Impact of Educational Intervention to Promote Jordanian Community Pharmacists’ Knowledge and Perception Towards Antimicrobial Stewardship: Pre-Post Interventional Study

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Objective: The aim of this study was to assess the impact of an online educational workshop on improving the knowledge, and perception of community pharmacists in Jordan towards the antimicrobial stewardship (AMS) and enhancing their ability to appropriately select correct antibiotic therapy.

Methods: This is a pre-post study that was conducted in Jordan in December 2020. An electronic questionnaire was used to assess the awareness, perception of community pharmacists towards AMS, and their ability to appropriately select correct antibiotic before and after the educational workshop. The two-days’ workshop was conducted on Zoom application. Analysis was conducted using Wilcoxon signed-rank test, McNemar’s test using SPSS version 22.

Results: During the study period, 100 community pharmacists attended the educational workshop. Pharmacists’ knowledge was assessed prior to their participation which revealed a relatively good knowledge score with a median score of 6/10 (IQR = 4); their scores have improved significantly following the educational workshop with a median score of 7/10 (IQR = 2), p-value<0.001. Although one-third of the participants knew the definition of AMS prior to the workshop, almost half of the respondents (n = 56, 56%) knew the definition after the educational workshop. Regarding community pharmacist’s ability to appropriately select correct antibiotic therapy, they showed a significant improvement in selecting the optimal antimicrobial for the virtual cases following the workshop (p-value < 0.05). Perceptions towards AMS were consistently positive before and after the workshop.

Conclusion: This study revealed the benefit of AMS-focused workshops for improving community pharmacists’ knowledge and appropriate antibiotic prescribing. Thus, efforts are required to implement more AMS educational workshops for community pharmacists.

Keywords: stewardship program, antimicrobial resistance, community pharmacist, workshop, knowledge, perception

Introduction
During the 21st century, antimicrobial resistance has become the biggest threat to public healthcare worldwide.1 Infections caused by resistant bacteria have led to increased mortality and morbidity rate, hospital stay, and costs on healthcare facilities.2,3 In 2013 the Center for Disease Control and Prevention (CDC) estimated that about 2 million people had been seriously infected with resistant bacteria...
in the United States, and about 23,000 individuals had died directly because of infections caused by resistant bacteria.\textsuperscript{1}

Antibiotic resistance occurs when the antibiotic loses its ability to inhibit bacterial growth.\textsuperscript{1} In this setting, bacteria are able to continue multiplying and cause further damage, despite therapeutic levels of antibiotics.\textsuperscript{4} Recently, researchers have found that there is a strong relationship between the irrational use of antimicrobial drugs and the emergence of bacterial resistance,\textsuperscript{5,6} especially in developing countries, due to the ease in antimicrobial accessibility and their frequent use.\textsuperscript{7} Thus, improving antimicrobial prescribing patterns has become an important issue for many healthcare sectors.\textsuperscript{8}

One of the critical interventions that can effectively control antimicrobial use and decrease antimicrobial resistance is the implementation of Antimicrobial Stewardship (AMS). Antimicrobial Stewardship as a term indicates that antimicrobial agents must be used wisely and responsibly, which includes developing actions that create a balance between appropriate patient therapy and sustained society access.\textsuperscript{9,10} Stewardship programs are divided into two sets of interventions, the first set is related to patient care and recommendation, such as following the guidelines for the management of infectious diseases. The second set is related to strategies that restrict over-the-counter use of antimicrobial agents and improve healthcare providers’ knowledge of and perception towards antimicrobial use.\textsuperscript{10}

In Jordan, community pharmacists are among the most accessible healthcare providers within the healthcare system with the ability to dispense antibiotics.\textsuperscript{11} Unfortunately, they are one of the most significant contributors to antimicrobial resistance, through dispensing antibiotics over-the-counter, which is illegal in many other countries.\textsuperscript{11} Therefore, it is essential to educate community pharmacists about AMS to combat the increasing rates of antimicrobial resistance.\textsuperscript{12,13} Educational programs can be put in place via conferences, workshops, and regular lectures/webinars for the healthcare sectors.\textsuperscript{14}

The literature is till now limited with respect to interventional studies to improve community pharmacists’ knowledge and perception towards AMS in Jordan. Therefore, this study aimed to assess the impact of an online educational workshop on improving the knowledge, and perception of community pharmacists towards the AMS and in enhancing their ability to appropriately select correct antibiotic therapy.

**Methods**

**Study Design and Study Participants**

This is a pre-post study conducted in December 2020 to evaluate the impact of implementing an educational workshop on enhancing community pharmacists’ awareness and perception about AMS and in improving their ability to appropriately select correct antibiotic therapy. Pharmacists engaged in the study met the following requirements: 1) registered licensed pharmacists, 2) currently working in community pharmacies, and 3) willing to participate in the study.

**Questionnaire Development**

The study questionnaire was developed following a comprehensive literature review,\textsuperscript{15–17} and consisted of several multiple choice questions. Experts in the field (three PhD holders in clinical pharmacy) had reviewed the questionnaire for structure and content validity to assess the clarity, understandability, and organization of the constructed questionnaire. They were asked to provide their feedback, and the amendment was done accordingly. Also, the final draft of the survey was pilot tested on a group of pharmacists to assure the clarity and comprehensibility of the questions, and the response from these pharmacists were excluded from the final analysis. It was estimated that filling-out the survey would take approximately 10 minutes before and 10 minutes after the workshop. A Cronbach’s alpha test was used to test its internal reliability, which yielded a 0.878, thus the current scale has reliable and has an acceptable internal consistency.

The questionnaire was designed in English language and it was divided into four sections. The first section was dedicated to respondents’ socio-demographic characteristics, which involve information about pharmacist’s gender, age, educational level, experience, and the type of pharmacy where they worked. The second section was about evaluating community pharmacy knowledge about antimicrobial resistance and AMS. The third section evaluated pharmacists’ perception towards AMS, the responses on this section were on a 5-points Likert scale (5: strongly agree, 4: agree, 3: neutral, 2: disagree, and 1: strongly disagree). Finally, the last section assessed pharmacists’ ability to appropriately select correct antibiotic therapy for four community pharmacy virtual cases.

For knowledge questions, participants gained one point for each correct answer and zero point for each incorrect answer. Then, the total knowledge score ranged from 0 to
10. A similar scoring were applied for the evaluation for the virtual cases, where participants gained one point for each correct selection of antimicrobial, and zero point for each incorrect selection.

Data Collection
Community pharmacists working in different areas in Jordan were invited to attend a two-day educational workshop using an advertisement posted on social media platforms (Facebook groups for pharmacists). Pharmacists who agreed to take part in the study were directed to a closed group created for the purpose of this study on a social media platform (WhatsApp) to further arrange for their participation.

Prior to the beginning of the first workshop session, pharmacists were requested to fill the pre-workshop online questionnaire, which was distributed to them through the closed group; they were allowed 20 minutes to complete the form, after that the link get deactivated. The same questionnaire was provided to the same cohort of subjects following the second workshop session to assess the impact of the education workshop on improving their knowledge, perception about AMS and enhancing their ability to appropriately select correct antibiotic therapy.

Educational Workshop
The educational workshop was conducted over two sessions on two consecutive days, Friday the 25th of Dec-2020 and Saturday the 26th of Dec-2020. The sessions were conducted using the Zoom virtual platform. Each session was an hour and a half long, through which PowerPoint presentations, videos, and clinical case scenarios were given.

The workshop material was guided by the World Health Organization (WHO) antimicrobial stewardship online course modules. The material was prepared by the authors, assessed and presented by two clinical pharmacists experts in the field with more than ten years of experience in the field of infectious diseases. Four lectures were prepared to cover the theoretical aspects related to 1) the basic concept of antibiotics, and principles of therapy, 2) antimicrobial resistance, 3) AMS, and 4) pharmacists’ role in stewardship programs.

A booklet containing some of the infection guidelines such as respiratory infections, skin infections, urinary tract infections was provided to the pharmacists through the closed group and was discussed through the first session of the workshop. The closed WhatsApp group was also used to share information about different smartphone applications that would help the pharmacist in their daily practice.

Ethical Consideration
The study protocol was submitted to obtain approval by the Ethics Committee at the Faculty of Pharmacy at Applied Science Private University (Approval No. 2020-PHA-20). The study was conducted following the ethical standards outlined in the World Medical Association Declaration of Helsinki guideline. Pharmacists were requested to approve an electronic informed consent, and they were informed that their participation in the study is voluntary, and they had the right to defer from submitting their filled forms at any time. Also, they were assured that their responses would be kept confidential and anonymous.

Statistical Analysis
Data was analyzed using statistical package for social science (SPSS) version 22 (SPSS Inc., Chicago, IL, USA). The descriptive analysis was done using mean and standard deviation (SD) for continuous variables and percentages for qualitative variables. Checking for normality was carried out using the Shapiro–Wilk test (with P-value > 0.05 indicating a normally distributed continuous variable). Wilcoxon sign rank test was used to evaluate pre-post changes in continuous variables, while McNemar’s test was used to evaluate differences in categorical variables between pre-workshop and post-workshop data. Cronbach’s α was used to evaluate the reliability of the questionnaire, with values ≥ 0.7 indicates acceptable internal consistency (19). For all statistical analyses, a P-value of ≤ 0.05 was considered statistically significant, and all tests were two-tailed.

Results
Community Pharmacists
Socio-Demographics
Overall, 269 community pharmacists participated in the first workshop session; among them, only 100 completed the second session and filled out the questionnaire post the workshop (completion rate of 37.8%). The mean age of the study participants was 30.9 years (SD= 8.8), with the majority being females (n= 85, 85.0%), and having a bachelor’s degree in BPharm or PharmD (n= 93, 93.0%). Pharmacists have an average of 5.8 years (SD= 6.3) of community experience, and around three-quarters
of them are working in independent community pharmacies (n = 76, 76.0%), while the remaining 24.0% (n = 24) are working at chain independent pharmacies. Almost 43.0% of the community pharmacists (n = 43) reported attending prior workshop regarding AMS. The sociodemographic characteristics are shown in detail in Table 1.

### Table 1 Demographic Characteristics of the Study Sample (N= 100)

| Parameter                      | Median (IQR) | n (%) |
|-------------------------------|--------------|-------|
| Age (years)                   | 30.9 (11)    |       |
| Gender                        |              |       |
| • Female                      | 15 (15.0)    | 15 (15.0) |
| • Male                        | 85 (85.0)    | 85 (85.0) |
| Educational level             |              |       |
| • Bpharm/pharmD               | 93 (93.0)    | 93 (93.0) |
| • MS.C                        | 4 (4.0)      | 4 (4.0) |
| • PhD                         | 3 (3.0)      | 3 (3.0) |
| Community practice experience | 5.8 (6.3)    | 5.8 (6.3) |
| Site of work                  |              |       |
| • Independent community pharmacy | 76 (76.0)   | 76 (76.0) |
| • Chain community pharmacy    | 24 (24.0)    | 24 (24.0) |
| Place of residence            |              |       |
| • Amman                       | 43 (43.0)    | 43 (43.0) |
| • Other                       | 57 (57.0)    | 57 (57.0) |
| Have you ever attended a course/workshop about Antimicrobial Stewardship programs? | | |
| • Yes                         | 43 (43.0)    | 43 (43.0) |
| • No                          | 57 (57.0)    | 57 (57.0) |

### Awareness About Antimicrobial Stewardship

Pharmacists were asked about their main source of knowledge about antibiotics and antibiotic use (Figure 1). Results showed that clinical textbooks (n = 88, 88.0%), clinical guidelines (n = 87, 87.0%), and university lectures (n = 86, 86.0%) were the most used sources by the pharmacists. Pharmacists stated that their source was practice, such as personal clinical experience (n = 82, 82.0%) and other pharmacist colleagues (n = 78, 78.0%). At the same time, half of the participants used websites or social media as a source of information, such as PubMed (n = 59, 59.0%), Wikipedia (the medical encyclopedia) (n = 58, 58.0%), and social media (n = 49, 49.0%).

All the participating pharmacists responded to 10 statements regarding antimicrobial resistance and antimicrobial stewardship programs before and after the workshop, and the results are presented in Table 2. Following an education workshop, some improvement of pharmacists’ knowledge was noted. In comparison to 59.0% of the respondent (n=59) knew that the statement “broad-spectrum antibiotic should always be used in place of narrow-spectrum to reduce microbial resistance” is an incorrect statement, this percentage was improved significantly to 81.0% (n= 81) after the workshop (P-value <0.001). Moreover, 60.0% of the respondent (n= 60) believed that the efficacy of the more expensive antibiotic

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![Figure 1](https://doi.org/10.2147/IDR.S324865)

**Figure 1** Community pharmacist’s main source of knowledge about antimicrobial and antimicrobial use during their practice (n= 100).
is not associated with better effectiveness and lower resistance, compared to 92.0% (n= 92) following the workshop (P-value <0.001). In addition, participants’ knowledge regarding antimicrobial stewardship was improved, where 32.0% of the respondents (n= 32) realize that the stewardship program would not increase the treatment duration to ensure therapeutic efficacy compared with a significantly higher percentage following the workshop (n= 56, 56.0%) (P-value <0.001). Finally, pharmacists showed an enhancement in their awareness that antimicrobial stewardship is a process that involves the appropriate duration of antibiotic therapy, where the percentage improved from 76.0% (n= 76) pre the workshop to 89.0% (n= 89) following the workshop (P-value = 0.019).

For the overall knowledge score (out of 10), the overall median knowledge score was improved from 6 (IQR= 4) pre the workshop to a median of 7 (IQR= 2) post the workshop (P-value <0.001). For more details, refer to Table 2.

### Table 2 Community Pharmacists’ Knowledge About Antimicrobial Resistance and Antimicrobial Stewardship (N= 100)

| Statements | Correct n (%) Pre-Workshop | Correct n (%) Post-Workshop | P value* |
|------------|----------------------------|----------------------------|----------|
| Broad-spectrum antibiotics should always be used in place of narrow-spectrum antibiotics to reduce resistance* | 59 (59.0) | 81 (81.0) | < 0.001* |
| The efficacy of the more expensive antibiotic is associated with better efficacy and lower resistance* | 60 (60.0) | 82 (82.0) | < 0.001* |
| If symptoms improve before the full course of antimicrobial is completed, your patient can stop taking it* | 89 (89.0) | 92 (92.0) | 0.508 |
| Antibiotic with resistance problem can become sensitive over time* | 45 (45.0) | 54 (54.0) | 0.175 |
| It is always better to under-prescribe antibiotics than over-prescribe* | 19 (19.0) | 22 (22.0) | 0.711 |
| Antimicrobial stewardship is a program that increases the treatment duration to ensure therapeutic efficacy* | 32 (32.0) | 56 (56.0) | <0.001* |
| Antimicrobial stewardship is a study of antibiotics* | 72 (72.0) | 74 (74.0) | 0.851 |
| Antimicrobial stewardship is a process that involves a suitable antibiotics dosing and route of administration* | 79 (79.0) | 88 (88.0) | 0.108 |
| Antimicrobial stewardship is a process that involves the appropriate duration of antibiotics therapy* | 76 (76.0) | 89 (89.0) | 0.019* |
| The role of antimicrobial stewardship is to encourage over the counter prescription of antibiotics agents* | 53 (53.0) | 61 (61.0) | 0.243 |
| Knowledge score (out of 10), median (IQR) | 6 (4) | 7 (2) | < 0.001*, $ |

Notes: *False, $true, *McNemar’s test, *using Wilcoxon signed-rank test, *significant at 0.05 significant level.

Pharmacists Ability to Appropriately Select Correct Antibiotic Therapy for Virtual Community Pharmacy Cases

All participants were asked to determine the preferred empiric treatment for four virtual community pharmacy cases (Figure 2). Regarding the urinary tract infection (UTI), pharmacists showed a significant improvement in their ability to appropriately select correct antibiotic therapy Nitrofurantoin (from 63.0% (n= 63) pre-workshop to 72.0% (n= 72) post the workshop (P-value = 0.049)). A similar finding was found for viral conjunctivitis, where only 56% of the pharmacists (n= 56) recognized that the patient does not need to start an antimicrobial agent. This percentage was significantly improved to 65.0% (n= 65) following the workshop (P-value = 0.049). Regarding the other two cases (tooth infection and cellulitis infection), no significant improvements were detected in pharmacists’ responses following workshop attendance (P-values >0.05 for both).
Perception Regarding the Importance of Antimicrobial Stewardship Program

Seven statements were used to assess pharmacists’ perception towards the antimicrobial stewardship program; most of the respondents showed a strong positive perception of antimicrobial stewardship programs before and after the workshop with no significant changes in their responses after the workshop (P>0.05 for all statements). Regarding community pharmacist responsibility in antimicrobial stewardship, 91.0% of them (n= 91) believed that they should take a prominent role in antimicrobial stewardship and infection prevention. This percentage increased to 97.0% (n= 97) after the workshop. Moreover, 91.0% of the respondent (n= 91) agreed/strongly agreed that community pharmacists should have sufficient education on AMS, and this percentage was increased to 93.0% (n= 93) after the workshop, which demonstrates community pharmacist’s awareness of the importance of stewardship program. For more details, refer to Table 3.

Satisfaction with the Training Workshop

All participants responded to eight statements with the aim of evaluating their satisfaction with the training workshop. They all agreed that the workshop helped them learn (n= 97, 97.0%) and understand the antimicrobial resistance (n= 95, 95.0%); participants also reported that the workshop improved their understanding of the concept of antimicrobial stewardship (n= 94, 94.0%). Most respondents strongly agreed/agreed that the educational workshop helped them understand the importance of stewardship programs (n= 96, 96.0%) and will be reflected in their daily practice (n= 93, 93.0%). For more details, refer to Table 4.

Discussion

The mortality and morbidity rates for infectious and communicable diseases increase proportionally in many countries. The level of antimicrobial resistance increased due to overprescribing, unlimited accessibility, and frequent antimicrobials prescriptions. Thus, several studies were conducted to better educate healthcare providers about AMS and increase their awareness about their responsibilities to follow the guidelines for antimicrobial stewardship in practice.

Out of 269 community pharmacists, 100 attended the two sessions of the workshop (completion rate of 37.8%). The reason for decreasing in attendance number can be explained by the country situation at that time; the first day of the workshop took place during the lockdown of the whole sectors because of COVID-19, while the second day of the workshop was held on a working day for pharmacists.

This study was conducted to assess the impact of conducting educational training on improving the awareness, knowledge, and perception of Jordanian community pharmacists towards antimicrobial stewardship. Up
to our knowledge, this study was the first study that evaluates these aspects regarding community pharmacists in Jordan. This study showed a significant positive improvement in the community pharmacist’s knowledge and perception. It revealed some improvement in their ability to appropriately select correct antibiotic therapy for virtual community pharmacy cases following the educational intervention (P-value <0.05), indicating that this educational workshop was useful and efficient to teach about AMS. Numerous previous studies elucidated the improvement in healthcare provider’s knowledge after conducting educational intervention.\textsuperscript{17,24–27}

This study showed that only one-third of community pharmacists were familiar with the definition of AMS before the educational intervention, indicating the poor awareness of pharmacists with AMS. Similar findings were reported in studies conducted in Egypt,\textsuperscript{17} and Ethiopia,\textsuperscript{28} which showed that less than half of the healthcare professionals were familiar with the term AMS. However, other studies reported higher awareness rates,

Table 3 Perception of Community Pharmacists Towards Antimicrobial Resistance and the Importance of Antimicrobial Stewardship Programs (\textit{N}= 100)

| Statements                                                                 | Pre-Workshop | Post-Workshop | P value* |
|---------------------------------------------------------------------------|--------------|---------------|----------|
| Strongly Agree/Agree n (%)                                                |              |               |          |
| Community pharmacists have a responsibility to take a prominent role in  | 91 (91.0%)   | 97 (97.0%)    | 0.109    |
| antimicrobial stewardship and infection prevention                        |              |               |          |
| I feel confident about my knowledge and practice in the area of antimicrobial prescribing | 81 (81.0%)   | 88 (88.0%)    | 0.143    |
| Sufficient education on Antimicrobial stewardship should be given to community pharmacists | 91 (91.0%)   | 93 (93.0%)    | 0.754    |
| Antimicrobial stewardship will improve the patient’s clinical outcomes    | 88 (88.0%)   | 94 (94.0%)    | 0.070    |
| Antimicrobial stewardship will reduce antimicrobial resistance             | 89 (89.0%)   | 96 (96.0%)    | 0.065    |
| Antimicrobial stewardship improves the cost-effectiveness of health care sectors | 85 (85.0%)   | 89 (89.0%)    | 0.503    |
| Antimicrobial stewardship improve the collaboration between healthcare providers | 90 (90.0%)   | 96 (96.0%)    | 0.109    |

Note: *McNemar’s test.

Table 4 Community Pharmacists’ Satisfaction with the Training Workshop (\textit{N}= 100)

| Statements                                                                 | Strongly Agree/Agree n (%) | Neutral n (%) | Strongly Disagree/Disagree n (%) |
|---------------------------------------------------------------------------|----------------------------|---------------|----------------------------------|
| The online workshop helped me to learn                                   | 97 (97%)                   | 3 (3%)        | 0 (0.0)                          |
| Trainers showed an interest in my needs during this workshop             | 94 (94%)                   | 6 (6%)        | 0 (0.0)                          |
| The PowerPoint lectures were easy to follow and understand               | 93 (93%)                   | 7 (7%)        | 0 (0.0)                          |
| The workshop made me understand the concept of antibiotic resistance     | 95 (95%)                   | 5 (5%)        | 0 (0.0)                          |
| The workshop made me understand the concept of antimicrobial stewardship | 94 (94%)                   | 5 (5%)        | 0 (0.0)                          |
| The educational workshop helps me understand the importance of antimicrobial stewardship | 96 (96%)                   | 4 (4%)        | 0 (0.0)                          |
| The cases integrated into the workshop gave me clear examples of the role of antimicrobial stewardship in reducing antimicrobial resistance | 93 (93%)                   | 6 (6%)        | 1 (1%)                           |
| The educational workshop will allow me to practice what I had learned in my daily practice at my practice site | 93 (93%)                   | 6 (6%)        | 1 (1%)                           |
such as studies conducted in South Africa (71.9%) and Australia (80%).

This inadequate awareness of community pharmacists about AMS could be explained by the lack of educational intervention and promotion of AMS programs across Jordan. Also, this study showed a good knowledge of community pharmacists regarding antimicrobial resistance. This result came in line with other studies about healthcare provider’s familiarity with antimicrobial resistance in Egypt and Ethiopia.17,28

Community pharmacists showed a positive perception regarding AMS before and after the educational intervention. This result aligned with another study that reported that about half of the participants knew the role and effectiveness of AMS before the educational intervention.29 In contrast to what was found in another study, which revealed that more than half of the respondents did not know about the role of AMS before conducting the educational program.17

Community pharmacist’s ability to appropriately select correct antibiotic has been assessed by evaluating pharmacists’ abilities in dealing with virtual community pharmacy cases. Results showed an improvement in pharmacists’ abilities in selecting the most appropriate antimicrobial as compared to prior to the workshop. This was also reported by another study where they showed that the poor practice of respondent pre-educational intervention, and they justified this result due to the absence of clinical education and skill expertise. However, they reported improving respondent practice after the educational intervention. Other studies supported these findings that showed a positive correlation between knowledge and practice.32–34

The training module’s impact was reflected in a good way on pharmacists, as shown through their satisfaction outcomes. The majority of pharmacists (93–97%) were more than satisfied with the training workshop; their satisfaction was detected in all aspects. It could be assumed that using real medical scenarios for a healthcare provider during the training sessions would make it more comprehensible and simple to be closer to professionalism.35

Although, this study is the first of its kind in Jordan, which gives it a great strength point, but it has several limitations. The main limitation of this study is that the training intervention’s influence was studied immediately after conducting the workshop. This may not reflect the actual effect of the training module on real practice long term. Thus, further studies are necessitated to evaluate the impact of conducting educational measures on pharmacists’ skills in implementing antimicrobial stewardship in the long term. In addition, pharmacists were invited to participate through social media which introduced selection bias; as some proportion of the community pharmacist do not have active social media profiles. This may limit the generalizability of results to the general population.

Conclusion
This educational workshop effectively improved community pharmacists’ knowledge about AMS and their abilities in selecting the most appropriate antimicrobial. Thus, efforts should to be intensified to increase perception, awareness, and skills in implementing AMS. These efforts should be focused at different levels, ranging from implementing educational modules in universities and presenting convenient training and educational programs for community pharmacy staff, at regular intervals.

Author Contributions
All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure
The authors declare that there are no conflicts of interest in this work.

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