquisition. S. G. supervised the study and participated in study design. S. D. participated in study design, manuscript supervision, and manuscript revision.

**Data availability.** The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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