

Original Research Article

Unused and expired medication disposal knowledge, attitude, and practices among healthcare professionals in Pune, India

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Abstract

Purpose: To assess healthcare professionals' knowledge, attitudes, and practices toward medication disposal.

Methods: This study employed a cross-sectional design, with data collected using an online Google form. The survey links containing 20 questions and demographic data were shared with the official WhatsApp groups and email addresses of various eligible participants. The collected data were presented as frequencies and percentages. A score was assigned to all responses, and an average mean score was used to categorize the respondents' knowledge, attitudes, and practices into good, moderate, and poor categories.

Results: A total of 233 participants responded to the questionnaire, and the majority were Nurses, 87 (37.3 %). The findings revealed that most respondents had poor knowledge, 95 (40.9 %), and practice, 98 (42.1 %), and the majority, 86 (36.9 %), had good attitudes.

Conclusion: The study revealed a significant gap in knowledge and practice among healthcare professionals toward medication disposal.

Keywords: Disposal, Expired medications, Healthcare professionals, Medication disposal, Unused medications, Knowledge, attitude and practice

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INTRODUCTION

Medications remain crucial in enhancing the quality of life; despite these benefits, their improper disposal practices negatively affect human health and environmental safety [1,2]. The increase in medications worldwide has led to a surge of unused and expired medicines among the public [2]. These medications expose the environment and its inhabitants to hazardous

consequences like pollution when they are improperly disposed of [3,4]. Several drugs are excreted into the environment as either active ingredients or metabolites through sewage [5]. This has led to negative consequences, mostly to aquatic species and by extension, humans [5].

According to the United Nations, when medications are disposed of properly, it offers a protective effect to the environment and its

inhabitants, which is one of the key initiatives of “Sustainable Development Goals” (Responsible Consumption and Production) and also one health approach of the United Nations (UN) [4]. This issue is not limited only to the harmful effects it poses on the environment and the public, but also as a contributing factor to antibiotic resistance and the wastage of finite resources in already stretched health budget expenditure, among others [3]. Additionally, unintentional overdose, accidental ingestion among children, the possibility of prescription drug misuse, and an increase in drug abuse are part of the consequences of improper drug disposal [1,6].

This issue has attracted the attention of several countries to enact policies regarding medication disposal systems [4]. In many developed countries like Canada, the United Kingdom, and USA, a medication return program is widely practiced in both public and private healthcare facilities [1,4]. However, many developing countries like Nigeria and India are facing challenges in medication management, which leads to the inability to use guidelines for medication disposal systems and a lack of systems for medication return programs [4,7,8]. Also, several agencies like the United States Food and Drug Administration (FDA) and the World Health Organization (WHO) developed guidelines for proper disposal practices of unused and expired medications for the public [1,4]. Many pharmaceutical companies have also recommended the disposal of produced medications to safeguard the public and the environment from their harmful effects [6].

Healthcare professionals are expected to educate the general population on proper medication disposal practices. However, several studies have highlighted widespread deficiencies in public knowledge, attitudes, and practices regarding medication disposal [9-12]. Despite this, limited studies have explored the extent of awareness and adherence to appropriate disposal practices among healthcare professionals themselves. This study seeks to evaluate the knowledge, attitudes, and practices of healthcare professionals concerning medication disposal, thereby identifying gaps that may impact both professional responsibility and public health safety.

METHODS

The study was conducted and reported according to the guidelines for strengthening the reporting of observational studies in epidemiology (STROBE) [13].

Study setting

The study was conducted in three multi-specialty hospitals in Pune, Maharashtra. Pune is an educational and industrial hub in the northern part of India. Recently, significant developments have been recorded in the health sector, and the population comprises Indigenous people and migrants [14].

Study design

The study is cross-sectional, descriptive, and questionnaire-based, and an online survey. The questionnaire survey link was shared with eligible participants via official social media platforms (WhatsApp) and personal emails. A weekly reminder was sent to the platforms to ensure all intended participants responded to the survey appropriately.

Ethics approval and consent to participate

The study protocol was reviewed by the institutional research and ethics committee of the Symbiosis International (Deemed University), Pune, India. Ethical clearance with reference number SIU/IEC/914 was obtained after the committee's approval. A written informed consent was obtained from each eligible participant, and all the information regarding the study was clearly written, with consent to participate in this study appearing before the research questions and an option to decline if they wished not to participate.

Study population and sample size

The target population is healthcare providers with a valid practicing license residing and working in Pune city. The eligible participants comprised doctors, nurses, and pharmacists who provide patient care and have direct access to the patients. Other healthcare professionals outside the inclusion criteria were excluded. A minimum sample size was determined using a single proportion formula ($n = Z^2 \cdot p(1-p) / d^2$) [15]. Assuming 50 % as the expected proportion of the healthcare providers who provide patient care and handle medications with a 0.05 % significance (alpha) level at a 95 % confidence interval, a minimum sample size of 384 was calculated. The sample size was stratified into 128 each for doctors, nurses, and pharmacists.

Data collection tool

A pre-validated, self-administered questionnaire was used for data collection. The questionnaire

was adapted after extensive literature from previous research [16]. It was then piloted among 20 healthcare professionals for face validity and relevance. An option of “Maybe” was recommended to be added to the Knowledge and Attitude domains of the questionnaire. A Cronbach’s alpha reliability showed an internal consistency coefficient of 0.746, 0.776, and 0.635 for the domains of Knowledge, Attitude, and Practice, respectively. The questionnaire was made up of two sections: Section A comprised the participant’s demographic data. Section B had 20 questions that evaluated Healthcare Professionals’ (HCPs’) knowledge, attitude, and practice regarding medication disposal practices. Six questions focused on the knowledge of the participants. Seven questions addressed participants’ attitudes and beliefs about expired/unused medicines. Finally, seven questions addressed the current practice of medicine disposal.

Study procedure/Recruitment

The data was collected for 2 months using an online survey, which was conducted and reported based on the Checklists for Reporting Results of Internet E-Surveys (CHERRIES) [17]. “Google Forms” was used to create the survey link containing the questionnaire. Later on, an online advertisement containing the survey link, study information, and eligibility criteria was designed.

This advertisement was shared with eligible participants via social media platforms (WhatsApp page) and their official emails. Consent to participate in this study appeared before the research questions, and the participants could only see the survey questions after clicking an informed consent to participate. The link was designed to accept only one response from a single participant.

Outcome measures

The primary outcome measures in the study are the knowledge, attitudes, and practices of healthcare practitioners toward unused and expired medications, which were measured by scoring the participants’ responses. These measures were assessed by scoring participants’ responses across all domains. Each knowledge item was scored one (1) point for a correct response and zero (0) for an incorrect response. In the attitude domain, responses reflecting a positive attitude were assigned two (2) points, neutral responses one (1) point, and negative responses zero (0) points. For the practice domain, correct responses received one (1)

point, while incorrect responses were scored zero (0). For each domain, total scores were computed separately for every respondent, and the mean score was calculated. Participants’ individual scores were then compared with the corresponding domain mean. Scores greater than or equal to one standard deviation above the mean ($X_i \geq \mu + \delta$) were categorized as good, scores falling within one standard deviation of the mean ($\mu - \delta < X_i < \mu + \delta$) were classified as moderate, and scores less than or equal to one standard deviation below the mean ($X_i \leq \mu - \delta$) were categorized as poor.

Data analysis

The data collected from the survey was transferred from the Google form into an Excel sheet for cleaning and then exported into IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp for analysis. Categorical variables were presented as frequencies and percentages, while numerical variables were presented as mean (standard deviation, SD). Chi-square was used to assess the relationship between the demographic data and the measured outcomes at a 95 % confidence interval.

RESULTS

Table 1 shows the sociodemographic results of the respondents. The majority, 90 (38.6 %), were in the 20-30 age group. Also, most respondents were female, 128 (54.9 %), with the majority being single, 119 (50.6 %). Nurses were the largest group of respondents, comprising 87 (37.3 %), while pharmacists had the smallest number of participants, at 64 (27.5 %). The highest qualification of the respondents was either a bachelor’s or a Master’s Degree, with 87 (37.3 %) and 84 (36.1 %) respondents, respectively. Most of them, 94 (40.3 %), had 5 years or less of experience.

As depicted in Table 2, 206 (88.4 %) respondents answered “Yes” to the question, “Can expired or unused medicines that are not properly disposed of pose hazards to public safety?” However, only a few of the respondents, 99 (42.5 %), answered the question, “Do you think the use of Ayurvedic, Homeopathic, and Veterinary drugs can affect the environment? With a positive response. Most of the other reactions are above 50 %, showing an average level of knowledge among the respondents. Also, the attitude of the respondents was proven to be good, with most respondents showing a positive response to almost all the surveyed questions. All the

questions were responded to correctly by at least 70 % of the respondents.

Moreover, in the practice domain, most of the respondents, 163 (70 %), showed they were counselling their patients or patients' relatives on how to dispose of medications properly. Also, 147 (63.1 %) respondents claimed not to have attended any seminar, workshop, or CME about medication disposal recently.

Table 3 shows the categories of knowledge, attitude, and practice of the respondents. 95 respondents (40.8 %) showed a poor level of knowledge on medication disposal, while 81 respondents (34.8 %) exhibited good knowledge

levels. The attitude of the respondents was good, with the majority of the participants, 86 (36.9 %) and 83 (35.6 %), categorized as having good and moderate attitudes, respectively. Also, 98 (42.1 %) of the respondents were categorized as having poor practice toward medication disposal.

The criteria for categorization into good, moderate, and poor classes are as follows:

$X_i \geq \mu + \delta$ = Good class; $\mu - \delta < X_i < \mu + \delta$ = Moderate class; and $X_i \leq \mu - \delta$ = Poor class.

Where: X_i = Individual score; μ = Mean score; and δ = Standard deviation of the score

Table 1: Sociodemographic characteristics of the respondents

Variable	Category	Frequency (%)
Age (years)	20-30	90 (38.6)
	31-40	84 (36.1)
	41-50	37 (15.9)
	51- above	22 (9.4)
Gender	Male	103 (44.2)
	Female	128 (54.9)
	Prefer not say	2 (0.9)
Marital status	Single	119 (50.6)
	Married	104 (44.2)
	Divorced	2 (0.9)
	Widowed	1 (0.4)
	Prefer not say	9 (3.9)
Designation	Medical Doctor	82 (35.2)
	Nurse	87 (37.3)
	Pharmacist	64 (27.5)
Educational level	Bachelor Degree	87 (37.3)
	Master Degree	84 (36.1)
	Doctorate Degree	28 (12)
	Fellowship	19 (8.2)
	Others	15 (6.4)
Years of experience	5 and below	94 (40.3)
	6-10	68 (29.2)
	11-15	31 (13.3)
	16-20	26 (11.2)
	21-above	14 (6.0)

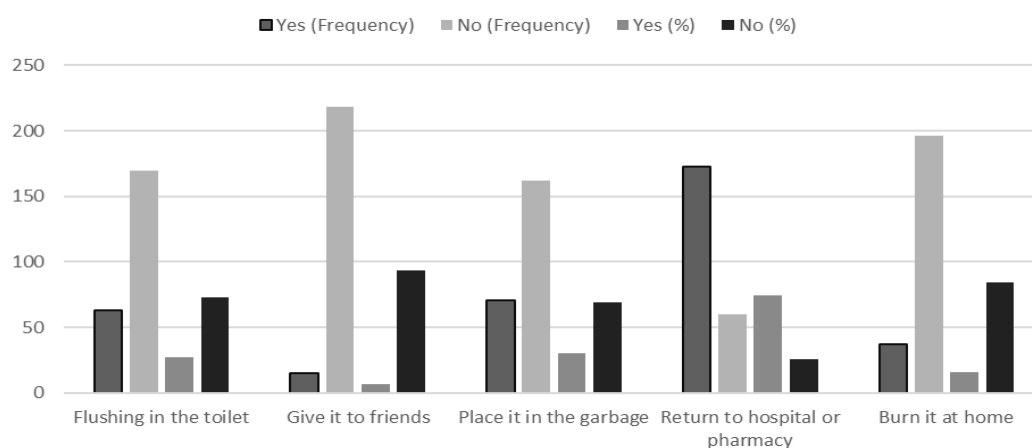


Figure 1: Shows the frequency and percentage of medication disposal preferred by the respondents

Table 2: Knowledge, Attitude, and Practice of the respondents towards unused and expired medication disposal

Domain	Variable	Responses	Frequency (%)
Knowledge	Can expired/unused medicines, which are not properly disposed of, pose hazards to public safety?	Yes	206 (88.4)
		No	16 (6.9)
		Maybe	11 (4.7)
	Could the pollution caused by pharmaceuticals potentially be a contributing factor to antibiotic resistance?	Yes	155 (66.6)
		No	25 (10.7)
		Maybe	53 (22.7)
	Have you read any media reports or articles about the environmental impact of pharmaceuticals?	Yes	145 (62.2)
		No	68 (29.2)
		Maybe	20 (8.6)
	Do you know if India has rules and regulations for minimizing the risk of drug entry into the environment?	Yes	147 (63.1)
		No	34 (14.6)
		Maybe	52 (22.3)
	Have you heard the terms "Green Chemistry" and "Green Pharmacy"?	Yes	129 (55.4)
		No	79 (33.9)
		Maybe	25 (10.7)
Attitude	Do your thoughts about disposing of unused or extra medication bother you	Yes	174 (74.7)
		No	34 (14.6)
		Maybe	25 (10.7)
	Knowledge of medication disposal will be relevant to my medical practice	Yes	209 (89.7)
		No	5 (2.1)
		Maybe	19 (8.2)
	There should be guidelines for the public to dispose of medications in an environmentally friendly manner	Yes	212 (91.0)
		No	3 (1.3)
		Maybe	18 (7.7)
	There should be collection boxes in hospitals and pharmacies to collect left-over/unused/expired medications	Yes	213 (91.4)
		No	10 (4.3)
		Maybe	10 (4.3)
	Manufacturers and pharmacies should collect unwanted/ left-over medications from the public	Yes	173 (74.2)
		No	33 (14.2)
		Maybe	27 (11.6)
Practice	Do you agree with the statement: "It is my responsibility to protect the environment from the harmful effects of pharmaceutical waste?"	Yes	193 (82.8)
		No	7 (3.0)
		Maybe	33 (14.2)
	Are you willing to actively engage in activities or initiatives related to medication disposal?	Yes	193 (82.8)
		No	10 (4.3)
		Maybe	30 (12.9)
	Do you buy drugs in bulk for family members?	Yes	75 (32.2)
		No	158 (67.8)
	Do you remove the drug from its container before throwing it in the garbage?	Yes	128 (54.9)
		No	105 (45.1)
	Do you counsel your patient or patient's relatives on proper drug disposal?	Yes	163 (70)
		No	70 (30)
	Do you pour leftover syrup/lotion from the bottle into the wash basin?	Yes	111 (47.6)
		No	122 (52.4)
	Have you previously attended any seminars/workshops/CME (Continuing Medical Education) about medication disposal?	Yes	86 (36.9)
		No	147 (63.1)
	Are you willing to dispose of unused medications through proper collection programs?	Yes	221 (94.8)
		No	12 (5.2)

As depicted in Table 4; in the knowledge domain, there was a statistically significant association between age and knowledge level ($p = 0.006$), with the highest proportion of individuals with good knowledge found in the 31 - 40 age group (42 individuals), while the 20 - 30 age group had the highest proportion of poor knowledge (48 individuals). Additionally, designation ($p =$

0.0000) and educational level ($p = 0.008$) showed significant associations with knowledge. Medical doctors and pharmacists had shown better knowledge than nurses, but individuals with higher educational levels (with master's degrees) had the highest knowledge (36).

Table 3: Knowledge, attitude, and practice category of the respondents

Variable	Category	Frequency (%)
Knowledge	Good	81 (34.8)
	Moderate	57 (24.5)
	Poor	95 (40.8)
Attitude	Good	86 (36.9)
	Moderate	83 (35.6)
	Poor	64 (27.5)
Practice	Good	45 (19.3)
	Moderate	90 (38.6)
	Poor	98 (42.1)

Table 4a: Association between sociodemographic characteristics and the respondents' knowledge and attitude

Domain	Variable	Category	Good	Moderate	Poor	P-value
Knowledge	Age	20-30	22	20	48	**0.006 (18.228)
		31-40	42	17	25	
		41-50	10	13	14	
		51- above	7	7	8	
	Gender	Male	44	25	34	0.076 (8.471)
		Female	37	32	59	
		Prefer not say	0	0	2	
	Marital status	Single	38	26	54	0.302 (9.502)
		Married	40	28	35	
		Divorced	1	1	0	
		Widowed	1	0	0	
	Designation	Prefer not say	1	2	6	**0.0000 (22.130)
		Medical Doctor	34	21	27	
		Nurse	19	16	52	
		Pharmacist	28	20	16	
	Educational level	Bachelor Degree	24	20	43	**0.008 (20.648)
		Master Degree	36	21	27	
		Doctorate Degree	14	9	5	
		Fellowship	4	6	9	
	Years of experience	Others	3	1	11	0.181 (11.374)
		5 and below	26	21	47	
		6-10	31	16	21	
		11-15	13	7	11	
		16-20	6	10	10	
Attitude	Age	21-above	5	3	6	**0.003 (20.071)
		20-30	30	37	23	
		31-40	44	23	17	
		41-50	10	13	14	
	Gender	51- above	2	10	10	0.064 (8.871)
		Male	48	31	24	
		Female	37	52	39	
	Marital status	Prefer not say	1	0	1	0.711 (5.426)
		Single	45	45	28	
		Married	36	35	32	
		Divorced	1	1	0	
	Designation	Widowed	1	0	0	0.089 (8.062)
		Prefer not say	3	2	4	
		Medical Doctor	38	27	17	
		Nurse	23	34	30	
	Educational level	Pharmacist	25	22	17	**0.025 (17.548)
		Bachelor Degree	30	36	21	
		Master Degree	41	24	19	
		Doctorate Degree	9	12	7	
	Years of experience	Fellowship	4	5	10	**0.000 (33.508)
		Others	2	6	7	
		5 and below	31	40	23	
		6-10	39	20	9	
		11-15	11	7	13	
		16-20	3	9	14	
		21-above	2	7	5	

****Statistically significant**

Table 4b: Association between sociodemographic characteristics and the respondents' practice

Domain	Variable	Category	Good	Moderate	Poor	P-value
Practice	Age	20-30	16	35	39	0.220 (8.250)
		31-40	15	34	35	
		41-50	7	18	12	
		51- above	7	3	12	
	Gender	Male	22	35	46	0.432 (3.816)
		Female	22	55	51	
	Marital status	Prefer not say	1	0	1	**0.035 (16.591)
		Single	17	53	48	
		Married	25	35	43	
		Divorced	2	0	0	
	Designation	Widowed	0	0	1	**0.003 (16.311)
		Prefer not say	1	2	6	
		Medical Doctor	15	29	38	
		Nurse	8	38	41	
	Educational level	Pharmacist	22	23	19	0.138 (12.306)
		Bachelor Degree	9	37	41	
		Master Degree	19	33	32	
		Doctorate Degree	9	10	9	
	Years of experience	Fellowship	3	5	11	0.116 (12.872)
		Others	5	5	5	
		5 and below	16	37	41	
		6-10	13	22	33	
		11-15	6	19	6	
		16-20	5	8	13	
		21-above	5	4	5	

**Statistically significant

However, gender ($p = 0.076$), marital status ($p = 0.302$), and years of experience ($p = 0.181$) do not have significant associations with knowledge, although males had slightly higher knowledge than females, and those with fewer years of experience showed poorer knowledge.

In the attitude domain, age ($p = 0.003$), educational level ($p = 0.025$), and years of experience ($p = 0.000$) show significant associations. The 31 - 40 age group had the highest good attitude (44), while the 20 - 30 age group had the highest poor attitude (23). Similarly, master's degree holders had the highest good attitude (41), whereas individuals with lower qualifications had poorer attitudes. Years of experience also played a role, with those having 6 - 10 years of experience demonstrating the highest good attitude (39), while individuals with 16 - 20 years of experience had the highest poor attitude (14). On the other hand, gender ($p = 0.064$), marital status ($p = 0.711$), and designation ($p = 0.089$) do not show significant associations with attitude, although medical doctors had slightly better attitudes than other healthcare professionals.

For the practice domain, significant associations are observed in marital status ($p = 0.035$) and designation ($p = 0.003$). Married individuals had better practice compared to single individuals,

while pharmacists demonstrated the highest good practice (22), whereas nurses had the highest poor practice (41). However, age ($p = 0.220$), gender ($p = 0.432$), educational level ($p = 0.138$), and years of experience ($p = 0.116$) do not have significant associations with practice. Although there is no statistical significance, younger individuals (20 - 30 years) had slightly better practice, and those with fewer years of experience (5 years or below) exhibited poorer practice.

Overall, age, designation, and educational level are significantly associated with knowledge and attitude, while years of experience significantly influenced attitude. Marital status significantly influenced practice, while gender did not significantly influence any domain. Designation played a crucial role in knowledge and practice, with medical doctors and pharmacists performing better than nurses.

DISCUSSION

The study assessed healthcare professionals' knowledge, attitudes, and practices toward unused and expired medication disposal using an online self-administered questionnaire. The findings revealed different knowledge levels among healthcare professionals, ranging from poor to moderate, and good. Most respondents

depicted poor knowledge, with most of them (52) being nurses. This knowledge gap is mostly associated with the respondents' responses to questions related to green pharmacy knowledge and the one related to the harmful effects of ayurvedic or veterinary drugs on the environment. These findings corroborate the findings of [16], which show similar trends in knowledge gaps. This may be attributed to the level of training for pharmacists during their undergraduate study, in which they were more exposed to formal training in terms of medication management and regulations, especially for pharmacists. Also, doctors had more medication knowledge in terms of their dangers and uses as compared to nurses.

Similarly, good knowledge was observed especially among pharmacists and doctors, which is largely attributed to questions like hazards of disposing of medication improperly, with a positive response of over 88.4 % and others that got a positive response of over 60 % (Table 2). This finding is in line with research conducted in Delhi that shows good knowledge of medication disposal among HCPs, but here with Nurses having better knowledge [19]. It is noteworthy to understand that there is an inconsistency in the knowledge level of medication disposal among healthcare professionals. Equipping healthcare professionals with the right knowledge can go a long way in curbing the dangers of improper medication disposal. Furthermore, the study revealed that most respondents have good and moderate attitudes, 36.9 and 35.6 % respectively, toward medication disposal. This is because most participants responded positively, with a response of over 70 % in all the assessed questions in Table 2. It is revealed that 74.7 % of respondents' thoughts of disposing of unused or expired medication bother them. These results agree with similar studies in Palestine and Saudi Arabia, which shows that 87.3 and 79 % of the participants are in agreement that improper disposal of medications will negatively affect the environment and its inhabitants [1,20].

Also, 82.8 % of respondents believed it is their responsibility to protect the environment from the harmful effects of pharmaceutical wastes. Similar studies on community pharmacists reported similar trends, with 93.8 % of the participants agreeing to be responsible for protecting the environment [1]. It is also imperative to note that a study of the knowledge, attitudes, and practices of healthcare professionals in Delhi on medication disposal shows that most healthcare professionals expressed their concerns towards protecting the environment [19]. Therefore, these

findings proved that healthcare professionals have a good attitude towards medication disposal irrespective of their profession, as contained in the findings with a p -value of 0.089.

The findings revealed that 42.1 % of the respondents had poor practice toward medication, with nurses contributing to the highest percentage (41.8 %). This is evident when 63.1 % of respondents reported not having recently attended any seminar, workshop, or CME on medication disposal. Therefore, attending seminars, workshops, and CME will improve the practice of healthcare professionals toward medication disposal. This is supported by findings in Palestine and Saudi Arabia, which show that participants who had previously attended courses had a higher level of awareness and good practice than others [1,20].

Of the preferred methods of medication disposal, most respondents choose returning it to the hospital or pharmacy, followed by placing it in the garbage and then flushing it in the toilet. This is evident in research conducted among community pharmacists in Nigeria, where most respondents choose a regulatory agency as the main route for disposing of their expired or unused medication [8]. These disposal methods were also previously reported by [1,19,21]. The strength of this study is the consideration of all healthcare professionals that directly interact with patients or patients' relatives, and their knowledge, attitude, and practice toward the disposing of unused or expired medications will help in addressing current challenges of improper disposal of unused or expired medications in society. Additionally, the findings will guide policymakers all over the world to form an informed decision that will address improper medication disposal, hence safeguard the environment while also helping in achieving the "One Health" initiative of the United Nations. One limitation of this study is the inability to reach the desired sample size, coupled with its self-reported online design, which may affect the reliability of response.

CONCLUSION

This study expressed a significant gap in the knowledge and practice level of healthcare professionals, with the majority having poor knowledge and practice toward unused and expired medication disposal. Despite the availability of guidelines, more work needs to be done in updating and implementing the guidelines while ensuring strict compliance with the guidelines. The government should also employ methods to ensure healthcare workers are well-trained in schools and provide regular

training to have up-to-date knowledge on medication disposal.

DECLARATIONS

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Ethical approval

The study protocol was reviewed by the Institutional Research and Ethics Committee of the Faculty of Pharmacy, Bayero University, Kano, Nigeria (approval no. SIU/IEC/914).

Use of Artificial intelligence/Large language models

The authors confirm that AI-based tools were used solely for language editing and manuscript polishing purposes (e.g., grammar, phrasing, and clarity). No AI tools were used to generate content, interpret data, or influence study design, results, or conclusions. All intellectual contributions, study analyses, and interpretations reported in the manuscript are the original work of the authors.

Use of Research Reporting Tool

The STROBE guidelines for reporting observational studies were used.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. U.S.H. conceptualized the idea and designed the method. U.S.H., N.A.S., and K.A.I. collected the data. U.S.H. wrote the first draft of the manuscript. K.A.I., M.A.Y., M.T.I., N.A.S., and

U.I.I critically reviewed, edited, and add intellectual content to the final draft of the manuscript. All authors contributed to the writing of the manuscript and approved the final version.

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