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Full Length Research Paper

Knowledge, perception and beliefs of human health workers and veterinarians on antimicrobial resistance in Ouagadougou, Burkina Faso

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Antimicrobial resistance (AMR) is a major public health problem in both hospital and community acquired infections. This study assessed knowledge, attitudes and perceptions on AMR among human health workers and veterinarians in Ouagadougou. A cross-sectional study using a self-administered questionnaire was applied among medical health and veterinary structures in Ouagadougou. on February 2020 to January 2021. A total of 34 question-items were self-administered. The collected data was analyzed using XLSTAT 2021.2 and Excel 2007. A total of 330 participants, 112 clinical health worker, 178 biologists and 40 veterinarians participated in the study. The overall response rate from participants was 92.7% (330/356). Overall, 198 (60.0%) of the participants had knowledge about AMR. more than 90.0% of participants agree that it is a public health problem for the world, Burkina Faso and our hospitals. The most important factors were self-prescription and self-medication (96.4%) and poor sensitization of prescribers (65.5%). The main perceived factors were the excessive and inappropriate use of antibiotics (92.7%). The most antimicrobial resistant bacteria according to participants were ESBL-PE with 70.9%. About potential interventions, the antibiotic use policy and training on prescription was considered with a frequency respectively 62.4 and 60.0%. This study made it possible to better understand the perceptions of human and animal health professionals on the problem of AMR. This information obtained on the knowledge of AMR can be useful for designing training plans and programs for controlling antibiotic resistance. More than half think of interventions as a good policy for the use of antimicrobial, training could reduce the dissemination of AMR.

Key words: Antimicrobial resistance (AMR), potential interventions, causes of AMR, Ouagadougou.

INTRODUCTION

All human and animal health professionals have an important role to play in maintaining the effectiveness of antibiotics (Dyar et al., 2017; Powell et al., 2017). The inappropriate and irrational use of antimicrobials, the availability of over-the-counter antibiotics and the lack of clinical microbiology laboratories for testing antimicrobial susceptibility, and the failure to follow infection control precautions are believed to be the major risk factors for antimicrobial resistance (AMR) (Vila and Pal, 2010). The recognition that the overuse of antibiotics causes antibiotic resistance has prompted calls for reform (WHO, 2014) because antimicrobial resistant bacteria have a negative impact on treatment such as increased morbidity, prolonged hospital stay and increased risk of mortality (Alabi and Sanusi, 2012). In addition, patients infected with the bacteria require more expensive treatment. Therefore, AMR has increasingly become a threat to patient safety in healthcare settings and leads to increased health care costs and burdens on families and societies (Alabi and Sanusi, 2012; Haeussermann et al., 2007). This is a difficult problem in low-income countries due to the high prevalence of infections (Kpoda et al., 2017). The development of AMR is accelerated by over-prescribing of antimicrobials (WHO, 2014). Every 10 min, almost two tons of antibiotics are used around the world, all too often with-out any prescription or control (Harbarth et al., 2015). The situation is more serious in developing countries due to the use of antibiotics without medical advice and inadequate regulation of antibiotics (Byarugaba, 2004). The containment of AMR requires changes in the antimicrobial prescribing behavior of health workers. To the best our knowledge, this is the first study undertaken to assess knowledge and perceptions of AMR among human and animal health professionals in Burkina Faso. The information generated in this study would help in the planning and implementation of AMR prevention and control interventions at national levels. Therefore, the emergence and transfer of AMR means that control solutions must be conducted from a "One Health" perspective (Collignon and McEwen, 2019). The aim of this study was to assess knowledge, attitudes and perceptions on AMR among human health workers and veterinarians in the city of Ouagadougou, in the public and private sectors. The aim of this study was to assess knowledge, attitudes and perceptions on AMR among human health workers and veterinarians in the city of Ouagadougou, in the public and private sectors. The objective of this study was to gain some understanding of this public health problem and to learn more about their perception about this problem. The information obtained

from this study could be useful in designing training plans and antibiotic resistance control programs.

MATERIALS AND METHODS

Study design

This was a cross-sectional study, based on a questionnaire, conducted among medical health and veterinary structures in Ouagadougou, Burkina Faso.

Study size

A sample size was determined using Kish, Leslie formula,

$$N = \frac{Z^2 p q}{d^2}$$

where N=minimum sample size for obtaining meaningful results, Z=confidence level (the typical value for the 95% confidence level is 1.96), p=proportion of a good knowledge of AMR, taking at 72.0% from study conducted in Addis Ababa, Ethiopia (Abera et al., 2014), q = (1-p) = (1- 0.72), d= the precision of the estimate expected which is 0.05. Therefore,

$$N = \frac{(1.96)^2 0.72(1-0.72)}{(0.05)^2}$$

N estimated was 310.

We took into consideration non-response rate of approximately 5% and rounded our sample size to 330. 356 participants based on the number of clinical health worker, biologists and veterinarians in each service were selected by simple random sampling using lottery technique. However, in service where the numbers of participants were less than ten, all participants were included.

Participants

The participants were human health workers and veterinarians from Ouagadougou. Human health workers included medical and care workers (physicians, nurses, midwives) and biologists. Biologists included microbiologists, pharmacists and laboratory technicians. The eligible personnel involved in the survey included doctors prescribing antibiotics, pharmacists involved in the sales and supply chain of antibiotics, biologists and technologists performing bacterial cultures and antibiograms, nurses and midwives and the veterinary personnel. Physicians from psychiatry, radiology, ophthalmology and anesthesiology were not included because they prescribe antimicrobial agents less often than other physicians. The eligible participants had to meet the following criteria:

1) be human or animal health worker in hospital or veterinarians office which fights against AMR.

- 2) give informed consent to participate in the study,
- 3) reside in Ouagadougou from February 2020 to January 2021.

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The letters of information were sent to all managers of hospital and Livestock National Laboratory. Information meetings were scheduled in each service included in the study. The study plan and procedure were explained to the participants. Those who gave their consent to participate received the questionnaire in paper version followed by an explanation of the questionnaire.

Setting and data collection instrument

Burkina Faso's largest city, Ouagadougou, has four university hospital centers (Yalgado Ouedraogo, Tengandogo, Bogodogo and Charles De Gaulle) all of which are in the fight against AMR resistance. In addition, there are two district hospitals (Boulmiougou and Nongremassom), three confessional hospitals (Paul VI, Schiphra and Saint Camille) and the livestock national laboratory. The six structures (Yalgado Ouedraogo, Tengandogo, Bogodogo, Charles De Gaulle, Paul VI, and Schiphra) were selected because they were involved in the fight against AMR (antibiotic purchase service, market control, microbiology laboratory service, clinical service prescribing antibiotics).

This study was conducted among medical heath and veterinary structures in Ouagadougou, Burkina Faso on February 2020 to January 2021. A questionnaire content was based on a previous survey described in an Indian study (Tennant et al., 2010), but modified for the purposes of our study. Before the data collection, the questions were tested at the local hospital to validate our modified questionnaire. Interviewees were given reasons why the information was collected and how it would be used, and a statement was read to them informing them that their participation was voluntary before the interview began and were assured that their responses are anonymous and confidential. Before the data collection, the questions were tested at the local hospital. A total of 8 sections and 34 items were self-administered to probe professional profiles, knowledge and attitudes about AMR. A selfadministered questionnaire was distributed in medical and veterinary structures. Questionnaires were distributed on site during working hours and participants were asked to respond immediately. Each participant was asked to complete all sections of the questionnaire. These sections deal with the socio-demographic characteristics, knowledge and attitudes of participants about antibiotic resistance. Section I of the questionnaire recorded the demographic characteristics of the participants, including their gender, age, position, specialty, number of years of experience, public or private service (7 questions). Section II also included 3 questions on participants' knowledge and assessment of the extent of the problem. Section III dealt with the causes of the problem and the participants gave 5 factors and he/she had to determine the importance of each factor in the problem. Section IV concerned the types of multidrug resistant bacteria (6 questions). Section V dealt with the prevalence situation of the main multidrug-resistant bacteria (3 questions). Section VII dealt with possible measures that can be applied to reduce the emergence of bacterial resistance. In addition to the closed questions, two other sections VI and VII were to choose from the participant's opinion on the local factors of resistance to antibiotics and the need of training for the participants; years of service, sources of information on AMR, training on AMR, exposure using results of antimicrobial susceptibility testing and working in public and private hospitals.

Statistical methods

For the knowledge assessment, each correct answer was given a score of "1" while a false or questionable answer was scored "0".

For both study participants, the mean knowledge scores <0.72 were considered to be below the expected level of knowledge, while the mean scores \geq 0.72 were at the expected level of knowledge. Scores from 0.15 to 0.88 were interpreted as negative beliefs, and scores ranging from 0.88 to 1 were considered as positive beliefs. The collected data were analyzed using XLSTAT 2021.2. Frequency analysis for different demographic data was presented towards work place, gender, and training on AMR. Categorical data were expressed as frequencies and percentages. To compare those who believe on potential interventions and those who do not believe, we used a Chi-square and P = 0.05 was considered statistically significant. Findings were presented as numbers and percentages in the form of tables and bar-charts. Categorical data were expressed as frequencies and percentages, while numerical data were expressed as means and standard deviations. The confidence interval was calculated to prove that the chosen sample is representative. The smaller the confidence interval, the closer the results will be to reality.

Ethical consideration

The study was approved by the director of Medical Biology laboratories, Health Ministry (Authorization No. MS/SG/DGAP/DLBM/ 2020-01, January 27, 2020). Written informed consent was obtained from all subjects participants before enrollment. Participants were enrolled voluntarily. The confidentiality of the obtained information from the subjects was respected.

RESULTS

Participant profiles and sources of information on AMR

A total of 330 participants took part in this study, 112 (33.9%; 95% CI=29.0 - 39.2) clinical health worker, 178 (53.9%; 95% CI=48.5 - 59.2) biologists and 40 (12.1%; 95% CI=9.0 – 16.1) veterinarians. Among the participants, there were 138 women and 192 men. The mean age of participants was $33(\pm 8)$. Other demographic and practice characteristics are listed in Table 1. The overall response rate from participants was 92.7%; 95% CI=89.4 - 95.0. All participants studying in the private hospital completed the questionnaires (response rate 100%). The overall mean year of service was 5.74 (SD ± 7.19). Participants were asked to identify their sources of information on AMR. Overall, 75.5% of respondents obtained information from university courses and training, 44.8% from the internet, 33.9% from books, 21.9% from scientific magazines and 17.6% from the media. Regarding the training followed, 56.4% of the participants replied that they had not undergone any specific training on AMR.

Knowledge of AMR

The awareness of AMR as a global and national problem

Table 1. Distribution of participants, according to profile, work place, gender, training followed on AMR and the source of obtaining information on AMR included in this study to February 2020 -January 2021 (N=330).

Variable	Clinical health worker (N=112)	Biologists (N=178)	Veterinarians (N=40)	Total (N=330) N (%)	
Variable	N (%)	N (%)	N (%)		
Work place					
Public	52 (46.4)	130 (73.0)	30 (75.0)	212 (64.0)	
Private	60 (53.6)	48 (27.0)	10 (25.0)	118 (35.8)	
Gender					
Male	64 (57.1)	98 (55.1)	30 (75.0)	192 (58.2)	
Female	48 (42.9)	80 (44.9)	10 (25.0)	138 (41.8)	
Training on AMR	30 (26.8)	84 (47.2)	30 (75.0)	144 (43.6)	
Source of information					
Books	38 (33.9)	52 (29.2)	22 (55.0)	112 (33.9)	
Internet	42 (37.5)	82 (46.1)	24 (60.0)	148 (44.8)	
Journals	18 (16.1)	40 (22.5)	12 (30.0)	70 (21.9)	
School course and training	81 (72.3)	142 (79.5)	26 (65.0)	249 (75.5)	
Media	14 (12.5)	36 (20.2)	8 (20.0)	58 (17.6)	

N: Number.

was high among the participants. The overall mean knowledge score was 0.60 (SD \pm 0.40). Thus, 198 (60.0%) of the participants were at the level of knowledge about AMR. Overall, the majority of participants knew that AMR is a global health problem for our country and hospitals with, respectively 91.5%; 95% Cl=88.0 – 94.1; 90.3%; 95% Cl=86.6 – 93.0 and 90.9%; 95% Cl=87.3 – 93.6 of correct answers. Participants' knowledge about the magnitude of the AMR problem at local, national and global levels is presented in Table 2.

Knowledge of the causes and prevalence of AMR

According to respondents, the main perceived causes contributing to the development of AMR were: the excessive and inappropriate use of antibiotics (92.7%; 95% CI: 89.4 – 95.1 by respondents), the bacterial mutations (83%; 95% CI: 78.6 – 86.7) and the lack of regulation for the acquisition of antibiotics (64.8%; 95% CI: 59.6 – 69.8) (Table 3). In addition, the assessment of knowledge on local factors in the spread of AMR was also supplemented by an open question. The most important local factors identified were as follows: 96.4% of responses for self-prescription and self-medication of patients, poor sensitization of prescribers was answered by 43.6%. Participants were asked to identify multi-antibiotic resistant bacteria in our hospitals

and globally by open question. Extended-spectrum betalactamase-producing Enterobacteriaceae (E-ESBL) was reported as 70.9%, Methicillin-resistant *Staphylococcus aureus* (MRSA) was reported as 67.3%. Multidrugresistant *Pseudomonas aeruginosa* 60.6% was listed. Multidrug-resistant *Acinetobacter baumannii* and carbapenemase-producing enterobacteria was evaluated as 45.5 and 41.2%, respectively (Table 3).

Beliefs about potential interventions for AMR

Establishing hospital infection control committees and establishing national AMR surveillance were not important for 61.8 and 60.6% of respondents, respectively. In addition, the most frequently considered interventions were the antibiotic use policy (62.4%) and the training of prescribers on AMR (60.0%) (Table 4).

DISCUSSION

Medical and paramedical staff, microbiologists and veterinarians are key players in the prevention and control of AMR through the judicious prescription of antimicrobials, the control of the transmission of antibiotic resistant bacteria and awareness raising. Thus, this study demonstrated the knowledge and perception of these professionals on AMR in Ouagadougou. In this study, the

Variable		Agree (%)	Desagree (%)	Don't know (%)
	Clinical health worker	87.5	5.4	7.1
	Biologists	92.1	4.5	3.4
AMR is worldwide problem	Veterinarians	100.0	0.0	0.0
	Total	91.5	4.2	4.2
	Clinical health worker	91.1	7.1	1.8
AMD is problem in Durking Face	Biologists	88.8	5.6	5.6
AMR is problem in Burkina Faso	Veterinarians	95.0	0.0	5.0
	Total	90.3	5.5	4.2
	Clinical health worker	92.9	3.6	3.6
	Biologists	88.8	1.1	9.0
AMR is a problem in your hospital	Veterinarians	95.0	0.0	5.0
	Total	90.9	2.4	6.7

Table 2. Percentage of human health workers' and veterinarians' rating the scope of AMR problem during February 2020january 2021 in hospital and veterinarians service in Ouagadougou, Burkina Faso.

Table 3. Human heath workers' and veterinarians' knowledge about the causes of antibiotic resistances, type of antibiotic resistant bacteria and local factors for development of AMR (N=330).

Variable	Clinical health worker (N=112) YES, N (%)	Biologists (N=178) YES, N (%)	Veterinarians (N=40) YES, N (%)	Total (N=330) YES, N (%)	95%CI
Causes of AMR					
Bacterial mutations cause of AMR	96 (85.7)	152 (85.4)	26 (65.0)	274 (83.0)	78.6-86.7
Unfavorable socio-demographic conditions	36 (32.1)	60 (33.7)	8 (20.0)	104 (35.1)	26.7-36.7
Excessive and inappropriate use of antibiotics	100 (89.3)	166 (93.3)	40 (100.0)	306 (92.7)	89.4-95.1
Absence of regulations for the acquisition of antibiotics	74 (66.1)	122 (68.5)	18 (45.0)	214 (64.8)	59.6-69.8
The variety and poor quality of antibiotics	72 (64.3)	90 (50.6)	14 (35.0)	176 (53.3)	47.9-58.6
Examples of antibiotic resistant bacteria					
ESBL-PE	84 (75.0)	116 (65.2)	34 (85.0)	234 (70.9)	65.8-75.5
CPE	40 (35.7)	84 (47.2)	12 (30.0)	136 (41.2)	36.0-46.6
MRSA	64 (57.1)	134 (75.3)	24 (60.0)	222 (67.3)	62.0-72.1
VRE	74 (66.1)	94 (52.8)	14 (35.0)	182 (55.2)	49.8-60.4
MDR P. aeruginosa	68 (60.7)	116 (65.2)	16 (40.0)	200 (60.6)	55.2-65.7
MDR A. baumannii	46 (41.1)	90 (50.6)	14 (35.0)	150 (45.5)	40.2-50.8
PDSP	46 (41.1)	40 (22.5)	8 (20.0)	94 (28.5)	23.9-33.6
Local factors for development of AMR					
Self-prescription and self-medication of patients	112 (100.0)	166 (93.3)	40 (100.0)	318 (96.4)	93.8-97.9
Inaccessibility of antibiogram data	58 (51.8)	66 (37.1)	20 (50.0)	144 (43.6)	38.4-49.0
Poor sensitization of prescribers	68 (60.7)	120 (67.4)	28 (70.0)	216 (65.5)	60.2-70.4

95% CI: Confidence interval of the frequencies of global knowledge of the causes of AMR; type of antibiotics resistant bacteria and local factors of AMR; MDR: multidrug resistant; PDSP: Pneumococci of decreased sensitivity to penicillin; MRSA: Methicilin resistant *Staphylococcus aureus;* CPE: Carbapenemase producers enterobacteria; VRE: Vancomycin resistant enterococcus; ESBL-PE: extended spectrum β-lactamase producing Enterbacteriacae.

Potential intervention	Useful [N (%)]	Not useful [N (%)]	p-value
Antimicrobial usage policy	206 (62.4)	124 (37.6)	<0.0001*
Reduction of antibiotic use for outpatient setting	138 (41.8)	192 (58.2)	<0.0001
Establish national AMR surveillance	130 (39.4)	200 (60.6)	<0.0001
Establish hospital infection control committee	126 (38.2)	204 (61.8)	<0.0001
Develop institutional guideline for antimicrobial use	164 (49.7)	166 (50.3)	0.939
Education on antimicrobial therapy for prescribers	198 (60.0)	132 (40.0)	0.015*
Establish microbiology diagnostic services	172 (52.1)	158 (47.9)	0.316

Table 4. Human heath workers' and veterinarians' beliefs on potential intervention to fight against AMR in Ouagadougou, Burkina Faso (N=330).

N: Number, Chi-square (comparison between those who believe in these potential interventions to fight AMR and those who do not believe in these interventions). *Statistically significant (p<0.05).

response rate was 92.7%, only 7.3% did not respond by completing the questionnaire. This strong participation can be explained by the fact that the fight against AMR is a topical subject and which has been communicated in health facilities (Suaifan et al., 2012). This awareness will allow a coordinated action, according to one health approach to reduce the emergence and the spread of multiresistant bacteria. In addition to this, men were more represented with 192/330, and the average age was 33 years. Indeed, civil servants are younger due to the minimum recruitment age which is 18 and 60 for retirement. According to the sources of information, 75.5% of the respondents learned about AMR through university courses and continuing education, less than 50% through the internet, scientific books and journals. This testifies to an insufficiency of workers in the search for scientific information, and also a lack of knowledge of bibliographic research. Therefore, clinicians, biologists, and veterinarians need structured training on AMR, as 56.4% did not receive specific training on AMR.

Regarding awareness of the magnitude of the AMR problem, the majority (more than 90%) of respondents agreed with antimicrobial resistance as a global, national and local public health problem. Indeed, 60% had a level knowledge about AMR. Indeed, the country has developed a national multispectral action plan 2017-2020 which explains the problem of AMR by including human, animal and environmental health. In this plan, a global analysis was carried out involving the actors of microbiology, care, pharmacy and veterinary (PAN, 2017). In addition, an awareness day is organized each year which brings together civil society, animal and human health professionals in order to raise awareness of the issues, causes, consequences and impact of AMR. In this study, the knowledge score was low, compared to 0.72%. These results differed from those of Wester et al. (2002) in which 87% of respondents agreed that AMR was a countrywide problem, but only 55% believed that their own hospital faced the problem.

In this survey, the top three causes of AMR were the excessive and inappropriate use of antibiotics (92.7% of respondents), the bacterial mutations (83%) and the lack of regulation for the acquisition of antibiotics (64.8%). These observations were made by Ouedraogo et al. (2017) which showed that these factors favored the emergence of multidrug resistance in West Africa. In our context, the access to antibiotics is uncontrolled, which explains the purchase of antibiotics without a prescription, taking antibiotics without medical advice. These practices increase self-medication, hence overuse which creates selection pressure in humans, animals and even the environment (Faizullah et al., 2017). Likewise, a study in Scotland, France and Spain indicated that too many prescriptions of antibiotics, too many broadspectrum antibiotics and inappropriate duration of antibiotic treatments were the main factors (Pulcini et al., 2010; Francisco et al., 2013). This study found that the most important local factors for the spread and development of AMR were the self-prescription and the self-medication according to 96.4% of the respondents. This result is similar to other studies that have shown that self-medication is a contributing factor to AMR (Kheder, 2013). The clinical and veterinary staff know better the extended beta-lactamase spectrum producina Enterobacteriacae (ESBL-PE) prevalence which is more than 50%, because the results of antibiograms reach them with the ESBL-PE mention and also the infections caused by the ESBL-PE is frequent and has therapeutic difficulties (Ouedraogo et al., 2016). Indeed, the more we use these drugs, the more we increase the speed of emergence and selection of resistant bacteria. In human use, around 80% of antibiotic consumption takes place in the community and at least half of this is considered based on incorrect indications, mostly viral infections (Harbarth et al., 2015). In addition, the lack of access to antibiotic susceptibility testing and the lack of prescriber awareness of AMR were mentioned as local factors. The wide spread use and inappropriate use were believed to

be the important general causes of resistance by about 92.7% of the respondents. In fact the use of antimicrobial agents, by itself, is considered to exert a selective pressure on resistance (Cars and Nordberg, 2005). The majority had mentioned the existence of bacteria resistant to antibiotics such as ESBL-PE (70.9%), MRSA (67.3%), And MDR *P. aeruginosa* (60.6%). These are superior to physicians' knowledge of multidrug bacteria documented in India (Tennant et al., 2010). The best known prevalence of ESBL-PE (70.9%), MRSA (67.5%), and *P. aeruginosa* (60.6%), would be explained by the fact that these bacteria are the most common in our hospitals and commonly isolated in microbiology laboratories.

Regarding potential interventions to fight against AMR, the majority of participants believed that the most appreciated actions were the antimicrobial usage policy, the education on antimicrobial therapy for prescribers and establishment of microbiology diagnostic services (Table 4). 62.4 and 60.0% of those questioned were respectively in favor of an antimicrobial usage policy and education on antimicrobial therapy for prescribers on an outpatient basis. Indeed 62.4% of respondents believed that the policy on rational use of antibiotics and 60% believe that training and good awareness could reduce the spread of resistance. These two interventions are among the objectives of the World Health Organization (WHO, 2014) on the fight against AMR and the action plan emphasizes these interventions in order to reduce the creation of other resistance and the spread. This finding is in agreement with a previous report on the beliefs of American physicians (Wester et al., 2002). However, our finding is different from Kheder et al. (2013) and Franscisco et al. (2013) who found that establishing local antimicrobial susceptibility testing and providing education on antimicrobial stewardship for healthcare professionals were identified as the most important interventions.

Limitations of the study

This study has certain limitations. First, as with most surveys, it is possible that respondents give socially desirable answers, rather than their true opinions or practices.

This could have an influence on the perceptions of the participants. Secondly, the results of this study could not be generalized or extrapolated without further research, as it focused only on the city of Ouagadougou. Indeed, some researchers have shown that respondents to questionnaire studies tend to underestimate the real situation, so our results could be inferior to reality. Recall bias was possible because the period of time in question was one full year and it was conducted in one city of our country.

Conclusion

Clinicians, biologists and veterinarians had knowledge on the causes, types of multidrug resistant Bacteria. In addition, self-medication and self-prescription are the local factors retained by the respondents. The majority agree that AMR is a health problem for the world, the country and the hospitals. More than half of the respondents think that intervention is a good policy for the use of antimicrobials and training of prescribers could reduce the dissemination of AMR. This study suggests that, to prevent the development of antibiotic resistance, we should further promote educational activities about antimicrobial therapy and create innovative strategies to attract physicians' attention to campaigns about AMR prevention. AMR is an epidemic that should be fought by everyone, the healthcare worker, biologists, veterinarians, the patients and the regulators. The adoption of appropriate educational interventions and strategies is the key that can unlock the initial step to curb the alarming increase in resistance.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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