A Computerized Decision Support System (CDSS) for Antibiotic Prescription in Primary Care: Implementation, Adoption and Sustainable Use in the Era of Extended Antimicrobial Resistance

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Background

To describe the implementation and use of a CDSS for antibiotic prescribing in primary care in France(*Antibioclic*). The CDSS targets 37 infectious diseases and is freely available on a website since 2011.

Methods

Description and implementation of the architecture of a CDSS for antibiotic prescription in general practice. Analysis of the queries performed between 2012 and 2018 on the CDSS by GPs. Analysis of 2 cross-sectional studies performed in users in 2014 and 2019.

Results

The number of queries increased from a median of 796/day [IQR,578–989] in 2012 to 11,125/day [5,592–12,505] in 2018. Unique users increased from 414/day [245–494] in 2012 to 5,365/day [2,891–5,769] in 2018. Time to perform a query was 2 minutes [1·9–2·1]. Among 3,542,347 queries in 2018, 78% were for adults. Six situations accounted for ≥50% of queries: cystitis; acute otitis media; acute sinusitis; community-acquired pneumoniae, sore throat and pyelonephritis. Queries concerned pathologies for which antibiotic prescription was systematic (63·7%), was conditional on additional clinical steps (34·5%), or was not recommended (1·8%). Most users (81%) were GPs, with median age 38-years [31–52] and 58% female. Among GP users, a large majority (96%) reported using the CDSS during the consultation, with 24% systematically using *Antibioclic* to initiate an antibiotic course and 93% having followed the CDSS recommendation for the latest prescription. Most GPs were comfortable using the the CDSS in front of a patient.

Conclusions

Antibioclic has been adopted and is widely used in primary care in France. Its interoperability could allow an adaptation and implementation in other countries.

INTRODUCTION

Worldwide, inappropriate use of antibiotics has led to an increase in Antimicrobial Resistance (AMR).[1,2] From 2007 to 2015, the burden of AMR has more than doubled in Europe and became equivalent to the cumulative burden of influenza, tuberculosis and HIV.[2] Despite having implemented AMR national action plans (NAPs) since 2001, antibiotic prescription is still very high in France compared to most of high-income countires.[1,3] As in other European countries, approximately ninety percent of the antibiotic prescription are written in primary care, and 71% of all prescriptions by general practioners (GPs). [4,5] Other primary care physicians (dentists, paediatricians, dermatologists, …) account for a 19% of all prescriptions and the rest is written in the hospital.4 In 2016, it was estimated that a French GP was initiating an antibiotic course every 6 consultations, corresponding to a 16·7% antibiotic prescribing rate per consultation and 29·9 defined daily dose (DDD) per 1,000 habitants per day.[6]

One of the ways to prevent the spread of AMR is to reduce the overall volume and improve the appropriateness of prescribed antibiotics.[5,7,8] In 2018, the French Ministry of Health has set an objective of 25% reduction of overall antibiotic consumption by 2022.[7] Since 2011, French primary care GPs have been eligible to a voluntary-based pay for performance (P4P) scheme to decrease their antibiotic consumption. The P4P objectives are: 1) to initiate less than 20 antibiotic therapy for 100 patients between 16 and 65-years, and 2) to reach less than 32% use of broad-spectrum antibiotics for initiated antibiotic therapy – *i.e.* amoxicillin-clavulanic acid, 3rd generation cephalosporins, or fluoroquinolones. Similar interventions have been conducted in Europe, such as the National Health System (NHS) Quality Premium (QP) in England in 2015/2016. A recent evaluation of the NHS Quality Premium trough an interrupted time series analysis shown a 3% relative reduction of antibiotic prescribing for respiratory tract infections (RTI) after its implementation.[9]

The efficacy of information campaigns on antibiotic consumption reduction is mitigated in Europe.[10] Multifaceted approaches have been associated with decreased antibiotic prescribing, especially in RTI.[10,11] Involvement of patients through shared decision-making with clinicians for antibiotic prescription has also been shown effective in the short-term, in RTI.[12] New technologies such as computerized decision support systems (CDSS) for antimicrobial prescribing could be effective and induce prolonged impact on practices.[11] CDSS are linking clinical observations to knowledge base, at the point-of-care, and might have the ability to support clinical decision-making and improve antimicrobial prescription.[13] This has been mainly demonstrated in hospital settings, where implementation of antimicrobial stewardship programs (ASP) is high, as compared to primary care.[8,13,14] Few studies of heterogeneous design and quality have been conducted on CDSS in primary care.[11,15,16] In a recent review, out of 58 CDSS, 18 had been specifically developed for primary care.[15] Of those, 11 were using syndromic approach to assist the practitioner for pulmonary and/or urinary tract infections (UTI). None of the CDSS covered all the infectious situations that are frequently encountered by GPs.[5,17] The impact at prescriber level was not consistently measured and none was tailored to demonstrate an effect on patients' hospitalization rate, or mortality.[15] Rawson *et al.* highlighted that when CDSS failed to demonstrate their primary outcome it was often related to a low uptake and a poor adherence to generated advice. Qualitative studies have shown that ease of use and integration into daily clinical practice workflow, with no impact on consultation time nor negative consequence for patient relationship, were key factors in improving CDSS uptake.[18,19] In addition, physicians have to follow the recommendations issued by the CDSS in order to improve antibiotic prescribing. According to the WHO, the main challenge in tackling AMR is the successful implementation of policies.[5] Many innovations in healthcare have been abandoned after their initial evaluation because of insufficient work on their implementation, and adoption.[20] The non-adoption, abandonment, scale-up, spread and sustainability (NASS) framework for digital technologies shows that the adoption of an innovation in healthcare is a dynamic process related to many factors from the micro to the macro level.[20]

In 2011, a French multidisciplinary team involving academic and non-academic GPs, infectious disease specialists and engineers co-designed a guideline-based CDSS focusing on GPs' antibiotic prescribing in primary care – *Antibioclic*.[21] The aim of *Antibioclic* was to improve the quality of antimicrobial prescribing in primary care, but to date, no high quality evaluation of its impact has been performed. Herein we describe the implementation, adoption and sustainable use of *Antibioclic* from 2012 to 2018, and provide future perspectives for development.

METHODS

Description of the CDSS

Antibioclic – http://www.antibioclic.com – is a French CDSS for antibiotic prescribing in primary care developed and released in October 2011.[21] Initial advertising was limited to an article in a French family medicine journal.[21] Since then, advertising is performed in medicine faculties to GP residents. Several communications or posters were also presented in French family medicine and infectious diseases congress (see acknowledgement section). It was co-designed by the *Antibioclic* steering committee, a team of academic and non-academic GPs, ID specialists, and engineers (IT). *Antibioclic* is a stand-alone web application and is not integrated into electronic health records (EHR). Since 2017 a smartphone application has been available. *Antibioclic* access and use is free of charge, does not require registration and is granted to any healthcare professional or service user 24/24-7/7.

Task-Network Model of Antibioclic decision tree

A systematic method was used to transform the clinical practice guidelines (CPG) from the French National Authority for Health (HAS) or the French Infectious Diseases Society (SPILF) into computer interpretable guidelines (CIG). We used a semi-formal decision-tree, implementing a Task-Network Model (TNM) where antibiotic prescription is described as a process with a set of predefined tasks and rules to obtain a decision.[22] The tasks of the TNM includes :

Data entry: for describing a clinical case

Required criteria

- Anatomical domain related to the pathology/infectious disease
- Name of the pathology/infectious disease
- Age group of the patient: adult versus children

Optional criteria

- Specific conditions that might impact choice of antibiotic therapy and drug-drug interactions: pregnancy (if adult), breastfeeding (if adult), and chronic kidney failure.
- Other specific condition related to the pathology/infectious disease, such as the CRB-65 score for community acquired pneumoniae (CAP), or the result of Point-of-Care testing for group A streptococci in sore throat.

Outcome: Guidelines to assist the physician

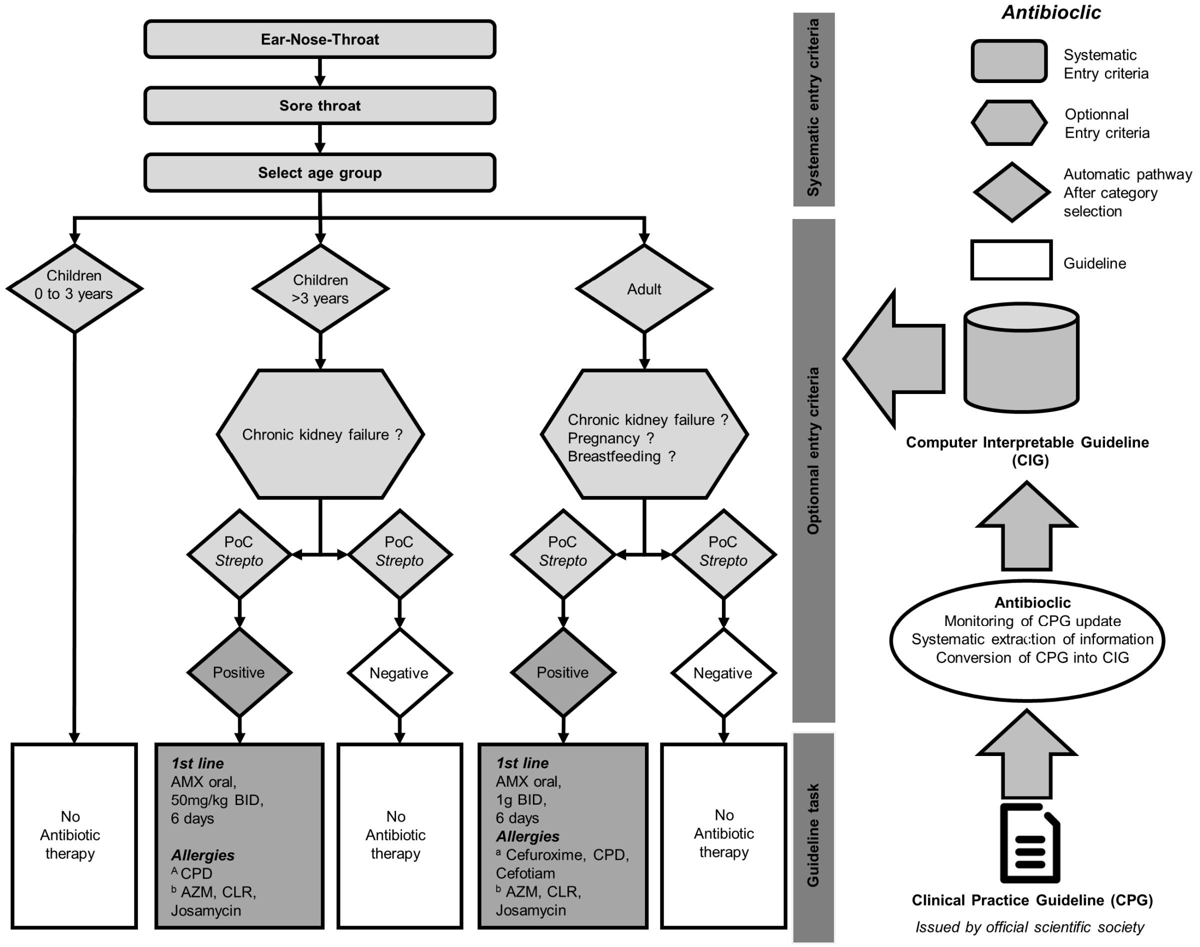
- Depending on the pathology, antibiotic prescription can be necessary, conditional or not recommended (Table 1).
    - Necessary prescription implies that an antibiotic treatment is always necessary but its choice depends on modifiers (= patient's characteristics).
    - Conditional prescription implies that an antibiotic treatment may be necessary according to modifiers (patient's characteristics) and/or the outcome of additional steps like a POC test.
    - Not recommended prescription implies that no antibiotic treatment should be prescribed.
- In any case, *Antibioclic* displays:
    - Link to the CPG
    - Date of the version update
- If an antibiotic is recommended, *Antibioclic* displays:
    - List of the recommended International Nonproprietary Name (INN), route of administration, dosage, and duration of recommended antibiotics
    - Alternatives in case of allergies
- When CPGs did not prioritize one antibiotic over others, *Antibioclic* steering committee chose a common recommendation for the preferred first line regimen. The decision is based on a systematic rule: 1) to prefer the molecule with the shortest treatment duration; 2) the least side effects; 3) and the narrowest spectrum.

Reliability

To ensure that *Antibioclic* follows official guidelines, a partnership with the French National College of Academic General Practitioners (CNGE) and the SPILF, has been developed. Each Society designed a representative member in the steering committee. The steering committee is monitoring official updates of national guidelines for each pathology/infectious disease. When national guidelines are issued or updated, the CDSS recommendations are updated accordingly by the steering committee using the TNM described above. From 2011 to end of 2018, the median rate of guidelines update was 3 [IQR, 2-4].

Service users can also contact the steering committee through a dedicated e-mail address.

Figure 1 represents the conversion of a CPG to a CIG using the example of sore throat.



PoC Strepto = Point-of-Care test result for presence of group A streptococci.

The steering committee extracts knowledge from clinical practice guideline (CPG) using a systematic procedure. CPGs are converted in computer interpretable guidelines (CIG) using the Task-Network Model (TNM) of Antibioclic – i.e. the extracted information is allocated to boxes in the decision-tree. The physician then selects the characteristics of the patient among lists or categories. After completing all the entry criteria, a guideline task is displayed. Standard abbreviations for antibiotics: AMX = amoxicillin, CPD = cefpodoxime, AZM = azithromycin, CLR = clarithromycin.

Figure 1: Antibioclic Task-Network Model for CPG to CIG conversion – the example of sore throat

Ethics, policies and funding

Antibioclic is a non-profit organization and is not linked by pharmaceuticals companies for the contents of the CDSS or funding. The steering committee members are volunteers and funding is obtained from competitive call for tenders from universities, the French health authorities or learned societies. Conflicts of interest of individual steering committee members are disclosed on the web site.

None of the collected data is shared with private companies. Confidentiality policy is fulfilling with European General Data Protection Regulation. The study has been approved by the ethics committee of the CNGE (N° 16051997).

Results of the study will be made available on the CDSS website.

Patient and Public Involvement

This research was done without patient or public involvement. Before publication, the results of this study were not disseminated to patients or the public.

Data collection on the use of the CDSS

Routine use

We used automated data collection by the Internet Service Providers (ISP) for our website to describe 1) date and time of request; 2) approximate geolocation based on the Internet Protocol (IP) address (In France, the accuracy of geolocation is 46% at the level of city within 10 km radius, and 76% at level of region.) Due to changes of ISP over the years, these data were available from week 42 of year 2011 to week 52 of year 2012, then from 2015 on.

We also used data logged specifically in our system regarding the details of the queries to the CDSS. These data allow determining the pages seen by a user, as well as the duration of interaction with the system. We described the nature of queries and the characteristics of user interactions over time. Due to change of ISP, these data were available from week 42 of year 2011 to week 52 of year 2012 then from week 42 of year 2017 on.

Cross-sectional studies

In addition to routine data collection, two cross-sectional studies on *Antibioclic* users were done in 2014 and 2019. The questionnaires were developed by the steering committee and covered: demographics, medical activity, CDSS usage, and users' compliance with CDSS recommendations. Participation was possible for all *Antibioclic* website users over a period of 2 months in both years, subject to one answer only for each IP address. No reminders were sent. Data was anonymized before analysis. The questionnaires are available in Table S2. Cross-sectional studies were compliant with the corresponding STROBE guidelines.

Statistical analysis

We computed mean number of queries to the CDSS per time period and according to location. Each unique IP address defined a user. We tabulated the number of queries according to disease, age and items specific to each query. We compared the responses to the survey in 2014 and 2019. Given the large number of participants, we focused on “large” differences (>10%) rather than on statistical significance in these comparisons.

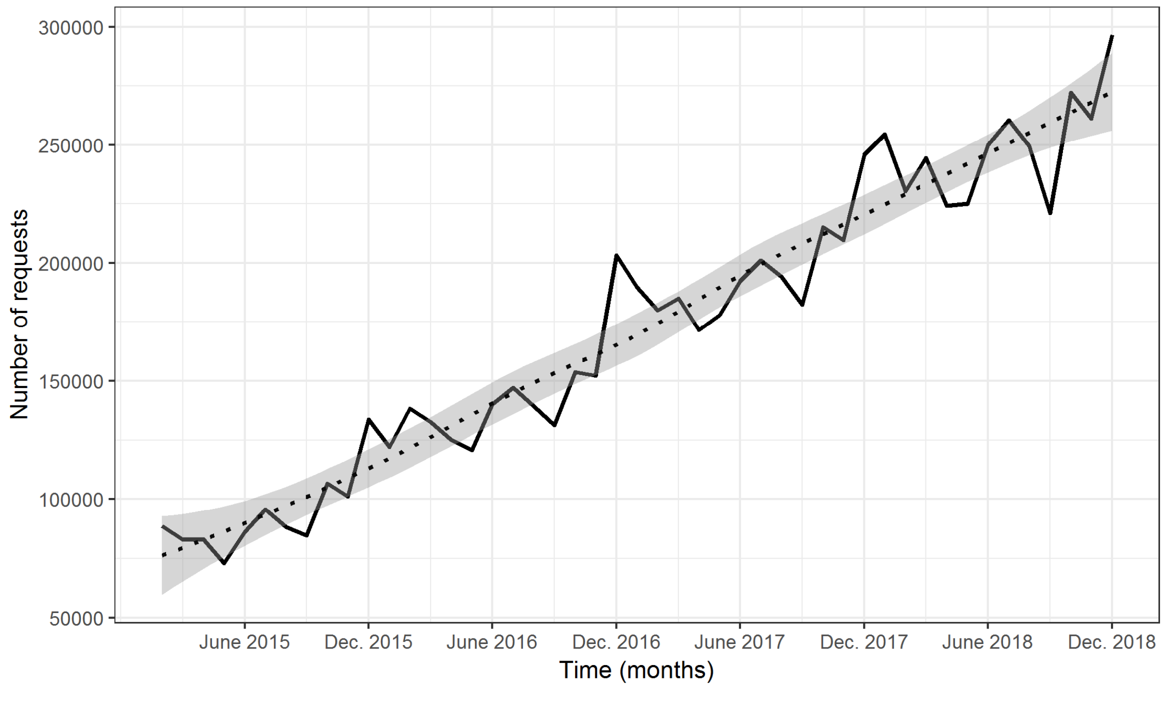
Results are reported as frequency and percentages or median and IQR as appropriate. Analysis were performed on R, version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Antibioclic use

The number of queries to the website increased from a total of 369,317 and a median [IQR] of 796 per day [578–989] in 2012, to 3,542,347 and 11,125 per day [5,592–12,505] in 2018 (+1397%). The number of users (unique IP address) increased from 414 [245–494] in 2012 to 5,365 per day [2,891–5,769] in 2018 (+1296%). In 2018, the maximum number users per day was 7,091. The increase in the number of queries did not lead to a saturation effect (Figure 2).

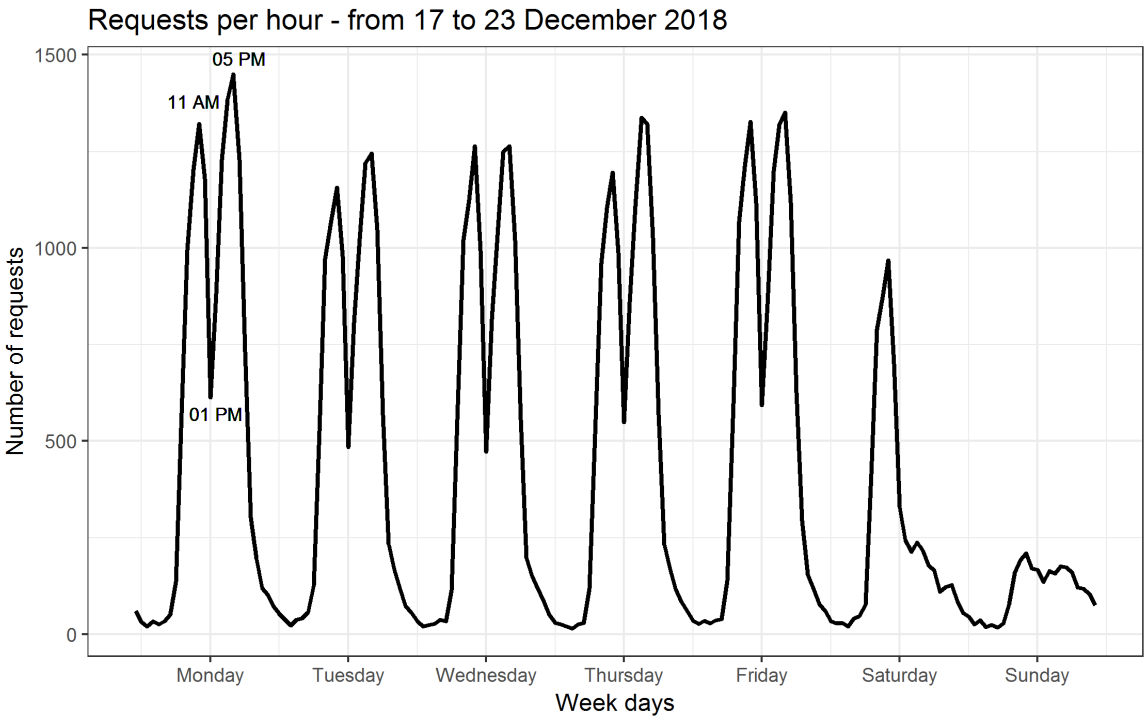
The median number of queries per user and per day was 2 [1·8–2·4] over the period 2015-18. The median time per query was 2 minutes [IQR, 1·9–2·1]. The median number of "clicks" to reach the page displaying the recommended action was 4 [IQR, 3–6].



The number of queries performed over time in months is represented. The linear tendency is also plotted as a dotted line with its confidence interval in grey.

Figure 2: Number of queries to the Antibioclic system between 2015 and 2018 per month.

The pattern of web-site traffic matched GP practice premises opening hours, with fewer queries over the week-end.[23] (Figure 3).



The number of queries performed over time in hours and according to weekdays of the week 51 of year 2018 is represented. Traffic peaks occur at 11 A.M. and 05 P.M., gaps at 01 P.M.

Figure 3: Number of queries to the Antibioclic CDSS per hour over week 51, year 2018.

Antibioclic users were all over France, with a median of 7,562 queries/100,000 inhabitants [IQR, 6,341–9,222], and a maximum of 12,191 queries/100,000 inhabitants in Paris area, Table S3 and Figure S1.

Among the 3,542,347 queries performed in 2018, 2,763,031 (78%) concerned adults. The three most requested anatomical domains in 2018 were: ear-nose-throat infections (ENT) with 968,737 queries (27·3%); UTI with 959,393 queries (27·1%); and skin and soft tissues infections with 535,755 queries (15·1%). Six situations accounted for more than half of the total number of queries: cystitis, 504,428 (14·2%); acute otitis media, 410,219 (11·6%); acute sinusitis, 340,128 (9·6%); CAP, 327,669 (9·3%), sore throat, 210,954 (6·0%), and pyelonephritis, 210,847 (6·0%). The details of queries performed are reported in Table 1. The outcome of the CDSS was that an antibiotic treatment was not recommended for 64,468 queries (1·8%); conditional for 1,223,013 queries (34·5%); and systematic for 2,254,866 queries (63·7%).

Table 1: Details of the queries performed on Antibioclic in 2018

Pathology	AB prescribing	Modifiers	N	%
ENT			**968,737**	**27·3%**
Acute Otitis Media	Conditional	Age group	410,219	11·6%
Acute sinusitis	Necessary	Age group Location	340,128	9·6%
Sore throat	Conditional	Age group PoC strepto [a]	210,954	6·0%
Rhinopharyngitis	Not recommended		7,436	0·2%
Urinary infections			**959,393**	**27·1%**
Cystitis	Necessary	Age group Complication Pregnancy	504,428	14·2%
Pyelonephritis	Necessary	Age group Complication Pregnancy ESBL[b] identification	210,847	6·0%
Masculine Urinary Tract Infection	Necessary	ESBL[b] identification	189,017	5·3%
Orchitis	Necessary		42,312	1·2%
Urinary colonization	Conditional	Pregnancy	12,789	0·4%
Skin and Soft Tissue Infection			**535,755**	**15·1%**
Lyme	Necessary	Age group Location / Dissemination	133,766	3·8%
Erysipelas	Necessary		107,455	3·0%
Impetigo	Conditional	Age group Severity	64,994	1·8%
Boil	Conditional	Age group Severity	51,543	1·5%
Paronychia	Conditional	Age group Surgery	51,992	1·5%
Scarlet fever	Conditional	Age group PoC strepto[a]	40,731	1·1%
Mammalian bites	Necessary	Age group	35,576	1·0%
Wound	Conditional	Age group Location / Dissemination	29,101	0·8%

Folliculitis	Not recommended		20,597	0·6%
Respiratory Tract Infections			**498,052**	**14·1%**
Community Acquired Pneumonia	Necessary	Age group CRB-65 score Influenza association	327,669	9·3%
COPD exacerbation	Conditional	FEV1[c] value Purulent sputum	98,767	2·8%
Bronchitis	Not recommended		36,435	1·0%
Pertussis	Necessary		29,158	0·8%
Bronchiolitis	Conditional	Acute Otitis Media Pneumoniae Fever > 38.5°C for 3 days	6,023	0·2%
Sexually Transmitted Infections			**292,332**	**8·3%**
Vaginitis	Conditional	Identified pathogen	181,056	5·1%
Uretritis	Necessary	Identified pathogen	60,710	1·7%
Cervicitis	Necessary	Identified pathogen	17,998	0·5%
Salpingitis	Necessary		14,398	0·4%
Syphilis	Necessary		12,731	0·4%
Rectitis	Necessary	Identified pathogen	3,606	0·1%
Lymphogranuloma venerum	Necessary		1,833	0·1%
Digestive infections			**269,933**	**7·6%**
Bacterial diarrhea	Necessary	Age group Identified or suspected pathogen	168,642	4·8%
Diverticulitis	Conditional	Immunosuppression ASA[d] score	55,622	1·6%
Helicobacter pylori infection	Necessary	Sensitivity to clarithromycin	25,605	0·7%
Parasitic infection	Necessary	Age group Identified pathogen	20,064	0·6%
Prophylaxis			**18,145**	**0·5%**
Endocarditis	Conditional	Age group Location of surgery	9,222	0·3%
Meningococcal meningitis	Necessary	Age group	6,083	0·2%
Tuberculosis	Necessary	Age group	2,840	0·1%

[a] PoC strepto = Point-of-Care test for group A streptococci

[b] ESBL = Extended Spectrum Beta-Lactamase

[c] FEV1 = Forced Expiratory Volume in 1 second

[d] ASA score = American Society of Anesthesiologists – Physical status classification system

The CDSS can recommend antibiotic prescribing or not, based on conditions. If conditions are impacting decision to recommend antibiotic prescribing, they are represented in the dedicated column.

Antibioclic users

The number of users taking the online survey was 1,848 in 2014 and 3,621 in 2019. Questionnaires were fulfilled by 1,366 (81%) participants in 2014 and 3207 (98%) in 2019. Overall, 352 (7%) were not medical doctors but most of them (54%) were health professionals (pharmacists, midwifes, dentist). Among the 4,607 (93%) who were doctors either in training or registered, 4,016 (81%) were GPs; the other medical specialties included emergency medicine (103), geriatrics (32), paediatrics (20), and gynaecology (11). The median age of the 4,016 GPs was 38-years old [31–52], 2,314 (58%) were women, 3,106 (77%) practiced in group-practices, and 460 (11%) were trainees.

The detailed results of the 2 surveys are reported in Table 2. For most questions that were posed on both occasions, the answers were similar (less than 10% change). Most GPs reported using the CDSS during the consultation before prescribing an antibiotic (96%), and 93% reported following *Antibioclic* recommendations. A large majority of users (94%) reported that the CDSS was not extending consultation duration, and that they were comfortable using the CDSS during the consultation. Using *Antibioclic* to update knowledge was less reported over time (83% in 2014 vs. 43% in 2019) – even though 90% of the 2019 reported that the CDSS was improving their knowledge in antibiotic therapy. Users were also fewer to use *Antibioclic* in each situation of antibiotic prescription (35% vs. 19%). A substantial portion of GPs (43%) reported using the CDSS to explain to patients why they did not prescribe antibiotics. From 2014 to 2019, the occurrence of a divergence with the recommendations grew smaller in terms of choosing the antibiotic, starting a cure when it was not recommended and extending the duration of the cure. Moreover, 93% of them reported following the CDSS recommendation in their last prescription, even if 20 to 30% of them acknowledged disagreements from time to time.

Table 2. Characteristics of general practitioner users – results of 2014 and 2019 cross-sectional studies

Characteristic of general practitioners	2014	2019
	N = 1,283	N = 2,733
	N (%), Median [IQR]	N (%), Median [IQR]
Demographics		
Resident	133 (10%)	327 (12%)
If physician, involved in residents training	522 / 1,150 (45%)	856 / 2,406 (36%)
Female	706 (55%)	1,608 (59%)
Median age (years)	37 [30 – 53]	36 [31 – 50]
Group practice [a]	794 (62%)	2,312 (85%)
CDSS impact on consultation		
CDSS is mostly used during the consultation, before antibiotic prescription	1,270 (99%)	2,596 (95%)
Consultation duration is not extended by CDSS use	1,206 (94%)	-
Comfortable with using CDSS in front of a patient	1,100 (86%)	2,299 (84%)
Users are using the CDSS		
To update knowledge	1,059 (83%)	1,168 (43%)
Every time they had to initiate an antibiotic therapy	447 (35%)	525 (19%)
To justify the non-prescription of antibiotic	-	1,176 (43%)
Compliance with CDSS recommendations		
Last antibiotic prescription was as the one recommended by the CDSS	1,191 (93%)	2,552 (93%)
Divergent antibiotic prescription – reasons		
Antibiotic different from the recommended one	366 / 897 (41%)	736 / 2,637 (28%)
Antibiotic initiation while not recommended	356 / 897 (40%)	866 / 2,637 (33%)
Extension of course duration	190 / 897 (21%)	534 / 2,637 (20%)
Other[b]	179 / 897 (20%)	301 / 2,637 (11%)
Users' vision of the CDSS		
Recommendations are reliable [c]	1,155 (90%)	2,401 (88%)
It is independent from pharmaceuticals companies [c]	1,105 (86%)	2,215 (81%)
It helps to improve knowledge in antibiotic therapy [c]	-	2,460 (90%)
It “deskills” the physician [c]	-	289 (11%)

[a] Group practice is defined as working in group facilities, medical health center, private or public hospital

[b] Other: Antibiotic is not prescribed while it was recommended, the duration is shorter than what was recommended, the posology is different from the recommended one.

[c] For these indicators, a 5-points Likert scale was used. Only “I agree” and “I strongly agree” were considered as positive answers in the computation of frequencies.

-: question not posed.

DISCUSSION

The number of users of *Antibioclic* has been steadily increasing over time with no saturation effect. Assuming that a unique IP address represents one user, and that 81% may have been GPs, this corresponds to a maximum of 5,700 GPs using *Antibioclic* daily, or about 10% of the 58,140 registered GPs in primary care.[24]

As proposed by Rawson *et al,* we discuss the rationale for development, implementation and assessment of our CDSS.[15] Having physicians follow recommended prescribing policies is a current challenge for the control of AMR.[5] Adoption of CPGs is often insufficient with up to 40% of patients not receiving the best care.[28] CDSS may lead to substantial improvements, though their efficacy in primary care has been variable.[28] In this respect, *Antibioclic* allows GPs to quickly get specialized advice at the time and place of decision making, using 3 systematic and 2 optional *entry criteria*. Our system includes the most prevalent situations in primary care and is in line with the situations recently targeted in England by the National Institute for Health and Excellence / Public Health England (NICE/PHE) antimicrobial prescribing guidelines.[17] Furthermore, it includes more situations for antibiotic prescriptions in primary care than other CDSS.[5,15,16] factors identified as being key of clinical practice improvement.[25] To ensure acceptability and integration in the GP workflow, *Antibioclic* has been co-designed since the beginning by a multidisciplinary team including GPs. This ensured including the CDSS' users perspective – *i.e.* the prescribers – into consideration. We also obtained feedback from users via e-mail and with the repeated cross-sectional studies. With a median time to perform a request of 2 minutes, users reported that it was possible to use *Antibioclic* during the consultation without extending its duration. Users were also very likely to trust the CDSS recommendations and reported the CDSS as a reliable source to update and improve their knowledge in antibiotic therapy. The more recent *Antibioclic* smartphone application has already been downloaded 38,170 times as of April 2019, and should further improve availability and timeliness of prescribing information at the point of care. To date, *Antibioclic* is not integrated into patients' EHR in primary care, but could easily evolve from a semi-formal to a formal CIG.[22,30] Through collection of individualized data, CDSS recommendations could then be more accurate and individualized.[22,30] So far, no formal assessment of *Antibioclic* impact has been made. Several studies have shown that an impact of CDSS on the appropriateness of antibiotic treatment in primary care is possible and mostly linked to the CDSS uptake level.[15,16] The continued increase in the number of users is therefore good news in this respect. Two small scale studies, independent from the team developing *Antibioclic*, reported encouraging results on the use of the system. Heslot *et al.* conducted a cross-sectional study among 142 GPs to investigate the impact of *Antibioclic* use on duration of amoxicillin course in CAP.[26] One hundred and twelve (79%) reported using *Antibioclic* to update their knowledge while 82 (58%) were directly looking at CPGs, 74 (52%) scientific literature, and 48 (34%) the website of the SPILF. Only *Antibioclic* users had an amoxicillin course duration ≤7 days (p<0·001).[26] Faucal *et al.* prospectively investigated 136 antibiotic prescriptions performed by 19 GPs.[27] Among the prescriptions, 31 (23%) were performed using *Antibioclic*.[27] The duration of antibiotic therapy was more appropriate to CPGs in case of *Antibioclic* use (81% versus 51%, p=0·038).[27] Since *Antibioclic* use is volunteer and self-initiated, a selection bias may be present in the participants described in these studies.[26,27] Physicians using *Antibioclic* may have a lower and more appropriate baseline antibiotic prescription level. This is suggested by the characteristics of the population surveyed in the cross-sectional studies that we conducted. Heslot *et al.* and Faucal *et al.* studies were conducted between our cross-sectional surveys and might have biased the conduction or the interpretation of our surveys. In order to better estimate the impact of *Antibioclic*, we are currently conducting a large scale observational study, comparing antibiotic prescribing and patient outcomes between all CDSS users and a control group of GPs. A social science perspective is also under way to understand how prescribers use the CDSS and how it may change clinical decision-making.

Secondary use of the data collected using this CDSS could provide information on the epidemiology of common infectious diseases in primary care. Collected data could be integrated in AMR NAPs surveillance system.[5,14] This would be of particular interest for microbiological data such as the level of resistance in UTI.[5] But such attempts would have to be handled carefully. For example, CAP queries were more frequent than COPD exacerbation and bronchitis, when the epidemiology of these conditions would suggest otherwise. It may be that users consult the the CDSS less frequently in situations where antibiotic prescription is not recommended (e.g. bronchitis) or that were already encountered before. This might lead to an under- use/reporting for those type of infections. In France, GPs in primary care are taking care of 92 to 97 patients per week, and antibiotic prescription rate is around 16.7%.[6,29] Over 3.5 millions of queries were performed on *Antibioclic* in 2018 and the median number of queries per day per users was stable at 2 [1·8–2·4]. Assuming a constant number of weekly patients across GPs and that each request corresponded to a situation in which an antibiotic could have been initiated, the rate of antibiotic prescribing would range between 14.4 and 15.2% in CDSS users.[29] These results support the fact that queries have been performed to manage real patients.

As of now, the design of the platform did not allow collecting the details of antibiotic prescription. This choice was made to improve user experience and ease its uptake.[25] Therefore, our study uses the analysis of queries as a surrogate marker for antibiotic prescription. It is not possible to differentiate situations in which a request has been performed for a real patient from queries unrelated to patient's care. However, queries analysis shows a clear correlation with the daily medical activity of GP in primary care, supporting that they are made at point of care.[23]

In *Antibioclic*, patients' interface and involvement are lacking. We plan to develop it through a collaboration with health authorities, in order to improve patient education regarding AMR and the shared decision making between patients and physicians.[5,22]

Finally, considering the international reach of AMR, and *Antibioclic'* interoperability, we believe that *Antibioclic* could be shared and adapted internationally. LMICs, where the rate of CPG development is low, data on ASP development and implementation are scarce, AMR is high and antibiotic consumption has been consistently increasing over the last 16-years could be prime targets for intervention.[3,31,32] In such settings, implementation and promotion of an adapted version of *Antibioclic* through multilateral collaboration, could be an inexpensive and easy way to avoid effort in *de novo* CPG development, and effectively support the implementation and adoption of integrated CDSS in primary care, at the point-of-care.[14,28,31–33]

In conclusion, *Antibioclic* was designed using a simple and systematic approach to convert CPG into CIG from the primary care physician perspective. *Antibioclic* allows a quick access to antibiotic prescribing recommendations for a large panel of primary care infectious diseases in accordance with up-to-date official CPGs. This study demonstrates that *Antibioclic* has been successfully implemented and adopted by French GPs with data supporting a sustainable use and a continuous increase of users. *Antibioclic* might have a positive impact on users' prescription, antibiotic consumption, AMR and patients' care. In an era where AMR is increasing while therapeutic innovation is rare, such systems should be promoted and developed in a global collaborative approach.

As compared with the results of the French Ministry of Health 2018 study on French medical physicians, *Antibioclic* users seemed younger, with a higher frequency of women, group practices, and involvement in training of residents.[6,24] Without good quality quantitative study, any observed difference between users and non-users could be linked to the CDSS, or to the users themselves. This also reinforce the need of a standardized framework for evidence-based reporting of CDSS analysis in primary care.[15]

Preliminary data from the 2019 cross-sectional study suggest that only 11% of surveyed GPs feel "deskilled", while 90% have the impression to improve their knowledge in antibiotic therapy. We are conducting a complementary qualitative analysis in order to further precise the place and role of *Antibioclic* within the medical consultation, its advantages and limitations from the GP's point of view, as well as their needs and expectations for future development. We will particularly consider common and potential unexpected consequences that are feared, such as the risk of "deskilling" physicians who use CDSS routinely, the risk of an automation bias or the risk of decreased interaction between the physician and the patient. A better understanding of how *Antibioclic* is being used will allow to gather valuable data to design and implement future systems and user interface, including systems using artificial intelligence.[30]

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- 2011: CMGF (communication); JNI (poster)
- 2014: CMGF (poster), RICAI (poster and communication)
- 2015: JNI (poster)
- 2016: CMGF (poster)
- 2018: CMGF (poster), JNI (poster) RICAI (poster)

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None to declare.

AUTHORS CONTRIBUTION

TD: Conceptualization, Funding Acquisition, Project administration, Data Curation, Formal analysis, Visualization, Original Draft Preparation

PJ: Conceptualization, Data Curation, Resources, Project administration, Funding Acquisition, Review and editing

SL: Conceptualization, Funding Acquisition, Project administration, Review and editing

JPA: Conceptualization, Funding Acquisition, Project administration, Software, Review and editing

NPS: Review and editing

PYB: Review and editing

EB: Conceptualization, Funding Acquisition, Project administration, Review and editing

FXL: Conceptualization, Funding Acquisition, Project administration, Review and editing

JLB: Conceptualization, Funding Acquisition, Project administration, Software, Supervision, Original Draft Preparation

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SUPPORTING INFORMATION

Year	2011[a]	2012	2013	2014	2015	2016	2017[a]	2018	2019
Date and time of request [b]	X	X			X	X	X	X	X
IP address [c]	X	X					X	X	X
Details of request according to TNM [d]	X	X					X	X	X

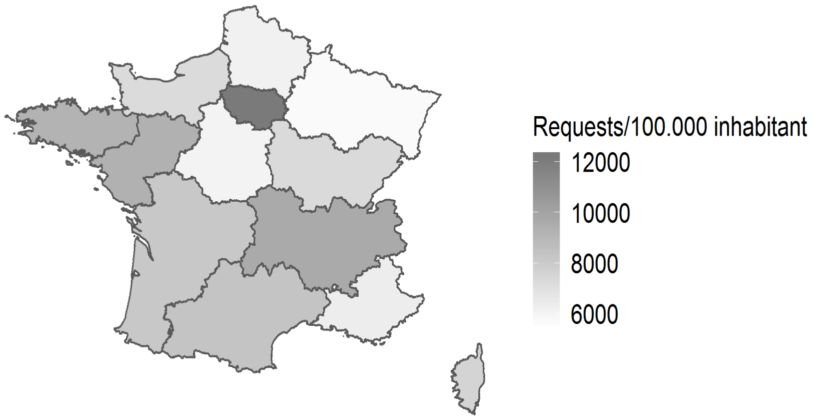
[a] *Collection process started in week 42 that year.*

[b] *Time is monitored in "hour,minute,second".*

[c] *Internet Protocol address – allow the geolocation of the request.*

[d] *The request details include the 3 systematic entry criteria and the 2 optional entry criteria.*

S1 appendix: Availability of data collected since 2011



For every administrative region of France, the number of queries per 100,000 inhabitants has been calculated and plotted on France map. The greyscale gradient corresponds to the level of use.

S2 Appendix: Number of queries per 100-000 inhabitants over French territory.