

# BMJ Open Practices and knowledge of community pharmacists towards the use of proton pump inhibitors: a cross-sectional study in Jordan

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## ABSTRACT

**Objectives** The widespread use of proton pump inhibitors (PPIs) raised concerns on the safety of long-term use of these drugs. Community pharmacists have great responsibility of educating patients on these drugs which requires having adequate knowledge. The aim of this study was to assess the practices and knowledge of community pharmacists regarding PPIs.

**Design** This was a cross-sectional study conducted by filling in a questionnaire. The questionnaire was developed after a comprehensive literature review and assessed knowledge and practices.

**Settings** Community pharmacists with at least 1 year of experience working in a community pharmacy were enrolled in the study.

**Participants** Community pharmacists with at least 1 year of experience working in a community pharmacy were enrolled in the study.

**Primary outcome measures** The knowledge, attitudes, and practices of community pharmacists towards PPIs dispensing.

**Results** A total of 459 community pharmacists were approached for participation in the study, 451 (98.3%) community pharmacists agreed to be enrolled. The most dispensed PPIs in Jordan were lansoprazole and the most commonly treated medical condition with PPIs was gastric ulcer. PPIs were dispensed by the pharmacists very frequently and one-fourth of the participants did not review instructions with patients to ensure their proper use of PPIs. Participants had an average knowledge of  $6.1 \pm 1.7$  (the highest knowledge score is 12). More than one-third of participants (180, 39.9%) had inadequate knowledge (a score of less than 6). Being a PharmD graduate was the only significant factor that predicted adequate knowledge in the logistic regression model, with an adjusted OR of 5.671,  $p=0.002$ .

**Conclusion** To provide adequate pharmaceutical care services, community pharmacists must possess appropriate knowledge on different aspects of PPIs concerning administration, efficacy and long-term and short-term side effects.

## INTRODUCTION

Proton pump inhibitors (PPIs) are one of the most prescribed drugs for treatment

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This was a cross-sectional study where data were collected using a Google Form.
- ⇒ Community pharmacists with at least a bachelor's degree and 1 year of experience were included.
- ⇒ The questionnaire included demographics, social data and different aspects of knowledge on proton pump inhibitors.
- ⇒ The participants were considered to have adequate knowledge if they scored  $\geq 50\%$ .

and prophylaxis of gastrointestinal problems. They are the medical care experts' best option for treatment of upper gastrointestinal issues like dyspepsia, gastro-oesophageal reflux infection and peptic ulcer illnesses.<sup>1</sup> Even though they are profoundly effective and have a more prominent degree of tolerability and safety, their irrational use may prompt unfavourable therapeutic results.<sup>2</sup>

In line with the focus on self-care and the resulting financial benefits for governments and insurance providers, an increasing number of medications, such as PPIs, have been made available without a prescription or over the counter (OTC).<sup>3</sup> Irrational use of PPIs is known to have adverse therapeutic outcomes. Abuse of PPIs may introduce expanded danger of bone fracture<sup>4</sup> and may prompt mineral and nutrient inadequacies and *Clostridium difficile* infection.<sup>5</sup>

It is estimated that over \$13 million sales of PPI prescriptions occurred worldwide.<sup>6</sup> This rise a concern about the overutilisation of PPIs, which will lead to significant high cost and undesirable outcomes such as *C. difficile*, acute interstitial nephritis and microscopic colitis.<sup>7</sup> In addition, they may lead to minerals and vitamins malabsorption such as calcium, magnesium and vitamin B<sub>12</sub>.<sup>8</sup>

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The introduction of a standardised guideline on prescribing PPI helped in decreasing inpatient use of PPI prescriptions, only among patients not receiving PPIs at the time of hospital admission.<sup>9</sup> This support that the majorities of prescriptions are among outpatient sittings and are taking care by community pharmacists (CPs).<sup>10</sup> The understanding and perspective of CPs about PPIs is crucial for optimising PPI use and preventing side effects, drug–drug interactions and improper PPI use.<sup>11</sup>

Worldwide, several studies have been done to assess the knowledge and attitude of CPs towards the use of PPIs. One study in the Kingdom of Saudi Arabia showed that almost all CPs recommend antiulcer drugs for their patients. The study showed a significant association between length of work experience in community pharmacy and reporting PPIs' adverse events.<sup>12</sup> Another study was performed in Riyadh and included a total of 414 surveyors. The results of this study showed that healthcare professionals in the Riyadh area are generally positive about the use of PPIs. However, increasing their level of knowledge and reducing their reliance on PPIs must be strengthened. Frequent professional development programmes and trainings for healthcare professionals are needed to minimise widespread PPI overuse.<sup>13</sup> Moreover, as concerns about the increasing use of PPIs rise, a study conducted in Australia recommends that PPIs continue to be overused worldwide and should be a focus for deprescribing programmes. Ongoing education and awareness campaigns for health professionals and patients, including electronic reminders at the point of prescribing, are strategies that have the potential to reduce PPI use in individuals who do not have an evidence-based clinical indication for their long-term use.<sup>14</sup>

In Jordan, only a few studies have elaborated on the attitude and knowledge of pharmacists towards the use of OTC or prescribed medications. Given the importance of CPs' role in achieving optimal PPI use and preventing possible adverse events or drug–drug interactions, this study aimed to assess the knowledge, attitude and practice of CPs towards the use of PPIs in relation to the recent overuse of PPIs. Up to the authors' knowledge, this is the first study in Jordan that sheds light on the knowledge, attitude, and practice of CPs regarding PPI use.

## METHODS

This was a cross-sectional study that was conducted between January 2023 and May 2023. A research assistant distributed the questionnaire to the CPs in a Google Form to ensure the inclusion of pharmacists who fulfilled the inclusion criteria and to answer any inquiries and improve the response rate. Convenience sampling was used to enrol participants. CPs were able to access the questionnaire if they agreed to participate.

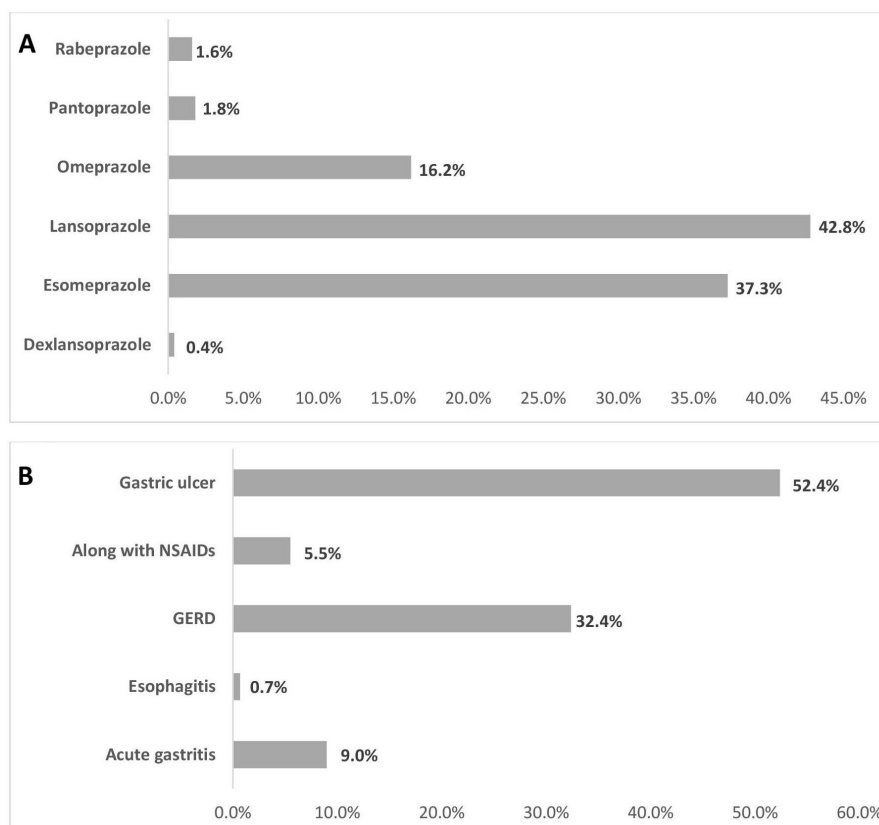
Inclusion criteria: Pharmacists with at least a bachelor's degree in pharmacy and with at least 1 year of experience working in a community pharmacy (to ensure practice with PPI use) were asked to participate in the study.

**Table 1** The general characteristics of the participants, N=459

	N	%
Gender		
Male	130	28.8
Female	321	71.2
Education		
Bsc in pharmacy	397	88.0
Pharm D	32	7.1
Masters in pharmacy	22	4.9
Area of the pharmacy		
In an urban area	204	45.2
In a rural area	42	9.3
In a commercial area	205	45.5
Location of the pharmacy		
North of Jordan	94	20.8
Middle of Jordan	281	62.3
South of Jordan	76	16.9
Type of employment		
Owner of the pharmacy	32	7.1
Employee	419	92.9
Average number of patients per day		
<30	112	24.8
30–70	235	52.1
>70	104	23.1
Monthly income/salary (JOD)		
<300	120	26.6
300–600	301	66.7
>600	30	6.7
University		
Governmental	225	49.9
Outside Jordan	18	4.0
Private	208	46.1
Years of experience		
<1 year	119	26.4
1–5 years	240	53.2
>5 years	92	20.4
JOD, Jordanian dinars.		

## Development of the questionnaire

The questionnaire was developed and written in the English language after a comprehensive literature review. The self-developed questionnaire was constructed based on the information that must be collected to achieve the aims and objectives of this study. The questionnaire included four sections: demographic, geographical region, and social data, knowledge of pharmacists on the correct use of PPIs, possible side effects of the correct duration, practice patterns of CPs, attitudes towards



**Figure 1** (A) The frequency of commonly used PPIs; (B) The most commonly treated medical condition with PPIs. PPIs, proton pump inhibitors. NSAIDs, non-steroidal antiinflammatory drugs. GERD, gastroesophageal reflux disease.

counselling and educating their patients, as well as their recommendations regarding PPI use. The geographical region in Jordan was included as a variable because the educational, economic level and cultural characteristics of the customers differ significantly from one region to another. Consequently, the practices of the CPs, personal experience and surrounding environment may affect their knowledge. In addition, most of the educational lectures and courses are centred in the middle and north regions which might affect the knowledge of the participants. The knowledge score was calculated by summing the correct answers related to the knowledge section, correct answers were assigned 1 and incorrect answers were assigned zero. The participants were considered to have adequate knowledge if they scored 6 out of 12,  $\geq 50\%$  (the highest knowledge score was 12) and inadequate knowledge if the score was less than 6,  $< 50\%$ .<sup>15–17</sup> The questionnaire was translated into Arabic by a language expert since some pharmacists received their education in Arabic. The Arabic version was matched with the English version and verified by two field experts. Pilot sample included 10 responses from known pharmacists, and they were asked to give comments on the clarity, comprehensiveness and suitability of the questionnaire and modifications were performed accordingly. The modifications were minor changes concerning the wording or rephrasing of certain questions for a clearer understanding and absence of

ambiguity and data presentation (whether continuous or categorical).

### Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

### Sample size calculations

Sample size was calculated using the Raosoft Sample Size Calculator.<sup>18</sup> Z is the statistic corresponding to the level of confidence; for a 95% CI, which is 1.96; P is expected prevalence, and it is assigned as 0.5 to give the largest sample and  $1-P=0.5$ ; and d is precision,  $d=0.05$ . Population size of community pharmacies was 4000, the approximate number of community pharmacies in Jordan. By using the above values, the sample size was calculated to be 351 participants. However, a larger sample size was targeted to provide more information.

### Statistical analysis

The data were analysed using IBM SPSS Statistics for Windows, V.25.0. (IBM). Descriptive analysis, including frequency and percentage, was used for categorical variables, and the mean and SD were provided for the continuous variables. Logistic regression was used to evaluate possible predictors of adequate knowledge. Variables included in the model were selected based on

**Table 2** Practices of pharmacists concerning PPIs dispensing

	N	%
How often do you dispense nonprescription PPIs for your patients?		
Rarely	87	19.3
Every day	105	23.3
Every week	259	57.4
PPIs represent your first nonprescription choice for your patients who suffer from indigestion?		
No	374	82.9
Yes	77	17.1
Do you ask your patients if he/she takes any other drug, to prevent any kind of drug-drug interaction with PPIs?		
No	59	13.1
Yes	392	86.9
Did you suggest lifestyle changes to improve the symptoms?		
No	15	3.3
Yes	436	96.7
Do you tell your patients on best time to take PPIs during the day?		
No	9	2.0
Yes	442	98.0
Do you tell your patients on the side effects of PPIs?		
No	148	32.8
Yes	303	67.2
Do you tell your patients on the duration of using PPIs?		
No	130	28.8
Yes	321	71.2
Do you tell your patients on the important drug-drug interactions of PPIs?		
No	144	31.9
Yes	307	68.1
If the patient does not improve on the PPIs, what is your recommendation?		
Add an H2 receptor blocker	26	5.8
Switch to another PPI	51	11.3
Switch to H2 receptor blocker	13	2.9
Refer to a physician	361	80.0
Do you recommend any supplements for patients taking the PPIs for a long period of times and suffer from iron, calcium, B <sub>12</sub> and magnesium deficiency?		
No	118	26.2
Yes	333	73.8
Do you review instructions with patient to ensure their proper use of PPIs?		

Continued

**Table 2** Continued

	N	%
No, because they are safe	19	4.2
No, there is no time	59	13.1
No, I never thought of that	40	8.9
Yes	333	73.8
PPIs, proton pump inhibitors.		

other studies that evaluated knowledge of pharmacists in different aspects of their pharmacy practice.<sup>19–21</sup> P values less than 0.05 are considered statistically significant.

## RESULTS

A total of 459 CPs were approached for participation in the study, 451 (98.3%) CPs agreed to be enrolled. Reasons for not participating were loss of interest and being too busy.

Most of the respondents 322 (70.2%) were young females with an average age of 27.80±6.798 years. The general characteristics of the participants are shown in [table 1](#).

The most dispensed PPI in Jordan was lansoprazole and the least dispensed was dexlanoprazole, most probably due to its high price. PPIs were dispensed mainly to treat gastric ulcer, GER and acute gastritis ([figure 1](#)).

Most of the pharmacists (404, 89.6%) thought that they had adequate information on gastrointestinal diseases. PPIs were dispensed by the pharmacists very frequently, almost half dispensed them daily, but they do not represent a first choice for indigestion. Almost one-fourth of the participants do not review instructions with patients to ensure their proper use of PPIs drugs view ([table 2](#)).

Only 345 participants (76.5%) reported having effective communications with their patients to ensure that they are treated safely and effectively. Their knowledge included information about long-term and short-term side effects, dosage regimens, and differences among PPIs (see [table 3](#)).

Participants had an average knowledge of 6.1±1.7 (the highest knowledge score is 12). More than one-third of participants (180, 39.9%) had inadequate knowledge (a score of less than 6). Being a PharmD graduate was the only significant factor that predicted adequate knowledge in the logistic regression model ([table 4](#)).

## DISCUSSION

PPIs in Jordan are considered OTC drugs; pharmacists can dispense them to the customers without a prescription. Therefore, appropriate knowledge and practices of the CP are pivotal to maintain patients' safety and adequate use.



**Table 3** Knowledge of pharmacists on different aspects of PPIs

	N	Frequency
1. The best time to take PPIs is:		
Before breakfast*	446	98.9%
After any meal	3	0.7%
With any meal	2	0.4%
2. Maximum duration for using PPIs without referral to a physician as an over-the-counter drug if symptoms persist is:		
Less than 1 week	47	10.4%
1–2 weeks*	164	36.4%
2–4 weeks	145	32.2%
More than 4 weeks	26	5.8%
PRN Regardless of the period	69	15.3%
3. Omeprazole has longer duration of action compared with esomeprazole		
No*	126	27.9%
Yes	325	72.1%
4. Is it advisable that the pharmacist increase the dose frequency rather than a single dose to improve effect?		
No*	350	77.6%
Yes	101	22.4%
Long-term side effect(s) of PPIs		
5. Significant vitamin (B <sub>12</sub> and C) and mineral (iron, calcium, and magnesium) deficiencies		
No	20	4.4%
Yes*	431	95.6%
6. Enteric and respiratory infections		
No	358	79.4%
Yes*	93	20.6%
7. Gastric polyps, gastric carcinoids and gastric cancer		
No	330	73.2%
Yes*	121	26.8%
8. Osteoporosis		
No	185	41.0%
Yes*	266	59.0%
Short term side effect(s) of PPIs		
9. Rash/hypersensitivity		
No	334	74.1%
Yes*	117	25.9%
10. Nausea/vomiting/abdominal pain/flatulence		
No	171	37.9%
Yes*	280	62.1%
11. Diarrhoea/constipation		
No	197	43.7%
Yes*	254	56.3%

Continued

**Table 3** Continued

	N	Frequency
12. Headache/dizziness		
No	327	72.5%
Yes*	124	27.5%

\*Correct answer.

PPIs, proton pump inhibitors; PRN, when necessary.

Most of the respondents were females which is expected since in Jordan the pharmacy profession, especially the community pharmacies, is dominated by females. PPIs were frequently dispensed by the pharmacists, almost 80% of the CPs dispensed PPIs at least once weekly. In a recent review, Shanika *et al* evaluated global use of PPIs in the general population. They identified 28 million PPI users (one-quarter of adults), of which two-thirds were on high doses.<sup>22</sup> In Iceland, a nationwide study showed an annual increase in PPI use from 8.5 per 100 persons to 15.5 per 100 persons.<sup>23</sup> Similar reports of increased PPI consumption were documented in many studies worldwide.<sup>24–25</sup> Regrettably, it is also common that patients are prescribed PPIs during their hospital stay and many continue taking them after discharge without an indication or appropriate termination schedule.<sup>26</sup> This confirms the finding of a study that revealed that 70% of patients take PPIs without appropriate indication.<sup>27</sup>

The widespread increase in the use of PPIs warrants a careful assessment of the practices and knowledge of prescribers/dispensers (physicians of prescription only and pharmacists for OTC drugs). Lansoprazole was the most frequently used PPI; in other countries different PPIs were mostly used. This is probably based on the availability of generic drugs and cheaper alternatives.<sup>11</sup> Strangely enough, one-third of the pharmacists do not tell their customers about the side effects of the PPIs and do not review the instructions with patients to ensure their proper use. Despite their relative safety, long-term use of PPIs exposes the consumer to many side effects including reduced calcium and magnesium absorption, vitamin B<sub>12</sub> deficiency, community-acquired pneumonia, *C. difficile*-associated disease.<sup>26</sup> Additional serious complications also include chronic kidney disease<sup>28</sup> through the inhibition of proton pumps in the renal tubule.<sup>29</sup>

Almost all the participants knew that PPIs should be given before breakfast, however, few knew that the duration of treatment with PPIs as OTC drug is 1–2 weeks and most of the participants thought that patients can receive them for longer durations as OTC drugs. This is lower than neighbouring countries, where in Saudi Arabia, 54.9% of CPs recommend treatment for 1–2 weeks.<sup>12</sup> Consumers should not use PPIs as an OTC longer than 2 weeks, and patients who need them longer should be encouraged to refer to a physician.<sup>30</sup>

CPs did not have appropriate knowledge concerning certain long-term and short-term side effects of PPI use.

**Table 4** Possible predictors of adequate knowledge using logistic regression analysis

	Univariate logistic regression			Multivariable logistic regression		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.981	0.954 to 1.008	0.165	0.968	0.927 to 1.011	0.139
Gender						
Male						
Female	0.664	0.433 to 1.017	0.060	0.664	0.411 to 1.074	0.095
Education						
BSc in pharmacy						
Pharm D	5.083	1.750 to 14.765	0.003	5.671	1.874 to 17.161	0.002
Masters in pharmacy	1.049	0.438 to 2.511	0.915	1.048	0.397 to 2.771	0.924
Area of the pharmacy						
In an urban area						
In a rural area	1.580	0.764 to 3.267	0.217	1.500	0.691 to 3.256	0.306
In a commercial area	0.824	0.555 to 1.222	0.335	0.759	0.499 to 1.156	0.199
Location of the pharmacy						
North of Jordan						
Middle of Jordan	0.770	0.474 to 1.251	0.290	0.856	0.856 to 0.488	0.586
South of Jordan	0.785	0.421 to 1.465	0.447	0.882	0.882 to 0.455	0.710
Type of employment						
Owner of the pharmacy						
Employee	1.185	0.574 to 2.448	0.646	1.034	0.418 to 2.558	0.942
Average number of patients per day						
<30						
30–70	1.371	0.870 to 2.161	0.173	1.531	0.929 to 2.523	0.095
>70	1.569	0.908 to 2.712	0.106	1.613	0.867 to 3.001	0.131
Monthly income/salary (JOD)						
<300						
300–600	0.863	0.560 to 1.332	0.506	0.780	0.465 to 1.311	0.349
>600	1.709	0.703 to 4.158	0.237	1.844	0.624 to 5.454	0.268
University						
Governmental						
Private	0.877	0.597 to 1.288	0.503	0.970	0.618 to 1.522	0.895
Outside Jordan	1.261	0.456 to 3.483	0.655	1.406	0.421 to 4.694	0.579
Years of experience						
<1 year						
1–5 years	0.895	0.569 to 1.409	0.633	0.943	0.561 to 1.584	0.824
>5 years	0.730	0.419 to 1.271	0.266	0.973	0.441 to 2.147	0.946

JOD, Jordanian dinars.

A mere 20% of the participants knew that PPIs caused enteric and respiratory infections, although an association was found between their long-term use and increased risk of enteric bacterial infections.<sup>31</sup> Additionally, pharmacists were not aware of the risk of gastrointestinal malignancies. Many studies proposed several mechanisms for gastric cancer, such as increased proliferation of enterochromaffin-like cells<sup>32</sup> and gastric colonisation by *Helicobacter pylori*.<sup>33</sup>

41% of the CPs did not know that long-term side effects of PPIs included osteoporosis. Although association between the risk of fracture and PPI use is controversial.<sup>34</sup> Patients with certain medical conditions, such as renal dysfunction, have higher risk. Consequently, CPs must know about this risk and vulnerable groups and should provide recommendations concerning routine prophylaxis for osteoporosis.<sup>35</sup> Knowledge concerning short-term side effects also was not adequate, headache/

dizziness, diarrhoea/constipation and rash/hypersensitivity were not known as possible side effects by many CPs.

This finding emphasises the need for appropriate knowledge by the CPs of long-term and short-term side effects of PPIs to be competent in providing recommendation to the consumers in terms of stopping unnecessary oral administration of PPIs. A recent study revealed that only 44% of PPI prescriptions in the Netherlands had an indication.<sup>36</sup> In Kuwait, 87.4% of surveyed physicians agreed that PPI overuse is common and that there is a need for education on appropriate use of PPIs for the public as well as physicians.<sup>37</sup> In the United Arab Emirates, 83% of pharmacists reported providing advice to their patients to stop long-term use of PPIs if there was no indication.<sup>38</sup> Despite the involvement of all healthcare professionals in providing advice on PPIs, disparities in knowledge are present. A large study that was conducted in China, investigated awareness of medical staff towards PPI use. Pharmacists showed significantly higher levels of awareness compared with doctors and nurses ( $p<0.01$ ).<sup>39</sup>

Unlike similar studies that explored the pharmacy education programme did not affect the knowledge of CPs.<sup>11</sup> In this study, the only predictor of adequate knowledge was having a PharmD degree. This emphasises the comprehensive and valuable education that they receive that endows them with great knowledge that can be transferred to the consumers.

To the best of our knowledge, this is the first study which has evaluated the prescribing pattern, knowledge and practices of CPs towards the use of PPI in Jordan. The information revealed by the study identifies gaps in knowledge and practices that must be addressed by healthcare services and regulatory bodies to guarantee safety of consumers.

Limitations of the study include the generalisability of the findings. Although CPs from different geographical regions participated in the study, differences within the same region and lack of randomisation (convenient sampling) limit the generalisability of the data but it still gives an approximate description of the current situation. The chosen knowledge cut-off of 50% is another limitation of the study since it is controversial and may differ in other similar studies where the cut-off is 60%. This will affect comparisons with other studies and the assumptions of having adequate knowledge.

Future studies should assess the association between the knowledge of the patients and the presence of side effects. Continuous professional development programmes should be implemented and the effect on the practices of CPs should be assessed.

## Conclusion

CPs frequently dispense PPIs to millions of consumers worldwide. To provide adequate pharmaceutical care services, CPs must possess appropriate knowledge of different aspects of PPIs' prescribing, efficacy and long-term and short-term side effects. CPs play an important role in the judicious use of PPIs, this includes educating

patients on appropriate use and possible side effects to minimise harm and maximise benefits. The practices and knowledge of CPs suffers from several gaps and disparities and can be addressed through educational programmes and continuous professional development activities.

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**Contributors** LG: conceptualisation, methodology, analysis, writing-original draft preparation, guarantor. MAA: conceptualisation, data curation, writing-original draft preparation. MIA-H, ED and RA: conceptualisation, data curation, supervision, editing the original draft. ZL: methodology, writing-reviewing and editing. ZZ: methodology, writing-reviewing and editing. LG is the guarantor.

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**Patient consent for publication** Not applicable.

**Ethics approval** The institutional review board's approval from Amman Al-Ahliyya University was obtained before starting the study (IRB/AAU/3/14/2021–2022) in September 2022.

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**Data availability statement** Data are available on reasonable request. Data can be shared through the corresponding author on reasonable request.

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