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Original Research

Source of medicines and medicine information by self-reported persons living with hypertension and diabetes in rural and urban Ghana

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Abstract

Objectives: This study was conducted to determine the source of medicines and medicine information of persons living with hypertension and diabetes in rural and urban Ghana and assessing if they are influenced by predisposing and enabling factors as defined by Andersen's behavioural model.

Methods: A population based cross sectional study was conducted in four (4) rural and four (4) urban districts in the Ashanti Region of Ghana. A multistage and proportional sampling method was used in enrolling participants aged 18 years and above. A pre-tested structured questionnaire was used to collect primary data from respondents. Data collected was exported to STATA for analysis. Descriptive analysis was performed. Chi-square tests/Fisher's exact test and multinomial logistic regression models were used to establish association between variables.

Results: A total of 336 self -reported persons with hypertension and diabetes were enrolled in the study with 199(59.23%) living in urban communities. The majority of participants with hypertension and diabetes living in the rural communities 77 (56.20%) were females contrasting with the male majority in urban communities 106 (53. 27%). In the rural communities, 49 (35.77%) of participants sourced medicines from the health centre while 45 (32.85%) and 35(25.55%) sourced medicines from the hospital and over the counter medicine shop (OTCMS) respectively. In the urban communities, 153 (76.88%) sourced medicines from the hospital while 33 (16.58%) sourced medicines from the pharmacy. The predisposing factor age (OR: 1.1, 95%CI 1.040-1.210) under OTCMS, age (OR 1.0, 95%CI: 1.002-1.066) under hospital and enabling factor socioeconomic status (OR: 0.3, 95%CI 0.085-0.855) under Hospital influenced participant's source of medicine in the urban communities. The results also revealed that majority of participants in both rural 99 (72.26%), and urban 164 (82.41%) communities sourced medicine information mainly from public healthcare facilities, pre-disposing factors; age (OR 1.1 95%CI 1.032-1.270) under family member, age (OR 1.1, 95%CI 1.022-1.167) under friend health professional, age (OR 1.1, 95%CI 1.050-1.147) under nearest health institution, marital status (OR: 0.004, 95%CI 0.003-0.441) under friend health Professional were found to influence participants' source of medicine information in the urban communities while in the rural communities the predisposing factor marital status (OR 10.6, 95%CI 1.044 -106.835), education (OR: 26.1, 95%CI 1.271-537.279) under friend health professional, age (OR 1.1, 95%CI 1.002-1.187), educational level (OR 30.6, 95%CI 1.718-546.668) under nearest health institution and enabling factor socio-economic status (OR 6.6, 95%CI 1.016 -43.510) under nearest health institution influenced one's source of medicine information.

Conclusions: Majority of inhabitants with hypertension and diabetes in both rural and urban communities, sourced medicines and medicine information from public health institutions though a larger proportion was recorded in the urban communities. More participants in the rural communities than in the urban communities sourced medicines and medicine information from community pharmacies. Participants' source of medicine and medicine information was influenced by both predisposing and enabling factors.

Keywords

Hypertension; Diabetes Mellitus; Prescription Drugs; Health Services Needs and Demand; Pharmacies; Pharmacists; Surveys and Questionnaires; Multivariate Analysis; Ghana

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INTRODUCTION

Non-communicable diseases (NCD) are now the leading cause of death worldwide. Sixty three percent (63%) of all annual deaths (which translates into over 36million deaths) are attributed to NCDs. About 80% of NCD deaths occur in low and middle income countries. Globally, cardiovascular diseases account for about 17 million deaths a year, nearly a third of the total deaths. Cardiovascular diseases have been identified to account for about a third of all deaths in

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middle income countries.[1] Complications from hypertension also accounts for 9.4 million deaths worldwide annually.[2]

Medicines are vital in achieving optimal health outcomes in a wide range of medical conditions.[3] However, irrational use of medicines may lead to adverse events or result in the waste of scare re-sources impacting negatively on an individual health status.

Patient outcomes are likely to improve if this information is understood and used effectively.[4] Although there has been an increased global attention to medicines, there are still problems associated with access to essential medicines especially in the management of chronic diseases in Low Medium Income Countries.[4] Inequities in the access to health care delivery lead to poorer individuals having difficulty in accessing healthcare as compared to the richer individuals.[5] To ensure an effective health system for any community, the healthcare seeking behaviour of the inhabitants should be considered in the development of healthcare policies and the design of programmes.[6] Achieving and sustaining health involves a multifaceted interaction between the individual's health needs, the social linkage in which the individual is entrenched, and the health systems available to meet these health needs.[7]

Health services in Ghana have been decentralized as part of health sector reform, services are therefore integrated as one goes down the hierarchy of the health structure from the national to the sub-district level. Curative and public health services are provided at the regional and district hospitals mostly mission or faith-based facilities. Most district hospitals with a bed capacity of 60-80 serve an average population of 100,000 - 200,000 inhabitants in a defined geographical area. At the sub-district level, both preventive and curative services are delivered by the health centres. Outreach programmes to the communities within sub districts are usually supervised by the District Health Management Team (DHMT) but offered by the health centres. Community-based Health Planning and Services (CHPS) have been introduced to manage minor ailments at the community and household level. Most district capitals have a district hospital that provides health care to inhabitants in the capital and adjoining towns. The private sector plays a very important role in the healthcare delivery system.

In most districts private hospitals, pharmaceutical shops and over the counter medical sellers play a significant role in meeting the medical needs of inhabitants. It is reported that services sought over the counter are on the rise.[8] Private health facilities on the other hand are increasingly being accepted by inhabitants in sub-Saharan Africa. Although the private health centres have its own challenges such as an observation made in a study by Tripti *et al*. (2014) which reported prescription errors in about half of total drugs requests submitted.[9] In Ghana, there is dearth of in-formation regarding source in public or private health facilities. Asigbie *et al*. (2016) raised concerns on equity and quality of pharmaceutical products offered in the various health centres in-country.[10]

This study focuses on sources of medicine and medicine information by persons with hypertension and diabetes in both rural and urban communities in Ghana. The study further assesses predisposing and enabling factors (as defined by Andersen's behavioural model of health service utilization) that influence participants' source of medicine and medicine information. Understanding the health seeking behaviour particularly on medicinal access by chronic patients, who are known to be increased medicine users[11,12] will offer useful policy guidelines on managing pharmaceutical supplies and information for efficient use.

METHODS

Study design

A population based cross-sectional study design was employed to determine the disease burden of persons, living in rural and urban districts of the Ashanti Region of Ghana. The study was carried out from January 2016 to March, 2016.

The study was conducted in four (4) rural and four (4) urban districts in the Ashanti Region of Ghana. Ashanti region is one of the 10 regions in Ghana with a population of 4,780,208 representing 19.4% of the country's population. It is therefore the highest populated region with a growth rate of 2.7% and an urban: rural population ratio of 1.5:1 and is located in the central belt of the country.

Study population

The study included persons at least 18 years of age, who have resided in the study area for not less than 2 years and consented to be part of the study.

A multi-stage sampling technique was used in selecting a representative sample from both the rural and urban population (online Appendix). The rural districts were defined as districts that had more that 50% of their in-habitants in rural communities as indicated by the 2010 population census report. Out of the 30 districts in the region 17 and 13 were categorized as rural and urban out of which 4 districts were randomly chosen. Five of the communities among the 20 largest communities as provided by the 2010 population and housing census report were randomly sampled. The number of prospective participants from each community was determined by calculating proportionally based on the 2010 population census report for each district. Every community was then divided into 4 clusters, and equal numbers of participants were recruited from each cluster.

The sample size for the survey was calculated to obtain a representative sample to estimate the population prevalence of NCD with a good precision. The sample size was therefore calculated using the formula as illustrated below:-

$$n= Z2 *p (1-p) /d2 + (Z2 *p (1-p)/N)$$

Where n = sample size
Z = statistic for a level of confidence-(CI 95%-1.96),
p= a rough approximation to the proportion (0.5)
d = allowable sampling error tolerated or accuracy of measurement (2.5%)
N=Total population of the selected districts

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Table 1. Demographic characteristics of persons with NCD (diabetes and hypertension)

Variable	Rural, N=137		Urban, N=199	
	Frequency	Percentage (%)	Frequency	Percentage (%)
Sex				
Male	60	43.80	106	53.27
Female	77	56.20	93	46.73
Age (years)	Median(IQR)=58.00(51.00-67.00)		Median(IQR)=54.00(45.00-63.00)	
<=25 years	4	2.92	3	1.51
26-35 years	3	2.19	11	5.53
36-45 years	15	10.95	39	19.60
46-55 years	38	27.74	55	27.64
56-65 years	37	27.01	54	27.14
>65 years	40	29.2	37	18.59
Marital Status				
Single	4	2.92	19	9.55
Married	82	59.85	135	67.84
Co-habiting	0	0.00	0	0.00
Separated	3	2.19	2	1.01
Divorced	11	8.03	5	2.51
Widowed	37	27.01	38	19.10
Religion				
Christian	104	75.91	174	87.44
Moslem	26	18.98	22	11.06
Traditionalist	1	0.73	1	0.50
Other	6	4.38	2	1.01
Educational Level				
None	47	34.31	27	13.57
Basic Level	69	50.36	48	24.12
Secondary Level	17	12.41	89	44.72
Tertiary Level	4	2.92	35	17.59
Income status				
Low	82	59.85	87	43.72
High	55	40.15	112	56.28
Socioeconomic status				
Low	54	39.42	14	7.04
Medium	26	18.98	34	17.09
High	20	14.60	25	12.56
Highest	37	27.01	126	63.32
Enrolled on the National Health Insurance Scheme				
Yes	119	88.15	190	95.96
None	16	11.85	8	4.04

IQR: Interquartile Range

Total Population Size = 2,465,180.

The minimum number of inhabitants required was one thousand five hundred and thirty seven (1537) however, to make up for incomplete responses by some of the study participants, an upward adjustment of 10% was done. One thousand seven hundred (1700) participants were therefore proposed as the sample size to be enrolled. Furthermore, to allow for the comparison of urban and rural populations, proportionate sampling of the urban and rural population was done based on a ratio of 3:2, 1000 inhabitants were therefore proposed to be recruited from the urban population and 700 inhabitants to be recruited from rural populations.

Ethics approval

Approval was sought and obtained from the Committee on Human Research Publications and Ethics (CHRPE), of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology (Approval number: CHRPE/AP/503/17). Participants were given comprehensive information on the purpose of the study, and the potential risks and benefits of the study by the trained data collectors. Voluntariness to participate in the study was stressed in the process. Participants who agreed to participate were then made to sign whiles illiterate participants were made to thumbprint the informed consent document to affirm their willingness to participate in the study.

Data collection

A structured questionnaire was designed based on the research objectives. The UNDP Global Multi-dimensional poverty index questionnaire served as a guide in developing the measure of income and socioeconomic status. Sixteen

Table 2. Study participants NCD status

NCD Status	Rural		Urban	
	Number (N=137)	Percentage (%)	Number (N=199)	Percentage (%)
Diabetes Only	26	18.98	28	14.07
Hypertension and Diabetes	11	8.03	24	12.06
Hypertension only	100	72.99	171	73.87

Table 3. Chi Square Test on Place of Residence of Participants (NCD) and Sources of Medicines

Source of medicines	Rural, n(%), N=137	Urban, n(%), N=199	P value
OTCMS	35(25.55%)	9(4.52%)	<0.001*
Family member	0(0.00%)	1(0.50%)	
Health Centre	49(35.77%)	3(1.51%)	
Hospital	45(32.85%)	153(76.88%)	
Pharmacy	4(2.92%)	33(16.58%)	
Others	4(2.92%)	0(0.00%)	

OTCMS- Over the Counter Medicine Shop. *Fischer Exact Test.

data collectors were recruited, two data collectors were assigned to each rural and urban district. Data collectors were invited for a one-day training programme to ensure standardization of the questionnaire. The sixteen trained data collectors pre-tested the questionnaire to ensure reliability and validity in non-selected communities. Data was then collected electronically after informed consent had been obtained from opinion leaders and from prospective participants in the selected communities. The questionnaire was used to solicit information on self-reported NCD status (defined as either having hypertension or diabetes or both), demographic characteristics of participants and source of medicines and medicine information (e.g. dosage and side effects) for managing NCD. Predisposing and enabling factors that influence the source of medicines and medicine information were also obtained.

Table 4. Sources from which participants with NCD sought Medicine Information

Source of Medicine Information	Rural, n(%) N=137	Urban, n(%) N=199	p value
Family Member	11(8.03%)	3(1.51%)	<0.001*
Friend Health Professional	19(13.87%)	7(3.52%)	
Pharmacy	1(0.73%)	24(12.06%)	
Nearest Health Institution	99(72.26%)	164(82.41%)	
OTCMS	6(4.38%)	0(0.00%)	
Others	1(0.73%)	1(0.50%)	

Nearest Health Institutions: Public Hospital, Health Centre. *Fischer Exact Test for Trend.

Data Analysis

The data were exported to Stata version 13.0 (StataCorp. 4905 Lakeway Drive Station, Texas 77845, USA) for statistical analysis. Basic summary statistics of socio-demographic variables were conducted. Respondents self-reported their NCDs status. Wealth index was constructed for income and socio-economic status of the study respondents. The index was constructed from household asset data using principal components analysis.[13] Income status index was built from three main income variables: Number of people who earn an income in the household, average monthly income of the household and an additional money support to the household. The income status index was categorized as low and high based on

Table 5. Multinomial Logistics Regression test of Predisposing factors and Source of Medicine in the urban and rural communities of the Ashanti Region

Source of Medicine	Urban				Rural			
	OR	p value	[95% CI]		OR	p value	[95% CI]	
Pharmacy (base outcome)								
OTCMS								
Age	1.1	0.003	1.040	1.210	0.9	0.266	0.866	1.040
Sex (male=ref)								
Female	1.1	0.950	0.188	5.947	0.6	0.664	0.040	7.729
Marital Status (not married = ref)								
Married	2.0	0.459	0.326	11.995	3.0	0.411	0.216	42.406
Educational Level (none = ref)								
Educated	2.1	0.574	0.160	27.385	2.0	0.551	0.203	19.781
Occupation (Unemployed = ref)								
Employed	4.3	0.290	0.286	65.739	1.0	0.985	0.041	23.084
Health Centre								
Age	1.0	0.626	0.879	1.081	1.0	0.438	0.882	1.056
Sex (male = ref)								
Female	1.7	0.682	0.125	24.002	0.6	0.715	0.046	8.263
Marital Status (not married = ref)								
Married	2.4	0.559	0.133	41.915	2.8	0.441	0.208	36.833
Educational Level (none = ref)								
Educated	-	-	-	-	0.8	0.835	0.087	7.179
Occupation (Unemployed = ref)								
Employed	0.3	0.394	0.016	5.090	1.0	0.980	0.053	17.676
Hospital								
Age	1.0	0.040	1.002	1.066	1.0	0.456	0.883	1.057
Sex (male = ref)								
Female	1.0	0.988	0.447	2.264	1.2	0.905	0.087	15.822
Marital Status (not married = ref)								
Married	2.1	0.088	0.896	4.886	1.8	0.648	0.136	24.757
Educational Level (none = ref)								
Educated	1.0	0.964	0.323	3.264	2.0	0.538	0.217	18.700
Occupation (Unemployed = ref)								
Employed	0.9	0.836	0.305	2.612	3.2	0.462	0.144	71.414

OR: Relative Odds ratio. CI: Confidence interval. ref: Reference point. $p < 0.05$ was considered statistical significant.

Table 6. Multinomial logistics regression test of enabling factors and source of medicines in the urban and rural Communities of the Ashanti region

Source of Medicine	Urban				Rural			
	OR	p value	[95% CI]		OR	p value	[95% CI]	
Pharmacy (base outcome)								
OTCMS								
Income Status (low = ref)								
High	4.5	0.091	0.786	25.901	5.0	0.189	0.453	54.637
Socio-economic status (high = ref)								
Low	-	-	-	-	-	-	-	-
NHIS (no = ref)								
Yes	0.2	0.250	0.009	3.447	-	-	-	-
Health Centre								
Income Status (low = ref)								
High	-	-	-	-	1.2	0.863	0.108	14.183
Socio-economic status (high = ref)								
Low	-	-	-	-	-	-	-	-
NHIS (no = ref)								
Yes	-	-	-	-	-	-	-	-
Hospital								
Income Status (low = ref)								
High	1.7	0.196	0.768	3.633	9.1	0.069	0.843	97.918
Socio-economic status (high = ref)								
Low	0.3	0.026	0.085	0.855	-	-	-	-
NHIS (no = ref)								
Yes	0.7	0.718	0.075	5.939	-	-	-	-

OR: Relative Odds ratio. CI: Confidence interval. ref: Reference point. $p < 0.05$ was considered statistical significant.

scree plot of eigenvalues after principal component analysis. Access to basic utilities, sources of drinking water, and water treatment practices; access to sanitation facilities, housing structure; crowdedness of dwelling spaces; and type of fuel used for cooking are physical characteristics of a household that are used to assess the general well-being and socioeconomic status of house-hold members.[13] Socio-economic status index for this study was constructed from thirteen variables using principal component analysis: earned an income, average monthly income, received additional support, completed senior secondary school, under-five children death, number of school going of under-five children, number of rooms, type of materials used to make the wall of the house, house wired, have toilet facility, type of toilet facility, type of fuel and number of meals served in a day in household The socio-economic status index was categorized as low, medium and high and highest based on scree plot of eigenvalues after principal component analysis. Chi-square test of association or Fisher's Exact where appropriate was used to compare categorical variables and Health Seeking Behaviour (HSB). Finally, Multinomial logistic regression model was used to establish an association between HSB and predisposing, and enabling factors as proposed by Andersen's behavioural model of Health Services. Multinomial logistic regression model is suitable for comparing more than two possible outcomes; it picks a base category and calculates the odds (Relative Odds, OR) of the other possible outcomes relative to it.

RESULTS

Demographic characteristics

A total of 1703 participants were enrolled, 1019 from the urban population and 684 from the rural population. The findings revealed 336 participants self –reported they had NCD (Diabetes and Hypertension) made up of 137 in the rural communities and 199 in the urban communities. The find-ings of this study showed that the highest percentage of participants living in the rural communities with NCD were above 65 years. The median age in the rural population was 58 (IQR: 51-67). While in the urban population the highest percentage of participants living with NCD were between the ages 46-55 years. The median age of the urban population was 54 (IQR: 45- 63) (Table 1). Participants living in both the rural and urban communities were predominantly Christians and married (Table 1). The majority of participants with NCD living in the rural 77 (56.20%) communities were females while majority in the urban 106 (53. 27%) communities were males. About half of the participants with NCD in the rural communities 69 (50.29%) had attained basic education, while 47 (34.31%) had no formal education. In the urban communities, 89 (44.72%) had secondary education, while 27 (13.57%) had no formal education.

In the rural communities 82 (59.85%) of the participants were in the low income bracket, while 112 (56.28%) of the participants in the urban communities were found in the high income bracket (Table 1). About 88% of participants with NCD (88.15%, 119/137) in the rural and 95.96% (190/199) in the urban communities had registered with the National Health Insurance Scheme (NHIS) (Table 1).

Source of Medicine

The findings indicated that participants with NCD in the rural communities sourced medicines mainly from the health centre 49 (35.77%) followed by sourcing from the hospital in the urban areas 45 (32.85%). In the urban communities, the majority of participants 153 (76.88%) sourced medicines from the hospital while 33 (16.58%) indicated the pharmacy was their source of medicines. In

Table 7. Summary of Multinomial Logistics Regression test of Predisposing factors and Source of Medicine information in the rural communities of Ashanti

Source of Medicine Information	Urban				Rural			
	OR	p value	[95% CI]		OR	p value	[95% CI]	
Pharmacy (base outcome)								
Family Member								
Age	1.1	0.011	1.032	1.270	1.0	0.517	0.941	1.129
Marital Status (Not married = ref)								
Married	0.9	0.922	0.040	18.253	2.3	0.484	0.228	22.544
Educational Level (none = ref)								
Educated	-	-	-	-	10.2	0.142	0.462	223.926
Occupation (Unemployed = ref)								
Employed	2.1	0.661	0.074	60.987	-	-	-	-
Friend Health Professional								
Age	1.1	0.009	1.022	1.167	1.1	0.171	0.973	1.167
Sex (male = ref)								
Female	-	-	-	-	-	-	-	-
Marital Status (Not married = ref)								
Married	0.04	0.009	0.003	0.441	10.6	0.046	1.044	106.835
Educational Level (none = ref)								
Educated	-	-	-	-	26.1	0.034	1.271	537.279
Occupation (Unemployed = ref)								
Employed	0.7	0.732	0.088	5.533	0.8	0.868	0.038	15.787
Nearest Health Institution								
Age	1.1	<0.001	1.050	1.147	1.1	0.044	1.002	1.187
Marital Status (Not married = ref)								
Married	0.7	0.474	0.208	2.074	6.0	0.090	0.756	48.331
Educational Level								
Educated	3.6	0.058	0.956	13.219	30.6	0.020	1.718	546.668
Occupation (Unemployed = ref)								
Employed	1.4	0.649	0.360	5.155	2.2	0.560	0.158	30.327

OR: Relative Odds ratio. CI: Confidence interval. ref: Reference point. $p < 0.05$ was considered statistical significant.

the urban communities the family member was least utilized as a source of medicine (Table 3).

A Fisher exact test of independence on the above trend observed in Table 3 indicates that there is a statistically significant difference among participants with NCD, place of residence and source of medicine (p-value<0.001) (Table 4)

Source of Medicine Information

The majority of participants with NCD in the rural 99 (72.26%) and the urban 164 (82.41%) communities sourced medicine information from the nearest health institution. In the rural communities, other sources of medicine information were from health professional friends 19 (13.87%) while in the urban communities it was from the pharmacy. A Fisher exact test of independence indicated an association between participant's place of residence and source of medicine information (p-value<0.001) (Table 4).

A test for association using the multinomial logistic regression model revealed that there was no relationship between participants with NCD and their health seeking behaviour in the rural communities with respect to source of medicine. In the urban communities, participants with NCD with increasing age were 10% (OR 1.1, 95%CI 1.040 - 1.210 p =0.003), more likely to source medicines from Over the Counter Medicine Shop (OTCMS) and 1.0 times (OR 1.0, 95%CI 1.002 -1.066 p=0.040), likely to source medicine from the hospital than the pharmacy (Table 5). The results also indicated that participants with low socioeconomic status were 0.3 times more likely to source medicines from the hospital than from the pharmacy (OR 0.3, 95%CI 0.085 - 0.855 p=0.026) (Table 6).

Furthermore, the relative odds for married and educated participants with NCD in the rural communities were 10.6 times (OR 10.6, 95%CI 1.044 -106.835, p=0.046), and 26.1 times (OR 26.1, 95%CI 1.271 - 537.279, p=0.034) more likely to seek information on medication from a friend Health Professional than from the pharmacy respectively.

With increasing age, participants were 1.1 times (OR 1.1, 95%CI 1.002 - 1.187, p=0.044), more likely to seek information on medication from the nearest health institution, than from a pharmacy. Again, participants with NCD in the rural communities who were educated were 30.6 times (OR 30.6, 95%CI 1.718 - 546.668, p=0.020), more likely to obtain information on their medication from the nearest health institution than from the pharmacy. Also, low socio-economic status of participants with NCD in the rural communities were 60% (OR 6.6, 95%CI 1.016 - 43.510), likely to seek information on medication from the nearest health institution than from the pharmacy (Table 8).

In the urban communities, increasing age of participants with NCD were 1.1 times (OR 1.1, 95% CI 1.032 - 1.270, p=0.011), likely to seek information on medication from a family member rather than from the pharmacy.

The results also revealed that with increasing age and been educated were 1.1 times (OR 1.1, 95%CI 1.022 - 1.167, p=0.009) and 0.04 times (OR 0.04, 95%CI 0.003 - 0.441) likely to source medicine in-formation respectively from a friend health professional than the pharmacy.

Table 8. Multinomial logistics regression test of enabling factors and source of information medicines in the rural communities of the Ashanti region

Source of Medicine	Urban				Rural			
	OR	p value	[95% CI]		OR	p value	[95% CI]	
Pharmacy (base outcome)								
Family Member								
Income Status (Low = ref)								
High	0.5	0.603	0.040	6.469	-	-	-	-
Socio-economic status (High = ref)								
Low	-	-	-	-	2.4	0.411	0.294	20.078
NHIS (no = ref)								
Yes	-	-	-	-	1.9	0.612	0.152	24.636
Friend Health Professional								
Income Status (Low = ref)								
High	0.9	0.856	0.153	4.765	-	-	-	-
Socio-economic status (High = ref)								
Low	0.7	0.814	0.066	8.431	0.4	0.386	0.044	3.348
NHIS (no = ref)								
Yes	-	-	-	-	1.6	0.704	0.133	19.752
Nearest Health Institution								
Income Status (Low = ref)								
High	1.6	0.301	0.659	3.852	-	-	-	-
Socio-economic status (High = ref)								
Low	0.3	0.052	0.072	1.010	6.6	0.048	1.016	43.510
NHIS (no = ref)								
Yes	-	-	-	-	0.3	0.285	0.021	3.096

OR: Relative Odds ratio. CI: Confidence interval. ref: Reference point. $p < 0.05$ was considered statistical significant.

In the urban communities, participants with NCD, with increasing age were 10% (OR 1.1, 95% CI 1.050-1.147), more likely to source medicine information from the nearest health institution than from the pharmacy.

DISCUSSION

Source of medicines

The Ghana health system operates at different levels: from the CHPS compounds being the lowest, to health centres, polyclinics, district and private hospitals, regional and tertiary hospitals being the highest. The services that are provided differ at each level and becomes more sophisticated as the level rises. Although the gate-keeper referral system is proposed by the MOH in collaboration with NHIS in a number of circumstances self- referral takes place because some of the facilities are not well re-sourced. The results revealed that most participants with hypertension and diabetes in the rural communities sourced medicines from the health centre while in the urban communities, the participants' source of medicines was from the hospital. This compares with a study conducted in Brazil where medications were mainly obtained with a medical prescription at the pharmacy or hospital.[14] In South Africa, chronic dispensing units are set up as the main sources of medications for stable patients with chronic conditions.[15] This practice is different from what pertains in Ghana, where patients with chronic diseases do not have designated places for medicines. Participants with hypertension and diabetes in both communities also obtained medicines from health institutions in the public sector, presumably, when they go for regular follow up visits. Most of the participants with hyperten-sion and diabetes are enrolled on the NHIS and hence are entitled to free medicines for the manage-ment of hypertension and diabetes when they go on follow–up visits.

Access to medicines plays an important role in the health care delivery system. It serves as an input that should be available for an efficient and effective service delivery. It has been found that health systems are usually strengthened when adequate structures are in place to ensure equitable access to good quality medicines.[16] In the rural communities there was no significant association between predisposing and enabling factors and source of medicine by participants after multinomial analysis. In the urban communities however, increasing age was associated with a more likelihood to source medicines from the Over the Counter Medicine Shop (OTCMS) than the pharmacy and an equal likelihood to obtain medicines from the hospital as pharmacy. Participants with hypertension and diabetes in the urban communities have more access to pharmacies than in the rural communities; likewise, also they are able to obtain medicines from the hospital as well. This finding compares with a study that identified age as a predisposing factor among others that influences health service utilization.[17] Essential medicines have been found to be a foundation of almost all public health programmes that aim at reducing morbidity and mortality.[18] Access and source of medicines therefore form part of the essential services that should effectively be accomplished to ensure improved health outcomes. The multinomial logistic regression analysis indicated that there was no significant association between the enabling factors of sourcing of medicines in the rural communities. However, in the urban communities, participants within low socioeconomic status were less likely to source medicines from the hospital than the pharmacy. This practice was observed since participants, especially those enrolled on NHIS could obtained their medications at the pharmacy. This finding is similar to a study conducted in Cambodia where it was

found that the social health systems in place ensured that persons with hypertension and diabetes had access to medicines appropriate for the management of disease conditions.[19] Availability of medicines alone however does not ensure improved health outcomes.[20]

Source of medicine information

The relevance of medicine information through education and counselling empowers patients in decision making, which can ultimately improve patient outcomes.[21] A study conducted in Finland indicated that parents' source of information regarding their children's medicine use regardless of the age was from health professionals, mostly from the physician and from patient information leaflet. Parents further indicated that information obtained from health care professionals including physicians and pharmacist were found to be reliable.[22] In this study, similarly, majority of participants with hypertension and diabetes both in rural and urban communities mostly sought medicine information from the nearest health institutions. Results of this study differ slightly from a study conducted in the US where patients with rare disease conditions used physicians and the internet more often as their medication information source. Male patients were found to use their spouse/partner more often than did female patients. Female patients however, were more likely to use medication package inserts and the internet and were less likely to use nurses than were the male patients.[23,24] A study conducted among Arabic speaking Australians revealed that there was limited access to verbal and written medication and disease information, hence the over-reliance on health care practitioners who do not provide quality and adequate information.[25] The need to obtain reliable and valid information is very critical for patients who have non-communicable diseases, hence the source of medicine information should be acknowledged as an important tool in improving patient outcomes, as adherence to medication will usually be based on information obtained from the health professional.

The source of medicine or drug information for patients is usually preferred from the physician, while the pharmacist is mentioned as the second preferred source.[26] This assertion was confirmed in this study as participants in both the rural and urban communities indicated they obtained medicine information from the nearest health institution, while the pharmacy was the second preferred choice. Further analysis to determine what influenced participants' choice using the multinomial logistic regression test revealed association of increasing age, educational level attained and marital status in both urban and rural communities. Increasing age of participants, increased the relative odds of seeking information on medicines from a family member, friend health professional and nearest health institution than a pharmacy, and less likely for married participants to seek medicine information from a friend health professional in urban communities. This is similar to studies that propose that the physicians are a key source of medicine information.[26,27] In the rural communities, married status and educational level obtained by participants with hypertension and diabetes increased the likelihood to source information on medicines from a friend health professional; also increasing age and educational level, were likely to source information from the nearest health institution than the pharmacy.

The participants with low socio-economic status in rural communities preferred to obtain medicine information from the nearest health institution than the pharmacy. This could be as a results of pharmacies are not closer to the rural folds and they to travel a long distances to access them. However, in the urban communities none of the enabling factors shown statistical significance with medicine information.

Limitations

Participants were classified as hypertensive and or diabetic based on their self-report. This could results in a lower prevalence of the disease since some participants are usually in a state of denial when they are diagnosed of chronic diseases such as hypertension and diabetes. Furthermore, some participants might be having the conditions but have not yet been diagnosed.

CONCLUSIONS

Participants with hypertension and diabetes in rural and urban communities sourced medicine and medicine information similarly with a few variations. Most participants with hypertension and diabetes sourced medicines and medicines information from public health institutions- the healthcare centre in the rural communities and the hospital in the urban communities. A few participants in the rural communities sourced for medicine information from friends who were health professionals whereas in the urban communities a few also sourced medicine and medicine information from the pharmacy. Participants' source of medicines and medicine information were influenced differently by the predisposing factors: age, marital status, education and enabling factor, and socioeconomic status in rural and urban Ghana.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

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Original Research

Knowledge of pharmacists and parents towards antibiotic use in pediatrics: a cross-sectional study in Lebanon

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Abstract

Objectives: to assess the knowledge of both parents and community pharmacists regarding antibiotics use and resistance in pediatrics in Lebanon.

Methods: A cross-sectional study was conducted between June and August 2017 in community pharmacies. A pre-established questionnaire targeting knowledge of parents and pharmacists regarding antibiotics use/misuse was carried out. An index of knowledge was computed to assess factors associated with good knowledge on antibiotics use/misuse.

Results: The study showed that 28.7% of pharmacists did not know which factors may contribute to antimicrobial resistance. Concerning the misuse of antibiotics, pharmacists blamed at first parents (90.1%), at second level physicians (72.8%), and third themselves (59.4%). Furthermore, pharmacists believed that the socioeconomic problems of the country (86.1%), the level of resistance to the molecule of choice (80.8%), the lack of consultation time (71.2%) and the lack of national guidelines/recommendations (66.3%) might be additional factors contributing to antimicrobial resistance. In case of acute otitis media, the majority of pharmacists chose the correct treatment, dose and duration according to international guidelines; this was in contrast to the results obtained in case of pharyngitis. Female pharmacists had a significantly higher knowledge score compared to their male counterparts (ORa=2.51). Half of parents (42.6%) declared that antibiotics act against both viruses and bacteria, 55.9% still believe that the presence of fever requires the administration of antibiotics, 50% didn't know the consequences of antibiotics misuse, 58.4% said that it is okay to give their child antibiotics without a physician's advice or based on a pharmacist's recommendation, and 66.7% trusted the pharmacist in the antibiotic prescription. Parents with a university level of education or a master's degree had significantly better knowledge compared to illiterate ones (ORa=9.04 and ORa=16.46, respectively).

Conclusions: Based on the results obtained, it would be necessary to implement educational campaigns in order to increase awareness on antibiotics misuse and resistance in pediatrics.

Keywords

Health Knowledge, Attitudes, Practice; Anti-Bacterial Agents; Awareness; Pharmacies; Pharmacists; Parents; Surveys and Questionnaires; Multivariate Analysis; Lebanon

INTRODUCTION

Since their discovery decades ago, antibiotics brought lifesaving benefits and constitute today a major source of drug-related health expenditures.[1] They were behind the eradication of many serious bacterial infections, particularly in pediatrics.[2] Indeed, children are major consumers of antibiotics, with findings showing a higher intake among children aged 1 to 5 years (65%), in comparison with teenagers (38%). However, antibiotics consumption, whether in adults or children, has not been always rational or appropriate and errors could be encountered in the antibiotic indication, choice, dose or duration, administration or even adherence to therapy.[3,4]

Thus, 'antibiotics misuse', referring to the irrational use or overuse of antibiotics, might threaten any patient from all age groups and might concern any antibiotic.[5-7] It is increasingly contributing to antibiotic resistance, and is currently considered a serious public health concern globally, with a particular focus on developing countries.[8] In fact, self-medication with antibiotics, considered a major driver of antibiotics misuse, is highly prevalent in the latter countries where awareness and regulations often lack reinforcement.[9]

In Lebanon, similarly to other developing countries, although by law antibiotics are prescription drugs only, they are being dispensed by community pharmacists as over-the-counter drugs.[10,11] Patients from all ages (even children and elderly) can easily buy antibiotics (local, oral or injectable) from pharmacies without any medical prescription. Socioeconomic and cultural issues are particularly challenging in reducing antibiotics misuse in the country since half of the population has no social security coverage[10] and people frequently tend to self-medicate due to misconceptions or difficulties to afford a medical visit.[11,12] Moreover, the number of community pharmacies is continuously increasing, inversely to the price of medicines, making the situation even worse. Relevant studies estimated that around 40% of the population self-medicate with antibiotics[11-14]; they tend to acquire antibiotics for self-medication from a local community

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pharmacy or a friend or relative. They might also use an old prescription or some leftovers from a previous prescription-based dispensing.[13]

As for antibiotic misuse in pediatrics, although critical, it has been rarely tackled in epidemiological studies. It could be related to several factors, such as the medication itself (e.g. taste acceptability, dilution and conservation), or the treating pediatrician (e.g. watchful waiting approach) or even the pharmacist (e.g. referral to pediatricians). Moreover, parents or caregivers could contribute to antibiotics misuse through their poor compliance to treatment, lack of knowledge and general negative attitudes towards the disease and treatment.[15-17]

In this context, we conducted the present study to evaluate the knowledge of both community pharmacists and parents towards antibiotics use and resistance among pediatrics in Lebanon. We also aimed to identify factors associated with poor knowledge among parents and community pharmacists in order to identify gaps and priorities in public health interventions against antibiotics misuse in the country.

METHODS

Study and population

A cross-sectional study was carried out between June and August 2017 in a representative sample of Lebanese community pharmacies distributed all over the country (Beirut, Mount Lebanon, North, South and Bekaa).

First, an exhaustive list of pharmacies was provided by the Lebanese Order of Pharmacists in order to select a random sample of community pharmacies all across Lebanon (via Microsoft Excel random function). We selected the minimum required sample size to which we added a 30% expected refusal rate.

Second, we aimed to recruit one pharmacist (i.e. owner or employee) and one parent (i.e. first eligible participant) from each selected pharmacy. Thus, at each pharmacy visit, we invited the pharmacist to participate in the study and after taking his written consent, we interviewed him to fill in a pre-established questionnaire. Then we waited for the first eligible parent to enter the community pharmacy and accept to take part in the study to fill another questionnaire.

Eligible parents are mothers or fathers of at least one child aged 12 years or less, and having administered an oral antibiotic to their child at least once in the last 12 months. Excluded were those not completing the questionnaire, and parents who only had children aged more than 12 years.

Sample size calculation

We fixed our expected frequency of adequate knowledge at 50% in the absence of similar studies and chose a precision level of ±7%. The Epi-info software version 7.2 (population survey) calculated a minimum sample size of 196 for each group (pharmacists and parents) to ensure a confidence level of 95%. Thus, we selected 280 community pharmacies from the list of pharmacies to take into account a 30% refusal rate.

Compliance with Ethical Standards

The Institutional Review Board of the Lebanese University waived the need for an approval based on the facts that it was an observational study that respected participants' autonomy and confidentiality and induced minimal harm to them. A written informed consent was obtained from all parents and pharmacists prior to the beginning of the data collection.

Data collection

A face-to-face interview was conducted with the participants by two well-trained PharmD candidates, after explaining the study objectives to them. Separate questionnaires were used to evaluate knowledge in parents and pharmacists respectively; a mean duration of ten minutes was needed to fill the questionnaire.

Misuse of antibiotics

The European Centre for Disease Prevention and Control (ECDC) definition was used to evaluate antibiotics misuse. The latter englobed (1) the unnecessary prescription of antibiotics for viral infections, against which they have no effect; (2) the too frequent prescription of broad-spectrum antibiotics, in place of a better targeted antibiotic, through more precise diagnosis; and (3) the inadequate use by the patient, not respecting either dosage or duration of the treatment.[18]

Community pharmacists' questionnaire

The pharmacists' questionnaire was prepared in French and English, the two languages used in Lebanese universities during pharmacy studies. The first part of the questionnaire included sociodemographic characteristics (sex, age, educational level, years of experience, pharmacy location). The second part was comprised of 4 questions, which evaluated the pharmacist's knowledge regarding antibiotics use in pediatrics, antibiotic resistance and the factors promoting it, duration of use of antibiotics after reconstitution, preservation, the reasons that would affect the proper use of antibiotics in children (i.e., inappropriate behavior of parents, doctors, pharmacists, lack of time to update the knowledge, socioeconomic problems of the country, the level of resistance to first choice molecules, etc.). In addition, small case scenarios concerning ear infection and pharyngitis in pediatrics were set to assess their knowledge update, and the conformity to guidelines of the chosen antibiotic, dose, and duration of treatment. Guidelines used to assess conformity were those of the Infectious Disease Society of America (IDSA) (Streptococcal pharyngitis 2012 guidelines)[19] and the American Academy of Pediatrics (AAP) (Acute Otitis Media 2013 guidelines).[20]

Parents' questionnaire

The parents' questionnaire was prepared in Arabic, the native language in Lebanon. It first included a section on sociodemographic characteristics (i.e., gender, age, region, marital status, educational level, profession, family income, number of children). The second section evaluated the knowledge of parents regarding antibiotics use, spectrum of activity, side effects and risks, reconstitution and conservation, along with antibiotics misuse (i.e., definition, causes and consequences). Finally, we added some opinion

Table 1. Questions assessing pharmacists' knowledge about antibiotics use in children.

Questions	Answers	Points
In your opinion, which factor contributes the most to antibiotic resistance?	Low dose	1
	Long duration	1
For how long are antibiotics used after reconstitution?	According to antibiotics/ manufacturer	1
Should all antibiotics be placed in the refrigerator after reconstitution?	No	1
A children <2 years presenting with severe painful earache and fever> 39 ° C, does he require an antibiotic in your opinion?	Yes	1
First choice antibiotic?	Amoxicillin/ Amoxicillin-clavulanic acid	1
Dose?	80-90 mg/kg/day	1
Duration?	10 days	1
A child> 2 years presenting with earache and fever > 39°C, does he require an antibiotic in your opinion?	It depends on other factors	1
First choice antibiotic?	Amoxicillin/ Amoxicillin-clavulanic acid	1
Dose?	80-90 mg/kg/day	1
Duration?	5 to 7 days	1
A child presenting with pharyngitis (intense sudden onset) and fever> 39 ° C, does he require an antibiotic in your opinion?	It depends on other factors	1
First choice antibiotic?	Amoxicillin/ Amoxicillin-clavulanic acid	1
Dose?	50 mg/kg/day	1
Duration?	10 days	1
Maximum total score		16

questions on giving an antibiotic without a medical prescription.

We mainly used closed-ended questions in both questionnaires, particularly those related to antibiotics knowledge, and few open-ended questions (i.e. dose and duration of treatment).

Knowledge index

Several questions were used to calculate the pharmacists' knowledge index, with the correct answers identified according to the IDSA and AAP guidelines.[19,21] Answers choices were given a numerical value of 1 if correct (good knowledge) and 0 if incorrect (bad knowledge). The total pharmacists' knowledge index ranged between 0 (reflecting low knowledge) and 16 (reflecting high knowledge) (Table 1), whereas the parents' total knowledge index ranged between 0 and 18 (Table 2). Since there was no cut-off point to assess poor and good knowledge, we used the index median as a cut-off point. Scores above the median would reflect a good knowledge, while scores below the median would reflect a poor knowledge.

Statistical analysis

Data entry was performed by one lay person who was not involved in the data collection process. Descriptive statistics were calculated for all study variables. This includes means and standard deviations (or medians and interquartile ranges IQR) for continuous variables, counts and percentages for categorical variables. A bivariate analysis was done to assess factors associated with a good knowledge index using Pearson Chi-Square test or Fisher's exact test when applicable for categorical variables, and Student t-test for quantitative variables. Multivariate logistic regressions reporting adjusted Odds Ratios (ORa) were carried out using variables that showed a $p<0.2$ in the bivariate analysis[22,23]; potential confounders may be eliminated only if $p>0.2$, in order to protect against residual confounding.[24] In the logistic regression, the dichotomous knowledge index was used as the dependent variable, taking the median as the cut-off point. Moreover, Cronbach's alpha was recorded for reliability analysis for the knowledge index used in pharmacists and parents. The statistical package SPSS version 23 was used for all

Table 2. Questions assessing parents' knowledge about antibiotics use in children.

Questions	Answers	Points
In your opinion, antibiotics :		
Act on:	Bacteria	1
Treat all diseases of your children:	No	1
Could affect your children if given incorrectly:	Yes	1
Could have side effects even if administered properly:	Yes	1
Can be kept after reconstitution for:	7 to 10 days	1
Should be kept in the fridge	According to antibiotics/ manufacturer	1
In your opinion, misuse of pediatric antibiotics:		
Includes a bad:	Indication	1
	Choice	1
	Dose	1
	Duration	1
	Dilution	1
	Preservation	1
	Adherence	1
Leads to:	Side effects	1
	Treatment failure	1
	Recurrent infections	1
	Loss of immunity	1
	Bacteria resistant to antibiotics	1
Maximum total score		18

Table 3. Case scenarios

Questions \ Case		Child < 2 years old severe painful Otalgia, and Fever > 39°C	Child > 2 years old of Otalgia, and Fever > 39°	Child painful Pharyngitis (intense with a sudden onset), and Fever> 39 ° C
Require an antibiotic	Yes	117 (57.9%)	73 (36.1%)	85 (42.1%)
	No	22 (10.9%)	20 (9.9%)	25 (12.4%)
	Depends on other factors	48 (23.8%)	97 (48.0%)	78 (38.6%)
	I do not know	15 (7.4%)	12 (5.9%)	14 (6.9%)
First choice of antibiotics		N=138	N=137	N=127
	Amoxicillin	**27** (19.6%)	**14** (10.2%)	**8** (6.3%)
	Co-amoxiclav	**97** (70.3%)	**101** (73.7%)	**60** (47.2%)
	Cefdinir	3 (2.2%)	6 (4.4%)	10 (7.9%)
	Cefuroxime	-	-	6 (4.7%)
	Cefixime	1 (0.7%)	3 (2.2%)	26 (20.5%)
	Cefpodoxime	1 (0.7%)	5 (3.6%)	8 (6.3%)
	Ceftriaxone	3 (2.2%)	-	-
	Azithromycin	-	-	1 (0.8%)
	Clarithromycin	-	-	4 (3.1%)
	Any antibiotic	6 (4.3%)	8 (5.8%)	4 (3.1%)
Dose		N=118	N= 120	N=107
	In ml / per spoon	26 (22.0%)	34 (28.3%)	34 (31.8%)
	According to the instructions	10 (8.5%)	13 (10.8%)	17 (15.9%)
	According to the weight	9 (7.6%)	14 (11.7%)	18 (16.8%)
	According to age	3 (2.5%)	-	-
	According to the physician	4 (3.4%)	-	-
	In mg\kg	66 (55.9%)	59 (49.2%)	38 (35.5%)
Dose of amoxicillin		**N=124**	**N=115**	**N=68**
	50 mg/kg/d	2 (1.6%)	3 (2.6%)	4 (6%)
	80-90 mg/kg/d	57 (46%)	41 (36%)	3 (4.4%)
Duration of treatment	5-7 days	16 (12.9%)	80 (69.5%)	50 (73.5%)
	10 days	93 (75%)	19 (16.5%)	7 (10.3%)

statistical analysis. Statistical significance was set at $p<0.05$.

RESULTS

Pharmacists' results

The study population consisted of 202 community pharmacists (giving a response rate of 72.1%) among whom 51.5% females (median age 30 years; IQR 26 to 37 years). Half of them had a post-graduate degree (Pharm.D. or Master's or both), 39.6% were working in a pharmacy located in Mount Lebanon and 50% had a six-year work experience or more (IQR 2 to 11 years).

Fifty two percent of pharmacists declared that a low antibiotic dose would promote more antimicrobial resistance, while 37.1% reported the same for high doses, 37.1% for longer treatment durations and 39.6% for shorter durations (data not shown). It is important to note that 28.7% of pharmacists did not know which factors may contribute to antibiotic resistance. Moreover, 39.6% of pharmacists declared that antibiotics should be discarded 14 days after reconstitution, and 48% that not all antibiotics need to be refrigerated after reconstitution.

The majority of the pharmacists confessed that the inappropriate parental behavior (90.1%), the inappropriate behavior of physicians (72.8%), and that of pharmacists (59.4%) were the major causes of antibiotics misuse. Furthermore, pharmacists declared that the socioeconomic problems of the country (86.1%), the level of resistance to the molecule of choice (80.8%), the lack of consultation time (71.2%) and the lack of national guidelines/recommendations (66.3%) might be additional factors contributing to antibiotics resistance.

More than half of the pharmacists (57.9%) declared that a child <2 years, with severe painful otalgia, and fever >39°C requires an antibiotic. Amoxicillin/clavulanic acid was the first choice for 70.3% of pharmacists. Concerning the dose, 55.9% of the pharmacists confessed that the dose would be calculated according to the weight of the child. For amoxicillin or amoxicillin/clavulanic acid, 46% of pharmacists gave a dose of 80-90 mg/kg/day, for a duration of 10 days (75%).

In case of otalgia with a fever of > 39°C for a child aged more than 2 years, half of the pharmacists (48%) confirmed that the need for antibiotics depends on other factors. For those who gave an antibiotic, amoxicillin/clavulanic acid remained the first choice (73.7%), at a dose of 80-90 mg/kg/day (36%) and a duration of 5-7 days (69.5%).

In the case of a child with pharyngitis (intense with sudden onset) and a fever of >39°C, 42.1% of pharmacists confirmed the need to give an antibiotic; again, amoxicillin/clavulanic acid was the first choice for 47.2% of them (Table 3).

Before conducting the bivariate analysis to assess variables significantly associated with poor/good overall antibiotics knowledge among pharmacists, we calculated the reliability of the knowledge index to assess the quality of our data. High Cronbach's alpha was obtained (0.768). Based on fairly adequate internal consistency, we believe that the findings were relatively reliable.

The bivariate analysis, taking the dichotomous pharmacists knowledge index (low vs high knowledge) as the dependent variable, showed that a significantly higher percentage of males had poor knowledge compared to their female counterparts ($p<0.001$), whereas a significantly higher percentage of pharmacists in Beirut and South had poor

Table 4. Bivariate analysis of sociodemographic factors associated with the knowledge index among pharmacists.

Variables	Good knowledge (N = 95)	Poor knowledge (N = 107)	P-value
Sex			<0.001
Male	32 (32.7%)	66 (67.3%)	
Female	63 (60.6%)	41 (39.4%)	
Educational level			0.377
Bachelor degree	45 (46.9%)	51 (53.1%)	
PharmD.	33 (53.2%)	29 (46.8%)	
Master's degree	11 (34.4%)	21 (65.6%)	
PharmD. and Master	6 (50%)	6 (50%)	
District			0.006
Beirut	13 (38.2%)	21 (61.8%)	
Mount Lebanon	45 (56.2%)	35 (43.8%)	
North	7 (46.7%)	8 (53.3%)	
Bekaa	15 (68.2%)	7 (31.8%)	
South	15 (29.4%)	36 (70.6%)	
Age	33.42 ± 8.64	31.34 ± 7.53	0.076
Years of experience	6.96 ± 6.78	9.20 ± 8.03	0.034

knowledge (p=0.006). In addition, a significantly higher mean number of years of experience was found in pharmacists with poor knowledge (p=0.034). No significant difference was found for the educational level nor age (Table 4).

Table 5. Sociodemographic characteristics of the parents.

Variables	N	%	
Sex			
Mother	128	62.7	
Father	76	37.3	
Region			
Beirut	19	9.3	
Mount Lebanon	116	56.9	
Bekaa	12	5.9	
North	7	3.4	
South	50	24.5	
Nationality			
Lebanese	166	81.4	
Other	38	18.6	
Marital status			
Married	177	86.8	
Divorced	19	9.3	
Widowed	8	3.9	
Educational level			
Illiterate	12	5.9	
Primary	36	17.6	
Secondary	40	19.6	
University	80	39.2	
Higher education	19	9.3	
Technical	17	8.3	
Occupation			
Working full time	76	37.3	
Part-time contract	46	22.5	
Retired	4	2.0	
Student	11	5.4	
Housewife	52	25.5	
Physician/other health professional	6	2.9	
Unemployed	9	4.4	
Family income			
<$ 1,000	25	12.3	
$ 1000 $ -2000	36	17.6	
$ 2000 $ -4000	22	10.8	
> $ 4000	5	2.5	
No answer	116	56.9	
Medical coverage (Yes)	136	66.7	
Drugs coverage (Yes)	132	64.7	
	Median	IQR	
Age (in years)	31	27	38
Number of children per family	2	1	3

IQR: Interquartile range

Parents' results

The sociodemographic characteristics of the parents are summarized in Table 5. Two hundred and four parents were finally included (62.7% females; median age 31 years, IQR 27 to 38 years) into the study. Half of them were university graduates or postgraduates and 13% were divorced or widowed.

The results showed that 19.2% of parents still believe that antibiotics are active against viruses, whereas 42.6% thought they act against both viruses and bacteria. More than half of the parents thought antibiotics were given to treat fever (55.9%), cold (26%), sore throat (49.5%) and diarrhea (29.4%). The majority (95.1%) confessed that antibiotics should be administered following a physician's prescription, whereas 51.5% following the pharmacist's advice. Moreover, 38.2% knew that antibiotics could have the same side effects even when administered correctly, whereas more than half of them (52.5%) did not know the correct length of antibiotics storage after reconstitution. Only 21.6% knew that antibiotics should be kept in the fridge following the manufacturer recommendations.

Half of parents declared that antibiotics misuse is due to a bad indication or bad choice, whereas 40.2% and 39.7% declared that it is due to a bad dose or lack of adherence, respectively. Moreover, 58.8% said that antibiotics misuse would lead to loss of immunity, 38.7% to treatment failure and 44.6% to recurrent infections. More than half of respondents blamed parents for antibiotics misuse (56.4%), whereas 52.5% and 37.3% blamed physicians and pharmacists, respectively.

More than half of parents (58.4%) reported that it is okay to give antibiotics without a prescription if they were unable to visit a pediatrician, 23.6% if they had enough experience with children, 66.7% if they trusted their community pharmacist and 22.1% if they knew how to administer the antibiotic.

Before conducting the bivariate analysis to assess variables significantly associated with good overall antibiotics knowledge among parents, we calculated the reliability of the knowledge index to assess the quality of our data. We obtained a high Cronbach's alpha (0.788). Based on fairly adequate internal consistency, we believe that the findings were relatively reliable.

Table 6. Bivariate analysis of sociodemographic factors associated with the knowledge index among parents.

Variables	Good knowledge (N = 87)	Poor knowledge (N = 117)	P-value
Age	31.89 ± 7.13	32.78 ± 8.47	0.431
Number of children per family			0.026
≤ 2 children	63 (48.5%)	67 (51.5%)	
> 2 children	24 (32.4%)	50 (67.6%)	
Gender			0.480
Mother	57 (44.5%)	71 (55.5%)	
Father	30 (39.5%)	46 (65.5%)	
District			0.121
Beirut	9 (47.4%)	10 (52.6%)	
Mount Lebanon	56 (48.3%)	60 (51.7%)	
North	4 (57.1%)	3 (42.9%)	
Bekaa	4 (33.3%)	8 (66.7%)	
South	14 (28.0%)	36 (72%)	
Nationality			0.001
Lebanese	80 (48.2%)	86 (51.8%)	
Other	7 (18.4%)	31 (81.6%)	
Marital status			0.583
Married	73 (41.2%)	104 (58.8%)	
Divorced	10 (52.6%)	9 (47.4%)	
Widowed	4 (50.0%)	4 (50%)	
Educational level			<0.001
Illiterate	2 (16.7%)	10 (83.3%)	
Primary	5 (13.9%)	31 (86.1%)	
Secondary	14 (35.0%)	26 (65.0%)	
Technical	7 (41.2%)	10 (58.8%)	
University	46 (57.5%)	34 (42.5%)	
Master degree	13 (68.4%)	6 (31.6%)	
Occupation			0.231
Full-time work	37 (48.7%)	39 (51.3%)	
Part-time work	17 (37%)	29 (63%)	
Retired	1 (25%)	3 (75.0%)	
Student	6 (54.5%)	5 (45.5%)	
Housewife	21 (40.4%)	31 (59.6%)	
Physician/health professional	4 (66.7%)	2 (33.3%)	
Unemployed	1 (11.1%)	8 (88.9%)	
Monthly family income			0.424
<1000 $	9 (36.0%)	16 (64.0%)	
1000 $ -2000 $	16 (44.4%)	20 (55.6%)	
2000 $ -4000 $	13 (59.1%)	9 (40.9%)	
> 4000 $	3 (60%)	2 (40.0%)	
No answer	46 (39.7%)	70 (60.3%)	
Medical coverage			0.001
Yes	68 (51.5%)	64 (48.5%)	
No	19 (26.4%)	53 (73.6%)	

The bivariate analysis, taking the dichotomous parental knowledge index (low vs high knowledge) as the dependent variable, showed that a significantly higher percentage of parents with more than 2 children had poor knowledge compared to parents who had 2 children or less (p=0.026), whereas a significantly higher percentage of parents with poor knowledge was seen among illiterate or those with a primary level of education (p<0.001). No significant association was found between knowledge and age, gender, district, marital status, occupation, or monthly family income (Table 6).

The results of a first logistic regression, taking the dichotomous pharmacists' knowledge index as the dependent variable, showed that female pharmacists had a significantly higher knowledge index compared to their male counterparts (ORa=2.51), whereas those working in Mount Lebanon and Bekaa had a significantly higher knowledge index than those working in other regions (ORa=2.5 and ORa=3.77, respectively). The results of a second logistic regression, taking the dichotomous parents' knowledge index as the dependent variable, showed that parents with a university level of education or a master's degree had a significantly better knowledge compared to illiterate ones (ORa=9.04 and ORa=16.46, respectively) (Table 7).

DISCUSSION

To our knowledge, this is the first study in Lebanon to evaluate the knowledge of both community pharmacists and parents towards antibiotics use and resistance in pediatrics. It sheds light on important issues that should be addressed in order to enhance antibiotics appropriate use in children.

Pharmacists' results

The results showed that according to 52% of pharmacists, low doses play a major role in antibiotic resistance while little importance was given to the duration of treatment (37.1% longer and 39.6% shorter durations). What is true for the dose is wrong for the duration of treatment since

Table 7. Multivariable analyses of factors related to a good knowledge index.

Logistic regression 1 taking the dichotomous poor/good knowledge index among pharmacists.			
Covariates	**ORa**	**95% CI**	**p-value**
Age	1.04	0.94-1.14	0.487
Years of experience	0.94	0.84-1.05	0.260
Gender			
Males	1	-	-
Females	2.51	1.32-4.76	0.005
Region			
Beirut	1	-	-
Mount Lebanon	2.50	1.03-6.09	0.043
North Lebanon	1.59	0.44-5.70	0.479
Bekaa	3.77	1.15-12.32	0.028
South Lebanon	1.06	0.39-2.89	0.907
Logistic regression 2 taking the dichotomous poor/good knowledge index among parents.			
Covariates	**ORa**	**95% CI**	**p-value**
Educational Level			
Illiteracy	1	-	-
Primary	1.12	0.17-7.55	0.906
Secondary	3.95	0.44-35.36	0.219
Technical college	4.41	0.42-46.60	0.218
University	9.04	1.00-81.62	0.050
Master degree	16.46	1.57-172.41	0.019
Nationality			
Syrian	1	-	-
Lebanese	0.54	0.11-2.79	0.466
Region			
Beirut	1	-	-
Mount Lebanon	1.10	0.38-3.15	0.867
Bekaa	0.33	0.06-1.69	0.182
South Lebanon	0.59	0.18-1.96	0.384
North Lebanon	0.69	0.11-4.22	0.685
Number of children			
≤ 2	1	-	-
> 2	0.63	0.31-1.26	0.186
Medical coverage			
No	1	-	-
Yes	1.61	0.69-3.76	0.272

lower doses allow low-resistant bacteria to multiply and increase their chances of being resistant, while a long treatment duration (10 days or more) has a more negative effect by exposing bacteria to antibiotics for longer periods, thus promoting the survival of more resistant bacteria.[19]

Concerning antibiotics misuse, pharmacists mainly blamed parents for self-medicating their children with antibiotics to treat "all problems", a result similarly found in a Saudi Arabian study.[20] At a second level, both pharmacists and parents blamed physicians to misuse antibiotics in pediatrics. Furthermore, the majority of pharmacists believed that socioeconomic issues contribute to antibiotic resistance, in agreement with a previous study.[11]

For the otitis case scenario, our findings showed that the majority of pharmacists followed the AAP 2013 guidelines, with amoxicillin/clavulanic acid remaining the first choice of prescription for the majority of pharmacists for a period of 10 days for children <2 years old and 5 to 7 days for those >2 years old, in line with a previous study.[14] However, only half of pharmacists knew and followed the right dose. For the pharyngitis case scenario, a very small percentage of pharmacists followed the 2013 IDSA guidelines. It is plausible that they follow other guidelines or lack knowledge on recent guidelines.

Our findings revealed that female pharmacists had an increased knowledge concerning antibiotics use in children compared to males, in contrast to another study[25] that showed no gender differences. Unfortunately, we did not inquire pharmacists about their parental status which might be of interest to explain the results. In fact, a higher percentage of mothers among female pharmacists would lead to a better knowledge and expertise in pediatrics.

A significant negative association was also noted between years of experience and good knowledge towards antibiotics use; poor knowledge was found in pharmacists with a higher number of years of experience. Similar results were found in a Saudi Arabian study, showing that pharmacists with a job experience ranging between three to four years had better knowledge towards the appropriate use of drugs compared to those with a nine to ten-year experience.[26] Thus, continuous education and regular interventions are required to update and improve pharmacists' knowledge towards antibiotics use in pediatrics.

Parents' results

Parents are still confused about antibiotics spectrum of activity and only 42% knew that they were used for bacterial infection. This finding is in agreement with the result of another survey conducted in India where more than 45.9% of parents believed that antibiotics can be used to treat both bacterial and viral infections.[15] This may be attributed to the fact that while counseling, physicians

usually use the term 'germs' with antibiotics, rather than specifying bacteria.[27] Also, as mentioned by Rousounidis *et al*.[28], people do not understand the difference between bacteria and viruses and hence, believe that antibiotics are effective against both. Moreover, recent findings showed that pharmacists don't have enough time to counsel patients because of the decreased number of staff and the financial situation of community pharmacists in Lebanon.[29]

A high percentage of parents (55.9%) still believe that the presence of fever requires the administration of an antibiotic, a result consistent with another study.[21]

Only 21.6% of parents were aware that not all antibiotics need fridge after dissolution. The storage conditions are considered important manufacturing instructions and should be strictly followed; while some antibiotic suspensions require refrigeration, some others do not.[30]

Moreover, this study showed that half of parents did not know the consequences of antibiotics misuse (adverse effects, recurrent infection and the emergence of resistant bacteria, etc.). Parents' poor knowledge about the harm of non-selective use of antibiotics is another finding that urges the need to further educate parents about misuse repercussions.

In addition, 52.5% of parents blamed physicians for the misuse; the latter questioning the physician-parent relationship. An ineffective physician-parent communication is found to be incriminated in the unnecessary prescription of antibiotics. In fact, several studies reported short interaction time between pediatricians and parents due to work overload or lack of a regulated procedure to assist patients in understanding the disease and treatment.[31] Thus, it is important to prolong the interaction time and train both parents and pediatricians to adequately communicate in order to improve the child's health.

Another problematic finding is that 58.4% of parents declared that it was okay to give their child antibiotics without a physician's advice or based on a pharmacist's recommendation. This finding raises the issue of over-the-counter sale of antibiotics for children in Lebanon. Strong and urgent policies are needed to reduce this practice. It is better to make these changes in collaboration with pharmacies owners to ensure their commitment. Moreover, 66.7% of parents trusted the pharmacist in the antibiotic prescription, in agreement with another recent survey conducted in Saudi Arabia.[32] The latter result can be used for the delivery of future health education. In addition, the community pharmacy framework can also be a great way to provide good education on antibiotics. The Order of Pharmacists, the Ministry of Public Health and community pharmacists can collaboratively play a crucial role in enhancing public awareness about antibiotics use, misuse and antibiotic resistance.

Finally, a significant association was noted between the educational level and knowledge towards antibiotics use, in line with previous studies where people of lower educational levels were found to lack more knowledge regarding antibiotics use and resistance.[15,33]

Limitations

This study has several limitations. First, pharmacists included in the study were relatively younger than the target population which might overestimate their knowledge level regarding antibiotics use in pediatrics. Second, we included parents of other nationalities which might introduce a selection bias into the study. However, considering the study period, modalities and allowances, and considering the high ratio of refugees to Lebanese in 2017, we were not able to exclude them from the study and we decided to adjust our results in the multivariable analyses according to the participant's nationality. Third, an acquiescence bias might exist in the parents' questionnaire where participants tend to agree or give positive answers on all statements. Finally, knowledge indexes were just conceived to conduct logistic regressions on factors associated with good overall knowledge about antibiotics use in pediatrics. They need to be carefully considered while interpreting results since many knowledge items were not taken into consideration and case scenarios' conformity were based on American guidelines in the absence of national recommendations.

CONCLUSIONS

In a country where self-medication abundantly exists, it was necessary to conduct the present study to assess parents and pharmacists' knowledge towards antibiotics use and resistance in a vulnerable field, i.e. pediatrics. Results revealed gaps in knowledge among community pharmacists and parents on antibiotics misuse and resistance. A high percentage of parents still believe antibiotics work on viruses and find giving antibiotics to their child acceptable without a medical prescription. Higher educational levels among parents and lower years of experience among pharmacists were associated with a better overall knowledge in our study. Practice and patient simulated surveys should be conducted in community pharmacies to assess rates of antibiotics self-medication and misuse in pediatrics. Continuous education and awareness campaigns should mainly target older pharmacists and parents of low educational levels.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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Original Research

Evaluation of a vancomycin dosing nomogram in obese patients weighing at least 100 kilograms

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Abstract

Background: There remains variability in both practice and evidence related to optimal initial empiric dosing strategies for vancomycin.
Objective: Our primary objective was to describe the percentage of obese patients receiving vancomycin doses consistent with nomogram recommendations achieving targeted initial steady-state serum vancomycin concentrations. Secondary objectives were to describe the primary endpoint in subgroups based on patient weight and estimated creatinine clearance, to describe the rate of supratherapeutic vancomycin accumulation following an initial therapeutic trough concentration, and to describe the rate of vancomycin-related adverse events.
Methods: This single-center, IRB-approved, retrospective cohort included adult patients ≥ 100 kilograms total body weight with a body mass index (BMI) >30 kilograms/m2 who received a stable nomogram-based vancomycin regimen and had at least one steady-state vancomycin trough concentration. Data collected included vancomycin regimens and concentrations, vancomycin indication, serum creatinine, and vancomycin-related adverse events. Patients were divided into two cohorts by goal trough concentration: 10-15 mcg/mL and 15-20 mcg/mL.
Results: Of 325 patients screened, 85 were included. Goal steady-state concentrations were reached in 42/85 (49.4%) of total patients.
Conclusions: Achievement of initial steady-state vancomycin serum concentrations in the present study (approximately 50%) was consistent with the use of published vancomycin dosing nomograms.

Keywords

Drug Monitoring; Vancomycin; Nomograms; Drug Dosage Calculations; Obesity; Retrospective Studies

INTRODUCTION

More than one-third of adults in the United States are obese and consequently at a significantly increased risk for heart disease, stroke, and type 2 diabetes.[1] In addition to these health implications, the physiologic changes from obesity also impact pharmacokinetic and pharmacodynamic properties of drugs. These changes can impact both efficacy and toxicity, especially in antimicrobials such as vancomcyin.[2]

Vancomycin is a tricyclic glycopeptide antibiotic commonly used as therapy for infections caused by Gram-positive organisms, most notably methicillin-resistant Staphylococcus aureus (MRSA).[3] Published adult dosing recommendations for vancomycin in the general population are 15 to 20 mg/kg per dose every 8 to 24 hours (based upon total body weight [TBW] and estimated renal function).[4] However, such recommendations may be inadequate in obese patients due to increases in vancomycin clearance and volume of distribution.[5] In addition, when applied to obese patients, the large single doses resulting from such weight-based recommendations increase the risk of dose-related toxicities.[5]

Variability in both practice and lack of evidence related to optimal initial dosing strategies for vancomycin exist.[5] For example, dosing based on TBW achieves target steady-state trough concentrations more frequently then when based on ideal body weight (IBW).[2] In contrast, one study5 demonstrated that use of adjusted body weight (ABW) provided the best predictor to serum concentrations, and another[6] recommended using 45 to 65 mg/kg/day based on IBW.[5-6] In addition to weight-based dosing, published dosing nomograms have also been extensively evaluated.[7-9] Their efficacy in achieving initial goal trough concentrations (10-20 mcg/mL) has been shown to range from 40-60% on the initial regimen, but the majority excluded patients weighing more than 120 kg or limited the maximum single dose to 2 gms.[7-9] Studies analyzing appropriate vancomycin dosing and monitoring in obese patients have reported variable success rates. In one, approximately 60% of initial vancomycin steady-state concentrations were subtherapeutic (<10 mcg/mL), leading to increased risk of resistance and treatment failure.[8] Another concluded that obese patients most often reached target trough

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concentrations when given 20-30 mg/kg/day based on TBW.[9]

There has yet to be a consensus or guideline recommendations for dosing and monitoring in obese patients. At Duke University Hospital, a validated empiric dosing nomogram for patients weighing 50-100 kg has been in place since 2010. In order to fulfill an increasing and unmet need, an empiric vancomycin dosing nomogram was developed at Duke Regional Hospital (DRH) in 2016 targeting patients weighing 100 to 160 kg (see Appendix). While we hypothesized this nomogram would provide appropriate initial vancomycin dosing guidelines in this population, it had not been previously evaluated. The purpose of our study was to evaluate this newly-implemented vancomycin dosing nomogram in achieving goal steady-state trough concentrations for obese adult patients.

METHODS

The primary objective of this single-center, retrospective cohort study was to describe the percentage of obese patients receiving initial vancomycin doses consistent with nomogram recommendations achieving targeted initial steady-state serum vancomycin concentrations. The secondary objectives were to describe the primary endpoint in subgroups based on patient weight and estimated creatinine clearance (CrCl). We also sought to describe the percentage of patients maintaining a target steady-state trough concentration, on a consistent regimen, for one subsequent level following an initial target steady-state trough concentration to assess the rate of accumulation. Lastly, patients were evaluated for vancomycin-related adverse effects, including new-onset kidney injury and Red Man syndrome.

This single-center, retrospective cohort study was approved by the Duke University Health System Institutional Review Board and conducted at DRH, a 369-bed community hospital in Durham, NC. Patients >18 years-old, admitted to a general medicine or surgery unit from December 1, 2015 to February 1, 2017 were included. Subjects who weighed >100 kg and had a BMI of >30 kg/m2 who received at least 2 scheduled vancomycin doses following the appropriate loading dose (per nomogram recommendations) were included if at least one steady-state trough vancomycin concentration (defined as following at least the third dose of the regimen and drawn within 2 hours of the next sequential dose) was measured. Patients were excluded for any of the following: renal dysfunction (defined as an estimated CrCl <10 mL/min), unstable renal function (defined as a change in serum creatinine (SCr) of 0.5 mg/dL or 50% reduction in estimated CrCl between initial dose and time of subsequent trough measurement), moderate to severe liver dysfunction at baseline (defined as aspartate aminotransferase or alanine aminotransferase levels >two times the upper limit of normal (ULN), or a total bilirubin level >two times the ULN), ascites, burns (>20% total body surface area), within 30 days of solid organ or hematopoietic stem cell transplantation, had cystic fibrosis, were patients in the critical care unit, or were pregnant.

Patients were identified utilizing the Duke Enterprise Data Unified Content Explorer (DEDUCE). Separate admissions for the same patient were counted as individual cases. Data were collected using a Microsoft Access database and entry form. Patient demographics collected included gender, age, weight, height, BMI, and the presence of chronic kidney disease (CKD). Other data collected included vancomycin indication, vancomycin dosing regimens, and vancomycin serum trough concentrations, dates, and collection times. SCr and estimated CrCl at time of vancomycin initiation and trough concentration of maintenance regimen utilizing a modified Cockroft-Gault equation (removing weight and 72 from numerator and denominator, respectively).[10] Of note, in patients >70 years old, a SCr below 1 mg/dL was rounded to 1 mg/dL to calculate CrCl. For initial loading doses, patients received 25 mg/kg TBW unless they had impaired renal function indicated by new-onset kidney injury or CKD Stage IV or worse. In this case, patients were loaded with 20 mg/kg TBW. However, we incorporated our institution's policy of vancomycin dose capping at 2500 mg. For patients with therapeutic serum trough concentrations that were continued on the same regimen, SCr was collected again at the time of the next trough concentration. Lastly, presence of Red Man syndrome and new-onset kidney injury at the time of concentration collection (defined as an increase in SCr by 0.3 mg/dL or more within 48 hours, or an increase in SCr to 1.5 times baseline or more within the last 7 days, or urine output less than 0.5 mL/kg/h for 6 hours) was collected.[11] The institutional nomogram was developed with the above in mind, utilizing traditional vancomycin pharmacokinetic calculations including the Matzke equation for the elimination rate constant. For patients receiving multiple courses of vancomycin during a single admission, only the first course was included in the study.[12]

Data Analysis

The primary endpoint (initial steady-state serum vancomycin concentration within the indication-specific target range) and patient demographics were characterized using descriptive statistics. For the secondary objectives, the endpoints utilized were percentage of therapeutic trough concentrations in the pre-specified cohorts, percentage of patients experiencing vancomycin accumulation to a supratherapeutic level following an initial therapeutic concentration, and percentage of patients experiencing a vancomycin-related adverse event such as new-onset kidney injury. Patients were cohorted by CrCl (10-39 mL/min, 40-69 mL/min, 70-99 mL/min, and 100+ mL/min) and weight (100-119 kg, 120-139 kg, 140-159 kg, and 160+ kg).

RESULTS

Of 325 patients weighing over 100 kg and on vancomycin identified and screened, 85 (26.2%) met inclusion criteria. Patients were excluded for the following: doses were not consistent with nomogram recommendations (n=168), no trough concentration level (n=36), critical care unit status (n=28), BMI <30 kg/m2 (5), and weight <100 kg at time of vancomycin initiation (3). The study population was predominantly male with an average age of 60 years. Remaining subject demographics are summarized in Table 1. All subjects had an estimated CrCl > 30 mL/min and the

Table 1. Baseline demographic characteristics of included subjects (by cohort)			
Parameter	**Cohort**		
	10-15 mcg/mL (n=28)	**15-20 mcg/mL (n=57)**	**All patients (n=85)**
Age, yr	56.1 (11.8)	57.5 (15.2)	56.9 (13.0)
Gender, n (Male:Female)	15:13	37:20	52:33
Weight, kg	133.2 (35.6)	122.0 (17.6)	125.1 (25.3)
BMI, kg/m^{2} [a]	44.8 (12.7)	39.5 (7.3)	40.9 (9.5)
CrCl[b], mL/min	98.8 (22.1)	72.7 (24.6)	81.3 (26.7)
Indications, n(%)			
SSTI[c]	26 (92.9)	17 (29.8)	43 (50.1)
Osteomyelitis	0	16 (28.1)	16 (18.8)
Sepsis	0	11 (19.3)	11 (12.9)
Pneumonia	0	6 (10.5)	6 (7.1)
Bacteremia	1 (3.6)	4 (7.0)	5 (5.9)
Intra-abdominal	0	3 (5.3)	3 (3.5)
Other	1 (3.6)	0	1 (1.2)
Vancomcyin regimen			
1.5g Q12H	11	11	22 (25.9)
1.75g Q12H	5	10	15 (17.6)
2g Q12H	4	8	12 (14.1)
1.75g Q18H	0	8	8 (9.4)
1.25g Q8H	0	6	6 (7.1)
Other	8	14	22 (25.9)
Baseline renal disease			
CKD[d] Stage III-V	1 (3.6)	9 (15.8)	10 (11.8)
a. Body Mass Index b. Creatinine clearance in normalized Cockroft-Gault c. skin and soft tissue infections d. Chronic Kidney Disease			

mean CrCl was 81.3 mL/min. The majority of patients were in the 15-20 mcg/mL goal trough cohort and were receiving therapy for complicated skin and skin structure infections (SSTI).

Goal steady-state trough concentrations were reached in 42 patients (49.4%) with 27 (47.4%) in the 15-20 mcg/mL cohort and 15 (53.6%) in the 10-15 mcg/mL cohort. In the total population, 24.7% had subtherapeutic levels at steady state and 25.9% had supratherapeutic levels. There was also a similar distribution of subtherapeutic levels and supratherapeutic levels in each goal trough subgroup (Figure 1). Trough levels ranged from 6.1-30.9 mcg/mL. When this data was combined, 58 patients (68.2%) had levels that fell in the 10-20 mcg/mL range.

When divided into pre-specified subgroups based on goal trough concentrations, weight, and estimated CrCl (Table 2), the majority of patients fell into the 100-119 kg groups (n= 47, 55%). There were a limited number of patients >140 kg (n=13, 15%), and only 28 patients had an estimated CrCl <70 mL/min. 69% of the pre-specified subgroups containing at least one patient in the 15-20 mcg/mL goal cohort and 67% of the subgroups in the 10-15 mcg/mL cohort had mean trough concentrations at goal, respectively (Table 2). Notably, 16/21 (76%) of total patients with subtherapeutic trough concentrations had an estimated CrCl >70 mL/min. However, there were more patients in these subgroups and the majority still achieved goal trough concentrations (n=30, 52.6%). There was a noticeably higher rate of

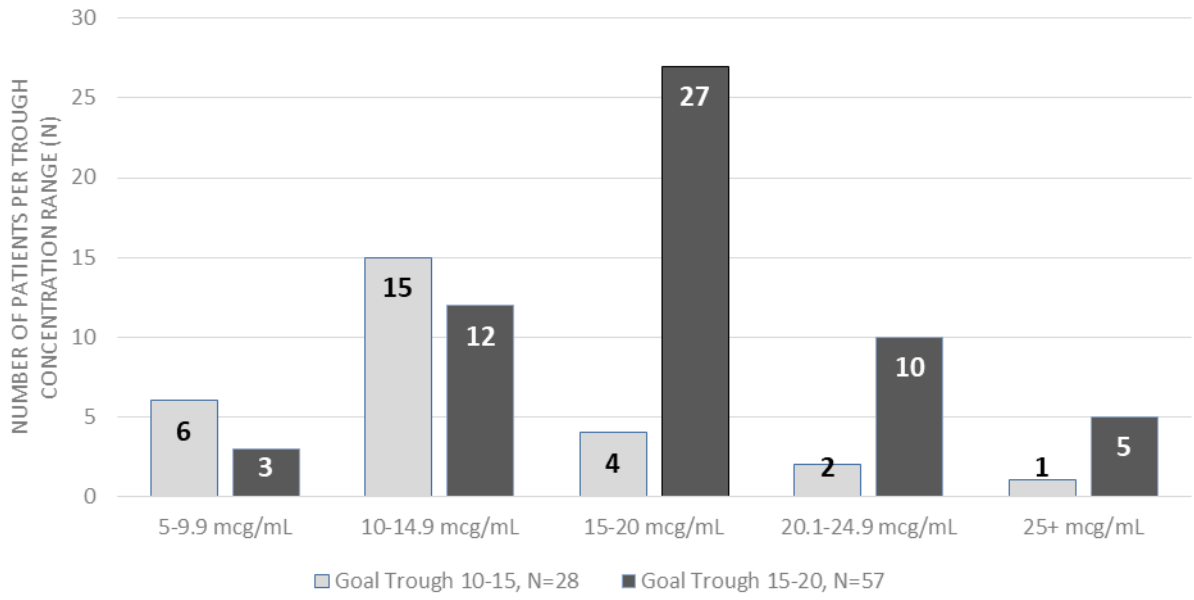

Figure 1. Number achieving trough concentrations based on target trough concentration goal.

Table 2. Subgroup analysis – average trough concentration (SD), mcg/mL

10-15 mcg/mL goal	**100-119 kg**	**120-139 kg**	**140-159 kg**	**> 160 kg**
10-39 mL/min	N/A	N/A	N/A	N/A
40-69 mL/min	17.0 (3.6)	22.8 (0)*	N/A	N/A
70-99 mL/min	14.4 (5.7)	11.5 (0)*	N/A	13.8 (1.6)
> 100 mL/min	10.7 (2.9)	9.8 (3.6)	14.5 (0)*	14.8 (3.8)
15-20 mcg/mL goal	**100-119 kg**	**120-139 kg**	**140-159 kg**	**> 160 kg**
10-39 mL/min	18.6 (2.4)	16.1 (0)*	N/A	N/A
40-69 mL/min	17.2 (4.8)	18.8 (4.3)	19.9 (0)*	14.2 + 6.1*
70-99 mL/min	16.9 (5.6)	18.7 (4.0)	11.5 (0)*	N/A
> 100 mL/min	12.6 (3.0)	23.2 (2.1)*	17.8 (0)*	15.4 (0)*

*<2 patients represented in the subgroup

patients reaching initial supratherapeutic trough concentrations in the CrCl <70 mL/min subgroups compared to those with a CrCl >70 mL/min (35.7% vs. 19.3%).

Very few patients were continued on the same vancomycin regimen following the achievement of a target trough concentration long enough to check a second concentration (n=11, 26.2%). Of these 11 patients, 5 experienced accumulation to a supratherapeutic trough concentration on the subsequent level, with a mean (SD) time to next level of 2.9 (SD=1.2) days. However, 3 (60%) of these patients developed new-onset kidney injury between the first and second concentration drawn.

No patients had to have vancomycin discontinued due to adverse events. Five patients experienced new-onset kidney injury during treatment and one patient was reported to have Red Man syndrome which was noted to improve when the infusion was administered at a slower rate. No other drug-related adverse effects were reported.

DISCUSSION

The results of our study found that our nomogram achieved target trough concentrations nearly 50% of the time. Prior attempts to utilize nomograms to provide initial dosing recommendations for vancomycin in obese patients have been met with variable success. One protocol employed a 20 mg/kg loading dose followed by 10 mg/kg/dose (based on TBW) every 12-24 hours in morbidly obese adults (BMI >40).[8] This dose was chosen based on previous findings that demonstrated a high rate of supratherapeutic concentrations with higher doses.[8] With this decreased dose, initial goal trough concentrations were achieved in 35.4% of patients, while subtherapeutic troughs occurred in 56.3% and supratherapeutic troughs in only 8.3% of patients.[8] Another recent retrospective study concluded that obese (BMI 30-40) and morbidly obese (BMI >40) patients most often reached target trough concentrations when given 20-30 mg/kg/day based on TBW.[9] However, this study had limitations which included a high rate of subtherapeutic trough concentrations (48%) and no loading doses were given.[9]

Compared to the aforementioned studies and another by Morrill et al, which utilized a similar dosing strategy and yielded 48% subtherapeutic initial trough levels, our study had a more even distribution of non-therapeutic trough concentrations.[7-9] Approximately 25% of patients had subtherapeutic trough levels with no level being lower than 6 mcg/mL, while another 25% of patients had supratherapeutic levels with only one level being greater than 30 mcg/mL (30.9). While we had a slightly higher rate of new-onset kidney injury during therapy compared to the previous trials, all patients experiencing kidney injury were on concomitant nephrotoxic medications including piperacillin-tazobactam, thiazide diuretics, and intravenous acyclovir.[8,9,13]

The results of this study fall within the range of results in previous studies evaluating vancomycin dosing nomograms, achieving goal steady-state trough concentrations nearly 50% of the time.[7,14-16] Unlike the majority of previous studies analyzing vancomycin nomograms, this study only included obese patients weighing at least 100 kg with no maximum weight.[4-7,14-16] When looking at the limited previous literature on vancomycin dosing in obese patients, our nomogram appears to be safe and similarly effective. Notable studies analyzing vancomycin dosing in obese patients have utilized protocols or nomograms that have based dosing on simplified mg/kg calculations paired with estimated renal function for determining frequency.[8,9,13] Our nomogram was developed utilizing traditional pharmacokinetic calculations for each subgroup using TBW for volume of distribution calculations and normalized CrCl which ultimately leads to a lower estimation of drug clearance in these patients. Utilizing this method of dosing, we predicted that our patients would receive large enough doses without experiencing toxic levels as a result of too frequent dosing.

This was also the first study to our knowledge to collect data on vancomycin accumulation in the real-world obese patient population. While our data is limited to 11 patients who were continued on their original therapeutic regimen long enough to receive a second trough level, it does reveal a concern for drug accumulation in this population. Nearly half (45%) of these patients experienced a subsequent supratherapeutic level following an initial therapeutic trough concentration and no change in dosing regimen. It is important to note that 3 of these patients had significant increases in SCr levels near the time of the follow-up level. Further studies are needed in this area to assess vancomycin adjustments in these patients to avoid potentially toxic accumulation.

Our study was not without limitations. Though our nomogram was designed using common calculations utilized in clinical practice, there are potential limitations with the pharmacokinetics of using the standard Vd, Matzke equation, and SCr rounding in the obese population.[12] However, there is no current consensus on the best method. AUC-based monitoring has also shown promising data, but until more implementable evidence

exists, many institutions will continue traditional vancomycin dosing.[17] With no active or historical comparator, we were only able to report descriptive statistics limiting ability to show any association with patient specific factors and vancomycin concentrations. We were also limited to a small sample size. Although over 300 patients were screened for inclusion, pharmacists were not required to utilize the nomogram during the evaluation period which led to many exclusions. We also excluded patients in the critical care unit per the institution's pharmacokinetic policy which limits extrapolation to these patients. This limited sample size and utilization also inhibited our ability to truly evaluate the effectiveness of our nomogram in patients with poor CrCl and those weighing over 140 kg. Lastly, we did not evaluate clinical outcomes of the patients.

CONCLUSIONS

Overall achievement of initial steady-state vancomycin serum concentrations in our study of obese patients (approximately 50%) was consistent with the use of published vancomycin dosing nomograms. Notably, our study had an even distribution of non-therapeutic trough concentrations (25% subtherapeutic and 25% supratherapeutic). Our study also added evidence for the risk vancomycin accumulation in continued dosing in this patient population. Future plans should include identifying patient-specific factors associated with non-therapeutic trough levels in the obese patient population and developing accurate pharmacokinetic models for this population.

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CONFLICT OF INTEREST

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Original Research

Falls in the elderly: assessment of prevalence and risk factors

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Abstract

Background: Falls in elderly people can lead to serious health problems. There is limited knowledge about the prevalence of falls, risk factors and causes of falls in the United Arab Emirates.

Objective: To assess the prevalence of falls among older adults aged 60 years and above and to determine the risk factors associated with falls.

Methods: This cross-sectional study was conducted using an anonymous, 20-item questionnaire which was developed in English and Arabic to be delivered as a semi-structured interview. The pre-piloted questionnaire was distributed to 510 families with at least one elderly person. The study was conducted in Sharjah and Dubai, United Arab Emirates, from September to November 2017.

Results: Participants were Arabs (368; 99.5%), living with family (339; 91.6%), females (256; 69.2%), married (240; 64.9%), holders of a university Bachelor's degree (110; 29.7%), and unemployed (154; 41.6%). Almost half of the participants (188; 50.8%) had a fall in the past two years, and three quarters (141; 75%) of those claimed that their illness was the reason for their fall. The results indicate that female and 70 years and above old participants are more likely to experience falls than males and younger counterparts respectively. A larger proportion of elderly participants not taking medications did not experience falls, while those on 1-4 medications fallers were less than non-fallers. However as the number of medications increased to 5-8 and more than 8 the number of those experiencing falls was significantly higher than non-fallers.

Conclusions: Falls are prevalent among the elderly population studied and efforts should be made to decrease the incidence of falls, identify those at risk and increase awareness about falls and their health consequences among the elderly and the general public.

Keywords

Accidental Falls; Risk Factors; Aged; Surveys and Questionnaires; United Arab Emirates

INTRODUCTION

Falls are defined as accidental events in which a person falls when his/her center of gravity is lost and no effort is made to restore balance or when this effort is ineffective.[1] Falls are considered as the most common cause of injuries among the older population. Forty percent of traumatic injuries-related hospitalizations are due to falls.[2] The most common fall-related consequences are pain, bruising, lacerations, fractures including upper extremity and hip fractures, and intracranial bleeding in severe cases. Frequent falls in the elderly population can lead to serious health consequences and efforts to reduce their incidence are necessary.[3-5] Nearly 28-35% of people aged 65 years and above fall each year[3,6,7] and this percentage increases to 32-42% for those over 70 years of age.[6-8] Moreover, 20% to 39% of people who fall experience fear of falling, which leads to further limiting of activity, independent of injury.[9]

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Risk factors for falls that have been identified include history of falling, use of assistive devices, environmental hazards such as poor lightening, and various health conditions including muscle weakness, vertigo, gait and balance impairments, visual and hearing disorders, cognitive and sensory impairments, orthostatic hypotension, diabetes mellitus and osteoporosis.[10-12] Several studies have also associated certain medications with an increased risk of falls among older adults.[13] The most common drugs that increase the risk of falls are different types of psychotropic drugs, such as hypnotics, sedatives, antipsychotics and antidepressants, which can cause sedation, impaired balance and coordination.[5,14-16] Furthermore, cardiovascular drugs such as diuretics and beta-blockers may cause or worsen orthostatic hypotension and falls.[17,18] Antihistamines and anticholinergic drugs may affect the cognitive skills of elderly patients and cause blurred vision, thereby increasing the risk of falls.[19] It has also been stressed by the same authors that polypharmacy and the use of psychotropic drugs, especially when combined with cardiovascular medications increase the risk of falls in the elderly.[19]

While some risk factors cannot be changed, many are modifiable. Many falls result from interactions among multiple risk factors, and the risk of falling increases linearly with the number of risk factors.[10] The incidence of falling changed from 8% among those with no risk factors to 78%

Table 1. Demographic characteristics of participants.

Criteria	Frequency N=370	%
Gender		
Female	256	69.2
Male	114	30.8
Age		
60-64	192	51.9
65-69	63	17
70-74	47	12.7
75 and above	68	18.4
Ethnicity		
Arab	368	99.5
Non-Arab	2	0.5
Marital status		
Married	240	64.9
Widowed	103	27.8
Single, never married	15	4.1
Divorced	12	3.2
Education		
illiterate	105	28.4
Less than high school degree	68	18.4
High school degree	59	15.9
Bachelor's degree	110	29.7
Higher degree (masters, PhD)	28	7.6
Employment status		
Unemployed	154	41.6
Retired	130	35.1
Employed for wages	54	14.6
Self-employed	32	8.6
Living situation		
Living with family	339	91.6
Alone	27	7.3
Living with friends/relatives	3	0.8
In a nursing home	1	0.3

among those with 4 or more risk factors according to a previous study.[8]

In United Arab Emirates (UAE), there is a lack of studies on falls in elderly people. Hence, the aim of this study was to assess the prevalence of falls in the past two years among older adults who are aged 60 years and above and to determine the risk factors associated with falls.

METHODS

Ethical approval

Ethical approval for the study was obtained from the Ethical Committee of the Medical Campus at the University of Sharjah. The study participants completed the questionnaire without providing any identification information. Participants were assured of confidentiality and anonymity of the responses provided and written informed consent was obtained.

Subjects and data collection

The inclusion criterion was elderly persons aged 60 years and above. A total of 510 families with at least one elderly from Dubai and Sharjah-UAE were approached to participate in the survey. The surveys were distributed by hand and were collected over the study period of three months (September-November, 2017).

Development of study design

This cross-sectional study was conducted using an anonymous questionnaire to be delivered as a semi-structured interview. The questionnaire consists of 4 sections and 20 questions and was designed by the researchers in both English and Arabic to collect specific data about the problem of falls in the elderly. All questions were close-ended questions, with 'Yes and No' as options. The questionnaire was pre-piloted by distributing it to 5 elderly persons who were interviewed face-to-face to check face validity of the questionnaire. Recommendations from the pilot study were considered to develop the final version of the questionnaire; however the participants were not included in the actual study. The first section of the questionnaire collects the socio-demographic characteristics of the participants. The second section is completed by participants who have experienced a fall and assesses the number, consequences and causes of falls and whether the participants visited a hospital for the fall. The third section discusses the health status of the participants, medications used and the number of medications. The fourth section includes questions to be answered by all participants concerning preventive strategies.

Statistical analysis

The data were analyzed using the program SPSS version 20 (Chicago, IL, USA). Pearson Chi-squared test was used to identify the influence of socio-demographics on the possibility of falling and differences between participants who experienced falls and those who did not with a significance level of $p<0.05$.

RESULTS

A total of 370 participants completed the questionnaire giving a response rate of 72.6%. Table 1 shows the demographics of participants. The majority of participants were females (256; 69.2%), Arabs (368; 99.5%), married (240; 64.9%), and living with family (339; 91.6%). More than half of the participants were in the age group of 60-64 years age (192; 51.9%). Participants who hold a Bachelor's

Table 2. The number of falls in the elderly who experienced falls in the past two years and their causes and health consequence.

Item	Frequency N=188	%
Number of falls		
1-2	118	62.8
3-4	48	25.5
≥5	22	11.7
Hospital visit after a fall		
Yes	112	59.6
No	76	40.4
Health consequences after a fall		
Pain	111	59
Bruising	103	54.8
Fracture	36	19.1
Laceration	23	12.2
Intracranial bleeding	0	0
Causes of falls		
My illness	141	75
Sense of dizziness when I stand up/balance problems	73	38.8
Loose carpets/ slippery floors	53	28.2
Vision problems	22	11.7
The shoes I'm wearing	20	10.6
The medications I take	19	10.1
Poor lighting	7	3.7

Table 3. Influence of selected socio-demographics on the possibility of falling.

Characteristic	Frequency (%), n=370		Total	Chi-square test p-value
	Fallers	Non-fallers		
Gender				
Female	146 (57)	110 (43)	256	< 0.001
Male	42 (36.8)	72 (63.2)	114	
Age				
60-64	80 (41.7)	112 (58.3)	192	< 0.001
65-69	30 (47.6)	33 (52.4)	63	
70-74	30 (63.8)	17 (36.2)	47	
75 and above	48 (70.6)	20 (29.4)	68	
Education				
Illiterate	79 (75.2)	26 (24.8)	105	< 0.001
Less than high school degree	36 (52.9)	32 (47.1)	68	
High school degree	23 (39)	36 (61)	59	
Bachelor's degree	44 (40)	66 (60)	110	
Higher degree (masters, PhD)	6 (21.4)	22 (78.6)	28	
Assistive device use				
Yes	78 (81.2)	18 (18.8)	96	< 0.001
No	110 (40.1)	164 (59.9)	274	

degree were 110 (29.7%) and 154(41.6%) participants were unemployed. About half (188; 50.8%) the respondents reported that they had a fall in the past two years. Table 2 shows the number of falls within the last two years in the elderly population studied. About two thirds (118, 62.8%) of the participants, who reported a fall, fell 1 or 2 times. More than half (112; 59.6%) of the participants who reported a fall visited a hospital after a fall (Table 2). The order of health consequences of the falls was pain (111, 59%), bruising (103, 54.8%), fractures (36, 19.1%) and laceration (23, 12.2%). None of the participants suffered intracranial bleeding during the study period.

Almost three quarters (141; 75%) of the 188 participants who reported a fall claimed that their illness was the reason for their fall while 73 (38.8%) of them reported experiencing a sense of dizziness when they stand up and have balance problems. Loose carpets/slippery floors accounted for the falls of more than one quarter (28.2%) of fallers. Other causes of falls are shown in Table 2.

As shown in Table 3, a statistically significant association was observed between the prevalence of falls and gender (p<001), age (p<0.001), education level (p<0.001) and the use of assistive devices (p<0.001). Falls were more common in females, patients 75 years and above, illiterate respondents and those using assistive devices.

Table 4. Health status of participants and the medications they use.

Item	Frequency (%), n=370		Total	Chi-square test p-value
	Fallers	Non-fallers		
Number of medications taken daily				
0	16 (36.4)	28 (63.6)	44	< 0.001
1-4	89 (42.6)	120 (57.4)	209	
5-8	54 (66.7)	27 (33.3)	81	
More than 8	29 (80.6)	7 (19.4)	36	
The medications used				
Hypnotics, sedatives	25 (71.4)	10 (28.6)	35	0.012
Diuretics	85 (65.4)	45 (34.6)	130	< 0.001
Antidepressants	16 (72.7)	6 (27.3)	22	0.034
Antipsychotics	4 (66.7)	2 (33.3)	6	0.433
Antihistamines	45 (60)	30 (40)	75	0.120
Beta blockers	89 (61.8)	55 (38.2)	144	0.002
Insulin	61 (66.3)	31 (33.7)	92	0.001
Laxatives	30 (69.8)	13 (30.2)	43	0.008
Anticonvulsants	4 (57.1)	3 (42.9)	7	0.735
NSAIDS	46 (63.9)	26 (36.1)	72	0.013
None	26 (30.6)	28 (63.6)	85	< 0.001
The existing health conditions				
Weak eye sight	73 (53.7)	63 (46.3)	136	0.401
Osteoporosis	72 (64.3)	40 (35.7)	112	0.001
Hearing problems	50 (71.4)	20 (28.6)	70	< 0.001
Sleep disorders	39 (53.4)	34 (46.6)	73	0.618
Obesity	51 (56.7)	39 (43.3)	91	0.273
Osteoarthritis	84 (59.6)	57 (40.4)	142	0.017
Chronic respiratory disorders	28 (66.7)	14 (33.3)	42	0.029
Anemia	16 (50)	16 (50)	32	0.924
Vertigo or balancing disorders	49 (70)	21 (30)	70	< 0.001
Dementia	5 (55.6)	4 (44.4)	9	0.773
Hypotension	10 (62.5)	6 (37.5)	16	0.339
Hypertension	88 (55.3)	71 (44.7)	159	0.130
Diabetes	83 (56.8)	63 (43.2)	146	0.061
Bladder or Bowel incontinence	25 (71.4)	10 (28.6)	35	0.010
None	8 (28.6)	20 (71.4)	28	0.014

The risk factors as related to the health status of the participant, the medications used and the number of medications on the prevalence of falls are shown in Table 4. There was a strong significant association (P< 0.001) between the number of medications taken daily and the increased risk of falls in elderly participants. The majority (29, 80.6%) of respondents who take more than eight medications daily experienced falls in the past two years. Among participants who take 5- 8 medications per day a total of 54 (66.7%) participants had a fall in the past 2 years. As the number of medications/day is reduced to 1-4 medications daily, the risk of falls decreased, and among those who take 1-4 medications, 89 (42.6%) experienced a fall. On the other hand, only 16 (36.4%) of those who do not take medications experienced a fall in the past two years (Table 4).

There was also a significant association (p<0.001) between taking certain medications and the incidence of falls. Participants taking beta-blockers comprised 144 (38.9%) and 89 (61.8%) of them fell in the last two years. The most common health condition reported by respondents was hypertension and about 88 (55.3%) of them had a fall. Nevertheless, there was a significant association between other co-morbid health conditions and the increased risk of falls; for example, of those (112; 30.3%) who stated that they have osteoporosis nearly 64.3% had a fall in the past two years.

Strategies used to prevent falls in elderly people include calcium and Vitamin D supplements, pharmacists counseling on drugs that may precipitate falls and participant's knowledge about fall prevention. Respondents taking calcium comprised only 165 (44.6%) and 186 (50.3%) participants were taking Vitamin D. The majority (292; 78.9%) of respondents reported that they have never received any counseling from a pharmacist regarding the possibility that their medications may cause falls and 230 (62.2%) of the respondents reported that they have no adequate information about strategies to prevent falls.

DISCUSSION

Falls in older individuals are common and may lead to serious health problems. They can be associated with various risk factors including intrinsic and extrinsic factors. Several studies assessed the prevalence of falls in older adults, and the related fall risk factors.[20-22] However, few studies addressed this issue in the Arab countries[20,23,24] and to the authors' best knowledge there is lack of such studies in UAE. Therefore, in the present study we aimed to assess the prevalence of falls in the past two years among older adults aged 60 years and above and to determine the risk factors associated with falls.

In the present study, the prevalence of falls in older adults was 50.8% as compared to 60.3% in Egypt[20], 34.7% in Ecuador[21], 27.6% in Brazil[22], 42.4% in UK[11] and 32% in USA.[25] It has been stressed that half of the cases of falls in people over 65 years of age are recurrent.[23,26] More than half of our responders visited the hospital after experiencing a fall and only 19.1% of participants who reported a fall reported that they had fractures after a fall. However, a study in Pakistan revealed that only 13% of participants had an emergency plan in case of falls, and showed that fractures were the outcome of 51% of the falls reported in their study.[27] Almost three quarters of the 188 participants who reported a fall claimed that their illness was the reason for their fall. Other reasons reported include; experiencing a sense of dizziness when standing up and having balance problems, loose carpets /slippery floors, vision problems, shoes, medications and poor lighting problem. Numerous studies identified environmental hazards like poor lighting, and a variety of health conditions, such as muscle weakness, vertigo or gait and balance impairment, visual and hearing disorders, cognitive and sensory impairment, orthostatic hypotension, diabetes, and osteoporosis as risk factors of falls.[10,12,13,28]

A primary finding of this study is that females are more likely to experience falls than males, and with advancing age, the prevalence of falls increases. This is consistent with earlier observations that females and advanced age (age above 75 years) were associated with a greater prevalence of falls.[21,22] Such a higher prevalence of falls in females may be a consequence of the decline in their bone mass that occurs faster than that of males especially after menopause. Among other risk factors, sarcopenia defined as loss of skeletal muscle mass that occurs with aging has also been associated with a higher incidence of falls in females.[29,30]

In the present study, illiterate elderly suffered more falls and the incidence of falls seems to decrease as the education level increase. Moreover, elderly people who use assistive devices such as canes are more exposed to falls. Such an influence of educational level on falls may be due to elderly people with low level of education perceive and worry less about their health status. Hence, they have fewer tendencies to engage in health recovery and are less aware of the preventive strategies and advice given by the healthcare professionals; therefore they are at increased risk of falls.[31] The health status of the participant, medications taken and number of medications are also predictors for falls and the significant association between the number of medications taken daily and the increased risk of falls in elderly participants may be explained by the increased possible occurrence of side effects and drug interactions as a result of polypharmacy. Several studies reported a strong relationship between the use of three or more medications and risk of falls.[32-35] These reports and the present study are further supported by earlier findings that the risk of falls increases significantly when more than four medications are taken regardless of the type of drugs taken.[36]

The present observation on the association between the prevalence of falls and medications used by the elderly participants such as hypnotics/sedatives, diuretics, antidepressants, beta-blockers, insulin, laxatives, and NSAIDs are in accordance with other reported observations.[37-39] It is known that hypnotics/sedatives and NSAIDs can cause sedation, dizziness and cognitive impairments while diuretics can result in postural hypotension, decreased alertness and fatigue. Sedation and postural hypotension by antidepressants and beta-blockers and the hypoglycemic effect of insulin also significantly contribute to the incidence of falls in the elderly.[5,18,37,38] In

addition, the use of diuretics and laxatives cause the elderly to get up frequently and rush at a fast pace to use the toilet, usually without assistance thus increasing the risk of falls.

Surprisingly no association was observed between the incidence of falls and antipsychotic, antihistamine, and anticonvulsant medications. This might be related to physician/ pharmacist instruction on type of and time when to administer such drugs. Medications are one of the modifiable risk factors for falls. Therefore, special caution is necessary when treating elderly patients at risk.[5,39] Dose adjustments or the use of alternative medicines with lower risks must be considered to reduce the risk of falls.

The most common risk related health condition reported by participants in this study was hypertension. Despite the fact that more than half of the participants with hypertension had a fall event during the study period, there was no association between the two. A similar finding was reported in a study in Qatar.[23] On the other hand, there was a significant association between osteoarthritis and the increased risk of falls. This is most likely due to gait disturbance and weakness associated with the condition.[21]

In agreement with the observation in Ecuador[21], urinary incontinence was also found to be a significant risk factor for falls in the present study. Falls related to incontinence are generally thought to result from loss of balance when rushing to the toilet and because these patients need to get up more times to use the toilet. In addition, similar to the findings in elderly Greeks[26], it has been observed in this study that vertigo or balance disorders also contribute to the increased risk of falls.

Calcium and Vitamin D supplements are necessary in the elderly for bone health and to prevent osteomalacia, osteoporosis, muscle weakness and protect against falls. In the present study, almost half of the participants take calcium and Vitamin D supplementation. A previous report revealed that 1µg alfacalcidol daily significantly decreases the number of falls in elderly.[40]

The majority of elderly included in this study reported that they have no adequate information about fall prevention and did not receive any counseling from the pharmacist regarding the possibility that their medications may cause falls. The value of educating elderly about medication-related fall risk has previously been stressed.[30] Both the physician and the pharmacist as forefront healthcare professionals have a major role to play in educating elderly patients and increasing their awareness of risk factors such as medication side effect in order to reduce the incidence of falls.

Limitations of the study

A major limitation of this study is the collection of retrospective data about falls that may be susceptible to recall bias, and some elderly subjects may under-report the number of their fall episodes, leading to possibility of a reported lower prevalence rate in this study.

Another limitation is that the falls may be due to other potential risk factors that have not been included in our study which may require further investigations. These are, among others, physical activity, poor nutrition, fear of falling, Parkinson's disease, thyroid disorders, foot problems, Alzheimer's disease. Finally, more detailed information about the drugs doses and frequency of administration may have provided better understanding of whether drugs greatly affect risk for falls in elderly patients.

CONCLUSIONS

Falls are prevalent in the elderly population and there is an urgent need for public health strategies to decrease their incidence and identify those who are at risk. Physicians and pharmacists should, through counseling, educate elderly patients and their families on how to reduce the incidence of falls. Such counseling should include reviewing the medications prescribed for the elderly that may precipitate falls, avoiding drug-drug and drug-disease interactions, minimizing the side effects, recommending vitamin D and calcium supplementation and suggesting lifestyle and living environment adjustments. Implementation of falls prevention programs can also significantly reduce falls in the elderly.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

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Original Research

Measuring the health literacy level of Arabic speaking population in Saudi Arabia using translated health literacy instruments

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Abstract

Background: Health literacy is an essential predictor of health status, disease control and adherence to medications.

Objectives: The study goals were to assess the health literacy level of the general population in Saudi Arabia using translated Gulf Arabic version of the short-version of the Test of Functional Health Literacy in Adults (S-TOFHLA) and Single Item Literacy Screener (SILS) tests and to measure the relationship between health literacy and education level.

Methods: The study was a cross-sectional with a convenience sample of 123 participants from the general population in Riyadh. Data were collected using the modified (Gulf) Arabic versions of both S-TOFHLA and SILS. Fisher's Exact test was used to measure the difference of the health literacy scores according to the education degrees and Cronbach's alpha was used to measure the internal consistency of the S-TOFHLA items.

Results: More than half (55.4%) of the participants were male, 50.4% had a middle school or less education level, and we found that 84.4% had adequate health literacy as measured by the S-TOFHLA, compared to 49.6% as measured by SILS. The Fisher's Exact test showed a significant difference (P<.05) in the S-TOFHLA and SILS scores according to education categories.

Conclusions: The level of education has a significant positive association with S-TOFHLA and SILS results. The Gulf Arabic version of S-TOFHLA is a reliable test with a good internal consistency and a significant positive correlation between the two parts of S-TOFHLA. We recommend the use of S-TOFHLA or SILS at the first patient visit.

Keywords

Health Literacy; Cross-Cultural Comparison; Psychometrics; Reproducibility of Results; Surveys and Questionnaires; Saudi Arabia

INTRODUCTION

Health literacy is the extent to which people have the ability to understand the basic health information needed to make suitable health decisions.[1] Health literacy is related to general literacy. However, it also refers more specifically to information in a healthcare context.[1] Health literacy has been found to be an essential predictor of health status and adherence to medications.[2-4] A systematic review of 35 health literacy studies found a significant positive correlation between health literacy and medication adherence.[4] Lack of knowledge about illness and treatment and poor medication adherence are usually associated with inadequate chronic disease control.[5,6] A study in a public hospital in San Francisco found significant positive relationship between education level and glycemic control among diabetes patients.[7]

This study used both short-version of the Test of Functional Health Literacy in Adults (S-TOFHLA) and Single Item Literacy Screener (SILS) which are important tools in the measurement of health literacy. The S-TOFHLA is relatively long test compared to the SILS which is a single short question. The Test of Functional Health Literacy in Adults (TOFHLA) was designed to measure patients' ability to read and understand the things people commonly encounter in healthcare settings using actual materials like pill bottles and appointment slips.[7] The TOFHLA evaluates both numeracy and reading skills. The reading part has three prose passages while the numeracy section includes 17 questions that evaluate the ability to read and understand prescription labels and appointment slips.[7] The S-TOFHLA is a shorter version with two prose passages and a numeracy section with four questions that evaluate understanding of glucose monitoring, prescription labels and appointment slips.[7] The English version of S-TOFHLA has good internal consistency and it is more practical than the full version as it takes a maximum of 12 minutes to finish instead of 22 minutes.[7] However, the time required to complete the test

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varies between people according to their ability to read and understand the test.[7] The SILS is a primary screening tool used to identify participants with inadequate reading skills who would like help reading health related information.[8]

According to World Federation of Public Health Associations, "the Arab World refers to the 22 countries of the Arab League" with population of 354 million.[9] An Arabic version of the S-TOFHLA and SILS tests was previously created and validated by Al-Jumaili and colleagues using 95 subjects in five pharmacies in Iraq.[10] However, in this study the Arabic language was modified to make it more understandable to the Arabic people of the gulf countries.

Arabic countries experience high prevalence of illiteracy. Saudi Arabia ranked among the top Arabic country leaders due to the advancement in the health and education with 87% of population have basic literacy (reading and writing) levels.[9,11] However, a recent study stated the percentage of uneducated people in Saudi Arabi ranges from 13 to 30%.[12] The study found prescription label misunderstanding is common among hospital patients.[12] Low education level may be associated with inadequate health literacy among Saudi population. The study goal was to assess the health literacy level of the general population in Saudi Arabia using translated Arabic version of the S-TOFHLA and SILS tests that represent Gulf countries and to measure the relationship between health literacy and education level.

METHODS

Study Design

This was a cross-sectional study conducted to translate the S-TOFHLA and SILS into formal Arabic and to assess the Arabic version of both S-TOFHLA and SILS among the Saudi population (online appendix). Additionally, the survey included basic demographic characteristics (age, gender, employment, monthly income, education level). At the end of the survey, participants were asked to give feedback regarding the newly translated version of the two tests using a five-point Likert scale (strongly agree, agree, neutral, disagree and strongly disagree) to respond to the questions. Before starting the data collection, we conducted pilot study to ensure the clarity of the modified instruments for Saudi people.

Data Collection

A convenience sample of 123 Saudi participants from the general population in different settings such as hospital, high schools, colleges, and public places in Riyadh was used to evaluate the translation. People who unable to read Arabic and children (less than 18 years old) were excluded.

After receiving verbal consent from the participants, the researcher provided in-person a paper form of the newly translated (Gulf) Arabic versions of both S-TOFHLA and SILS. After several minutes, the participants answered the questions and returned the survey in-person. The research was approved by Institutional Review Board (IRB) at College of Medicine, Imam Mohammad Ibn Saud Islamic University (IMSIU) in Riyadh, Saudi Arabia.

The Short-version of the Test of Functional Health Literacy in Adults (S-TOFHLA)

This study added written instructions to the participants about how to answer the S-TOFHLA. The study used the S-TOFHLA to measure both the reading and numeracy skills of the participants. The reading section includes two prose passages that describe how to prepare for an upper gastrointestinal (GI) X-ray, and Medicaid rights and responsibilities. An expert panel of eight bilingual physicians from IMSIU College of Medicine conducted forward translation (English to Arabic) and backward translation (Arabic to English) to validate the translation.[13] A pilot survey helped to identify the difficult words. The eight researchers translated the two S-TOFHLA sections and modified the language of the Medicaid Rights' passage to be understandable to Gulf countries people who use a different dialect from other Arabic countries. Thus, the authors introduced few specific Gulf country terms to the Arabic validated instruments.

The numeracy section includes four questions that measure a patient's ability to understand glucose monitoring, prescription labels, and appointment memos.[7,14] As Al-Jumaili and colleagues did, this study deleted the third item in the GI X-ray passage because it does not make sense in Arabic.[10] This study also added detailed written instructions on how to answer the S-TOFHLA questions on the first page. The two prose passages in the reading section have a total of 35 cloze items (each blank has 4 choices) totaling 70 points (two points for each item).[10] The reading section of the S-TOFHLA asks participants to fill the blanks with the most appropriate answer to complete the sentence grammatically and contextually from a list of four words.[7,10] The total score for the whole S-TOFHLA is 100 points, with 70 points for the reading section and 30 points for the numeracy section (7.5 points for each item). The score is classified into one of two health literacy levels: 0-66 indicates inadequate or marginal health literacy, and 67-100 indicates adequate health literacy.[7,10] The S-TOFHLA Arabic cloze items were reviewed by the same co-author who translated the items to Arabic in Iraq to assure the content validity.

Single Item Literacy Screener (SILS)

The Single Item Literacy Screener (SILS) is a primary screening tool for patients with inadequate reading skills who may need help to read health-related information.[8,14] The SILS has a single question: "How often do you ask someone for help to read the instructions and leaflets from a doctor or pharmacy?" A patient can choose one of the followings (5-point Likert scale): 1-never, 2-rarely, 3-sometimes, 4-often, or 5-always. If a patient chooses sometimes, often, or always, it suggests that the patient has a limited reading ability of health materials. On the other hand, if a patient chooses never, or rarely, it indicates adequate reading ability.[8,14] We did minor modifications to the question and choices of Al-Jumaili's Arabic version of SILS.[10]

Statistical Analysis

Statistical Analysis System (SAS Inc., Cary, North Carolina, USA) was used to conduct data analyses. Descriptive

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Table 1. Characteristics of the participants

Characteristics	Frequency (N=123)	Percentage
Gender		
Male	62	55.4
Female	50	44.6
Age (years)		
18-40	64	52
40s – 50s	46	37.4
≥60	13	10.6
Occupation		
Employee	78	77.2
Non-Employee	23	22.8
Income Level (SAR)		
<5000	64	58.7
6000-10,000	29	26.6
≥11,000	16	14.7
Education Level		
Middle school or less	62	50.8
High school	9	7.4
College/Graduate degree	51	41.8

analysis of the participants' characteristics was conducted including mean, range and standard deviation, frequencies, and percentages. Fisher's exact test was used to measure the statistical difference in the S-TOFHLA and SILS scores according to the participants' education degree, income level, and age. The Fisher's Exact test measured the relationship between these categorical variables. The significance level was 0.05. Pearson correlation (r) was used to measure the relationship between the two health literacy tests, and between the numeric and reading section scores of S-TOFHLA. Cronbach's alpha, a reliability test, was conducted to measure the internal consistency of the items on the Gulf Country Arabic version of S-TOFHLA and SILS. This had also been used in three previous studies.[7,10,15]

RESULTS

A total of 123 participants were recruited for the study and more than half (55.4%) were male (Table 1). Sixty-one (50%) of the participants were patients from the university hospital, 26 (20%) were students from colleges and high schools and the remaining 36 (30%) were general people from coffee shops. More than three-quarters (77.2%) of the participants were employed and the majority (58.7%) had an income level of less than 5000 Saudi riyal a month. Education level was categorized into three categories: middle school or less (50.8%), high school (7.4%), and college/graduate degree (41.8%) (Table 1).

Table 2 shows the results of S-TOFHLA and SILS according to education level, income level, and age. A Fisher's exact test showed a significant difference ($p<0.05$) in the S-TOFHLA and SILS scores according to education categories (Table 2). The participants with higher academic degrees (college/graduate degree) had higher health literacy scores according to both S-TOFHLA and SILS tests compared to the participants having lower academic degrees. More than three-quarters (84.4%) of the participants had adequate health literacy as measured by the S-TOFHLA, compared to approximately half (49.6%) as measured by SILS. According to the S-TOFHLA scores, less than half (47.2%) of the participants had a middle school or less education level, and three-quarters 74.2% of these participants had adequate health literacy. In contrast, 96% of the highly educated group (college/graduate degree) had adequate health literacy (Table 2). According to the SILS question, half (50.4%) of the participants had a middle school or less education level, and one-third (37%) of this group had adequate reading ability (Table 2). One-quarter (25%) of

Table 2. The results of S-TOFHLA and SILS per education level, income level, and age.

A. The Results of S-TOFHLA. N (%)			
Characteristics	**Inadequate-marginal (0-66)**	**Adequate (67-100)**	**p-value**
[a] Education Level			0.0037
Middle school or less	16 (25.8)	46 (74.2)	
High school	1 (12.5)	7 (87.5)	
College/Graduate degree	2 (4)	49 (96)	
Monthly Income Level (SAR)			0.118
≤5000	13 (20.3)	51 (79.7)	
6000 ≤	4 (8.9)	41 (91.1)	
Age (Years)			0.059
18- 40	9 (14.1)	55 (85.9)	
40s – 50s	5 (11.1)	40 (88.9)	
≥60	5 (38.5)	8 (61.5)	
B. The Results of SILS. N (%)			
Characteristics	**Limited (always, often, sometimes)**	**Adequate (rarely, never)**	**p-value**
[a] Education Level			0.0005
Middle school or less	39 (62.9)	23 (37.1)	
High school	6 (75)	2 (25)	
College/Graduate degree	15 (30)	35 (70)	
Income Level (SAR)			0.0504
≤5000	37 (58.7)	26 (41.3)	
6000-≤	17 (38.6)	27 (61.4)	
[b] Age (Years)			0.0012
18-40	22 (35)	41 (65)	
40s – 50s	29 (64.4)	16 (35.6)	
≥60	10 (77)	3 (23)	

[a] Fisher's Exact test showed significant difference ($p<0.05$) in S-TOFHLA and SILS scores according to education categories. [b] Fisher's Exact test showed significant difference ($p<0.05$) in SILS scores according to age categories.

Table 3. The mean and standard deviation of answers for the three participation satisfaction questions. N=67

Participant satisfaction item	Mean (SD)	Min	Max
The questions were clear and I faced no difficulties	1.52 (0.76)	1	4
I found no grammatical mistakes or any word that needed more explanation	1.45 (0.80)	1	4
In general, the tests were clear for me	1.52 (0.68)	1	4
5-likert scale: 1-Strongly Agree, 2-Agree, 3-Neutral, 4-Disagree, 5-Strongly Disagree.			

the participants with a high school degree had adequate reading ability. The Fisher's Exact test showed significant difference ($p<0.05$) in SILS scores according to age categories (Table 2).

Sixty-seven of the participants answered the three items about the clarity of the translated S-TOFHLA and SILS tests. The participants agreed that the two tests were clear and understandable with an approximate mean of 1.50 where 1 refers to strongly agree and 2 refer to agree (Table 3). The Cronbach alpha of the 35 S-TOFHLA reading items was good (alpha=0.9), and of the 4 numeric items was acceptable (alpha=0.6). The validity was also assessed by the Pearson's correlations between the numeric and reading sections of S-TOFHLA, and between the two health literacy tests S-TOFHLA and SILS. The reading section of S-TOFHLA showed a significant (p-value=0.008) positive correlation with the numeric section (Pearson's r=0.3). However, the correlation between S-TOFHLA and SILS was non-significant (p-value=0.089). Cronbach alpha measured internal consistency while the positive correlation of S-TOFHLA results with the education level (Pearson's r=0.4, p-value=0.0001) measured the criterion validity. It means the education level (measure) predicts the S-TOFHLA scores (outcome).

DISCUSSION

Half of the participants were highly educated (with high school diploma or higher) because public education in Saudi Arabia is free, which means everyone has the opportunity to get into school. However, children of low-income parents may leave school earlier looking for job to support their families. More than three-quarters (84.4%) of the participants had adequate health literacy according to the translated Arabic version of S-TOFHLA. The percentage of participants with adequate health literacy in this study was higher than that from an American study.[7] The English version of TOFHLA and S-TOFHLA showed that 54% of American participants had adequate health literacy.[7] The majority (74.2%) of the participants with low education levels had adequate health literacy as well. This result is comparable to the Iraqi study finding showing that 77.8% of the middle school participants had adequate health literacy.[10] Most of the participants with low education level had adequate health literacy may be due to the fact that is S-TOFHLA is a reading test written in Arabic and most elementary and middle schools in Saudi Arabia emphasize Arabic language teaching.

The SILS results were similar to the Iraqi study findings where the majority (83.3%) of the middle school participants was found to have limited reading ability [10]. According to the SILS test, participants with a middle school or less degree had higher health literacy (37%) than those with a high school degree (25%). The participants with lower educational levels received higher SILS scores simply because they answered "never" or "rarely" to the question about how often they needed help. According to the SILS score, the younger participants (18-40 years) had significantly higher health literacy level than elder age participants (40 years and above). This may be because the younger generations have higher rate of school completion compared to elder generations. Because SILS depends more on self-reports (how often do you need help for medical/medication instructions?) than on an objective assessment of participant actual ability, we agree with the Iraqi study which described SILS as a subjective test.[10] In contrast, the S-TOFHLA is reading and numeric assessment test. In other words, the SILS is a subjective test relying on self-assessment of health literacy and S-TOFHLA is more objective test relying on the participant rest scores Therefore, the correlation between the results of the two tests was non-significant. In fact, the S-TOFHLA test, particularly the reading section had good internal consistency. In our study, half of the participants had a limited health literacy level according to SILS. In contrast to a most recent Saudi study (2017) looking for factors influencing patient's understanding of medication label instructions found that most of the participants in their study (59.5%) had a low health literacy level according to the SILS test.[12] Since half of the participants need help to read healthcare instructions, we recommend having Arabic versions of all medical and medication brochures to enhance medication adherence and avoid any language barriers facing Saudi patients.

The answers for the three satisfaction questions showed the participants agreed upon the clarity of the two tests (Table 3). The study has some limitations. Although the study used a convenience sample, the participants represent the general Saudi population from different settings with various levels of education. Thus, the study participants can represent the general Saudi population. Because the interview-time was short and there was no compensation, only 55% (67) of the participants answered the three satisfaction questions at the end of the tests. Finally, the study was conducted in one city.

CONCLUSIONS

More than three-quarters of the participants had adequate health literacy as measured by the S-TOFHLA, compared to approximately half as measured by SILS. The level of education has a positive significant association with both S-TOFHLA and SILS results, which indicates the participants with higher education level have higher health literacy. According to the SILS score, the younger Saudi generations had significantly higher health literacy level than the elder generations. We successfully translated and validated the Gulf country Arabic versions of S-TOFHLA and SILS health literacy tests. These versions are appropriate for Arabic speakers in general as well as Gulf country population. The

modified (Gulf) Arabic version of the S-TOFHLA is reliable test with good internal consistency and a significant positive correlation between its two parts. In conclusion, health literacy may influence medication adherence and affect patient health outcomes. S-TOFHLA and SILS are important tools for the evaluation of health literacy among patients in healthcare settings Therefore, we strongly recommend the use of S-TOFHLA or SILS at the first visit to clinic/hospital, and to include these tests as part of the routine healthcare measures in Saudi Arabia to improve the quality of patient care.

CONFLICT OF INTEREST

There are no conflicts of interest to disclose.

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Original Research

Assessing pet owner and veterinarian perceptions of need for veterinary compounding services in a community pharmacy setting

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Abstract

Background: Pets, pet owners (referred to as clients in veterinary medicine and throughout this article), veterinarians, and community pharmacies may all benefit from veterinary compounding services provided in community pharmacies, but the benefits of this service are not well-documented in the literature.

Objectives: This study identified perceived benefits and barriers and evaluated the need for veterinary compounding services in community pharmacies; it also evaluated current business practices related to veterinary compounding services.

Methods: A cross-sectional survey was administered to three groups: 1) clients who filled a pet prescription at a study pharmacy, 2) clients who had not filled pet prescriptions, and 3) local veterinarians. Eligible participants were 18 or older; clients must have owned a pet in the past five years. The surveys collected demographic information and assessed benefits, barriers, need, and business practices regarding veterinary compounding services. Demographics were evaluated through descriptive statistics. Responses to Likert-scale items were compared between groups using the Mann-Whitney U test. Qualitative responses were assessed for emerging themes.

Results: One hundred eighteen clients and 15 veterinarians participated in the study. Seventy-two of 116 clients (62%) and eight of 10 veterinarians (80%) agreed that clients would benefit from veterinary compounds provided in community pharmacies. Only 40% of veterinarians agreed that community pharmacists have the knowledge to compound pet medications, compared to 67% of clients (P=0.010). Similarly, 47% of veterinarians agreed that community pharmacists have the skills to compound pet medications, compared to 72% of clients (P=0.016). Forty-eight of 118 clients (41%) would travel 10 miles or more out of their way for veterinary compounding services at community pharmacies.

Conclusions: This study assessed client and veterinarian perceptions of veterinary compounding service benefits, barriers, and need in community pharmacies. Clients identified more opportunities for veterinary compounding services in community pharmacies when compared to veterinarians. Both groups identified a need for veterinary compounding services and agreed community pharmacies providing these services would benefit pets and clients.

Keywords

Drug Compounding; Pets; Community Pharmacy Services; Pharmacies; Pharmacists; Veterinarians; Health Knowledge, Attitudes, Practice; Surveys and Questionnaires; Kansas

INTRODUCTION

Sixty-eight percent of American households are estimated to have at least one pet, with 63% of clients considering their pets to be members of the family.[1] In 2016, the American Pet Products Association (APPA) reported that clients in the United States spent nearly USD 16 billion on veterinary care, including routine veterinary visits and prescription medications.[2] With recent advances in medicine, pets are living longer, just like their human counterparts. A longer life expectancy means more animals develop chronic diseases, which can be costly to manage.[3,4] In 2015, the average amount of money spent on veterinary care per pet in the United States was about USD 1,300.[2]

Pets develop many of the same chronic diseases as humans, including hypothyroidism, arthritis, diabetes, and cardiovascular disease.[3-5] Veterinary medications play a significant role in the management of these diseases, yet one study showed more than one-third of clients find administering medications to their pet to be challenging.[5] Pets injuring their owners at the time of administration, avoiding medications due to lack of palatability, and refusing to swallow tablets or capsules are all barriers to effective medication adherence.[6]

Community pharmacists are uniquely positioned to help clients find solutions to medication issues and to collaborate with local veterinarians to provide the best care for their mutual patients.[7] Prescription filling trends show that clients increasingly seek to fill their pet's medications at community pharmacies.[8] In many cases, pets are prescribed generic human medications which are available at low cost from community pharmacies. In addition, some

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veterinary medications can be compounded by a pharmacist into a dosage form that is more clinically appropriate for both pet and client than commercially available products. Pharmacies that specialize in compounding regularly serve pets and their owners, but most community pharmacies do not currently offer this service. Additionally, community pharmacies often offer more convenient locations and hours of operation than compounding pharmacies and veterinary practices. Therefore, community pharmacies offering veterinary compounding services could offer low cost medications, solutions to medication administration challenges, and convenient hours and locations to clients.[1,2] Veterinarians could benefit through decreased drug inventory costs by outsourcing medication dispensing to a community pharmacy.[9] Veterinarians may also benefit by partnering with a community pharmacy to address therapeutic gaps and overcome drug shortages for their mutual patients.[8,10] Thus, all parties involved may benefit from community pharmacies providing veterinary compounding services, but the benefits of this service are not well documented in the literature.

Despite these possible benefits, working relationships between pharmacists and veterinarians may be less established than pharmacists' professional relationships with other prescribers.[8] As more clients fill pet prescriptions, including compounds, at community pharmacies, the pool of patients being mutually cared for by veterinarians and pharmacists grows.[7,8] As clinical practice evolves, education for pharmacy professionals must adapt to continue providing the best possible care for these patients. Increased access to veterinary resources and education may help decrease pharmacist errors when preparing veterinary prescriptions and aid in the removal of this barrier to effective community pharmacist-veterinarian collaboration.[7,8,11-13]

The purpose of this study was to identify perceived benefits, barriers, and need for veterinary compounding services in community pharmacies and to evaluate current veterinarian business practices regarding veterinary compounding services.

METHODS

Study Setting

Study pharmacies included three Balls Food Stores Pharmacies; Balls Food Stores is a supermarket chain operating 27 supermarkets with 21 pharmacies in the Kansas City metropolitan area. Balls Food Stores Pharmacies offer compounding services, but currently fill very few veterinary compounds; thus, it is an area for possible business expansion.

Study Design

Two cross-sectional surveys were distributed in person, via mail, or via e-mail to eligible participants. Clients and veterinarians were analyzed separately. The project was granted exemption by the University of Kansas Medical Center Human Subjects Committee prior to commencement of the study.

Inclusion and exclusion criteria

Participants were eligible if they were 18 years of age or older. Clients were eligible if they had owned a pet at any time between January 1, 2012 and February 28, 2017. Two groups of clients were targeted: those who filled a prescription for a pet at a study pharmacy between January 1, 2012 and February 28, 2017 and those who had never filled a prescription for a pet at a study pharmacy. Pharmacy staff designated any type of animal as a pet when adding them to the dispensing system, while a free-response item on their survey allowed clients open interpretation of the term "pet". All practicing veterinarians in the Kansas City metropolitan area were also eligible. Clients were excluded if the contact information on their pet's prescription in the pharmacy system was inaccurate and they could not be reached for survey distribution.

Survey Tools

Two separate but similar surveys were developed, one for clients and one for veterinarians. The surveys both collected demographic information in addition to assessing perceived benefits, barriers, and need for veterinary compounding services through multiple-choice, free-response, and five-point Likert scale (1=Strongly Disagree to 5=Strongly Agree) survey items. The veterinarian survey also assessed current business practices regarding

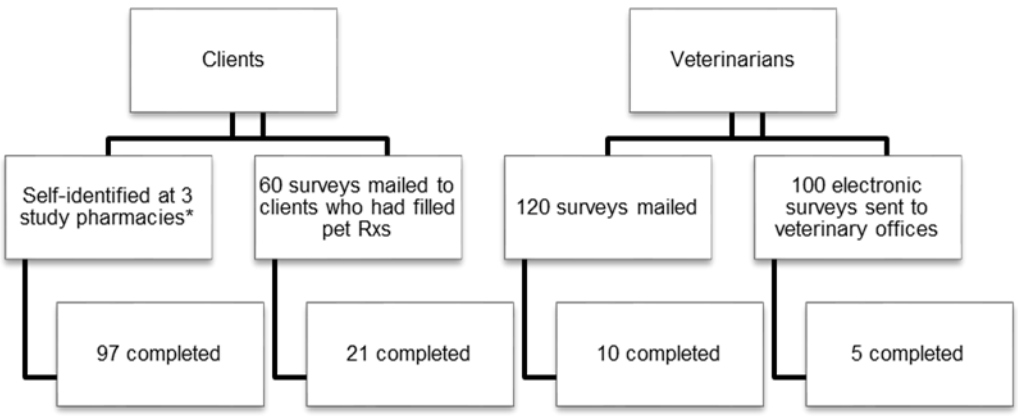

Figure 1. Survey Distribution and Completion.
*Total number of surveys distributed using this method was not measured.

Table 1. Survey Respondent Demographics

	Client n (%)	Veterinarian n (%)
Gender	n=114	n=14
Female	86 (75.4)	12 (85.7)
Age (years)	n=112	n=14
18-29	9 (8.0)	0 (0)
30-39	16 (14.3)	5 (35.7)
40-49	13 (11.6)	2 (14.3)
50-59	34 (30.4)	4 (28.6)
60-69	30 (26.8)	3 (21.4)
>70	10 (8.9)	0 (0)
Race/Ethnicity	n=109	n=14
White	98 (89.9)	13 (92.9)
Spanish, Hispanic, or Latino	7 (6.4)	0 (0)
More than one race	2 (1.8)	1 (7.1)
Black or African American	2 (1.8)	0 (0)
Education	n=101	
High School/GED	15 (14.9)	
Some College	26 (25.7)	
Undergraduate Degree	29 (28.7)	
> Master's Degree	31 (30.7)	
Annual Household Income	n=84	
< USD25k	9 (10.7)	
USD25k - USD49k	18 (21.4)	
USD50k - USD74k	15 (17.9)	
USD75k - USD100k	15 (17.9)	
USD100k - USD125k	10 (11.9)	
USD125k - USD150k	8 (9.5)	
> USD150k	9 (10.7)	

Abbreviations: GED = general education development; k=thousand dollars. Some numbers may differ from text due to omitted responses from survey participants. Percentages may not equal 100% due to rounding.

veterinary compounding services. The client survey contained 26 items (online Appendix 1), while the veterinarian survey contained 28 items (online Appendix 2). Pet owners are referred to as "clients" throughout this article to follow current veterinary medical terminology. Both surveys were pilot tested by five people prior to distribution.

Recruitment

Signs were posted at the study pharmacies to encourage clients to self-identify and participate in the survey. Prescription fill history through myDataMart® (Columbia, MD), a data analysis tool, was also used to identify prescriptions filled for pets at the study pharmacies. Pharmacy dispensing software allows designation of a patient as a pet; these reports included all prescriptions, whether compounded or commercially available prescriptions, and were used to mail surveys to identified clients. In addition, in-person surveys were given to clients at study pharmacies. Surveys were distributed via mail and email to veterinarians.

The Yellow Pages™ (Glendale, CA) was the primary source used to identify area veterinarians for the survey. Investigators also reached out to three local veterinary medical associations to recruit veterinarians to participate in the survey; investigators did not receive confirmation from any of these associations that the survey link had been distributed. Additional surveys were distributed to veterinarians via mail and e-mail at their practice sites by the primary investigator to encourage increased participation.

For all participants, a cover letter was provided containing information about the survey and instructions for survey completion. Hard copy surveys were distributed with pre-numbered envelopes and cover letters; participants were instructed to return the survey to the pharmacy or primary investigator in the sealed, numbered envelope. Participants identified in-person were encouraged to complete the survey onsite, but take-home surveys were allowed on a case-by-case basis. Upon receipt of a sealed envelope, pharmacy staff awarded a USD 5 incentive to the participant. Veterinarians also received a link to an electronic survey created using Qualtrics® (Provo, UT). Veterinarians who completed the electronic survey had the opportunity to enter their contact information into a second survey so that a USD 5 incentive could be mailed to them.

Statistical Analysis

Veterinarians and clients were analyzed as separate subgroups. To adequately power the study and obtain statistical significance, 105 client surveys and 60 veterinarian surveys needed to be completed. Participant demographics were evaluated through descriptive statistics. Responses to survey items utilizing five-point Likert scale and multiple-choice formats were compared between groups using Mann-Whitney U with an a-priori alpha value of 0.05. SPSS v.22 (Armonk, NY) was used for quantitative analysis. Qualitative responses to open-ended survey items were assessed for emerging themes.

RESULTS

One hundred eighteen clients and 15 veterinarians participated in the study (Figure 1). Incomplete surveys were included in data analysis (nine client surveys and five veterinarian surveys). The most common section not completed by survey respondents was the demographics section.

The majority of survey respondents in the client and veterinarian groups were female, 75% and 86% respectively (Table 1). Additionally, the overwhelming majority of survey respondents identified themselves as being white [98 of 109 (90%) clients, 13 of 14 (93%) veterinarians]. Age was more evenly distributed between groups. Client education and income demographics were also evenly distributed. Veterinarian education and annual household income were not assessed as these were not likely to contribute meaningful information to the study.

Client and veterinarian responses to Likert-scale survey items were compared (Figure 2). While all comparisons seemed to show a difference between the two groups, only two of these comparisons reached statistical significance. Seventy-eight of 116 (67%) client respondents agreed or

Table 2: Emerging Themes From Client Comments (n=30)

Theme	n (%)
This service would be beneficial	6 (20)
My pet's medications come from the vet's office	5 (16.7)
Cost would be a factor in my decision to use this service	4 (13.3)
Convenience would be a factor in my decision to use this service	3 (10)
Other	12 (40)

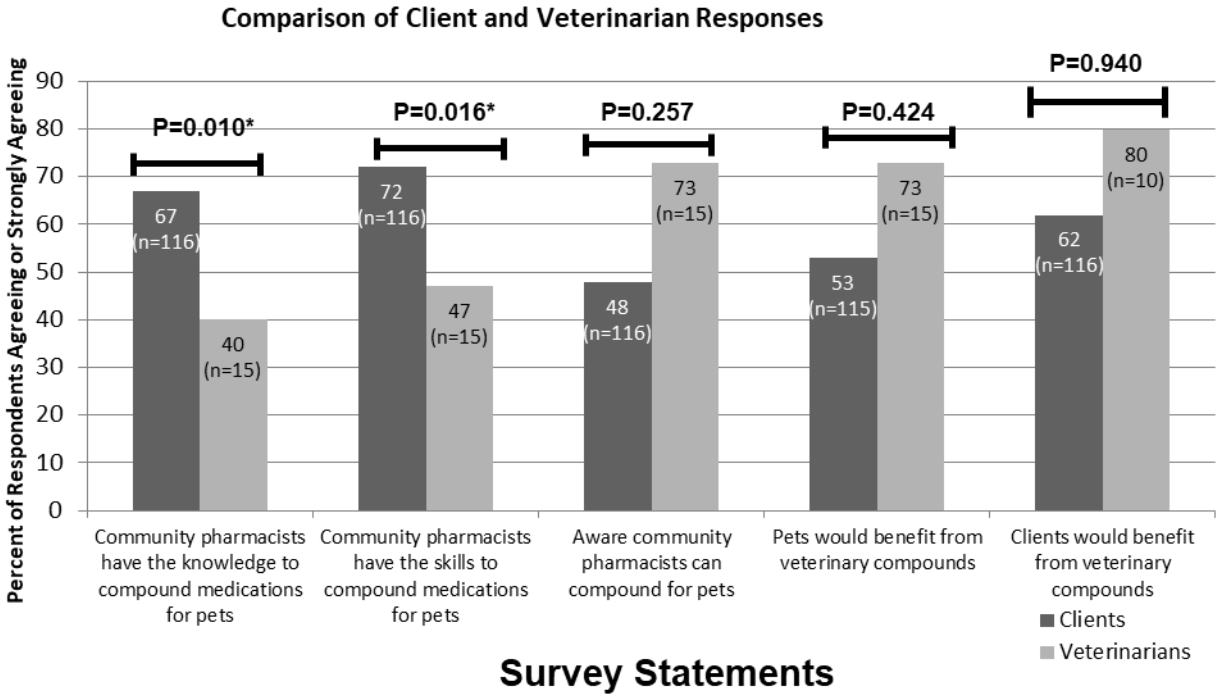

Figure 2. Comparison of Client and Veterinarian Responses. Compares responses to the same Likert-scale survey items. *denotes statistical significance (P<0.05).

strongly agreed that community pharmacists have the knowledge to compound medications for pets, compared to only six of 15 (40%) veterinarian respondents (p=0.010). Eighty-three of 116 (72%) client respondents agreed or strongly agreed that community pharmacists have the skills to compound medications for pets, while only seven of 15 (47%) veterinarian respondents shared the same view (p=0.016).

In addition to the results noted above, three of 15 (20%) veterinarian respondents currently perform compounding at their practice. Ten of 15 (67%) veterinarian respondents would prescribe more compounds if they had a trusted compounding resource. Further, 35 of 89 (39%) clients whose pets had previously taken medications indicated it was "difficult" or "extremely difficult" to administer medications to their pets. Pet refusal to eat or swallow medication was the most commonly reported barrier to giving pets medications. This was reported by 46 of 90 (51%) of clients whose pets took medications and by 14 of 15 (93%) veterinarians. Forty-eight of 118 (41%) client respondents reported they would travel 10 miles or more out of their way to pick up compounded medications for their pets.

Client and veterinarian comments left in the final free-response survey item were assessed for emerging themes (Table 2, Table 3). The item invited participants to write any additional comments they wanted to share. Some themes from clients included: clients believe veterinary compounding services would be beneficial and the decision whether or not to utilize the service would be impacted by cost and convenience. Twelve of 30 (40%) client comments that were left did not fit into a theme; some examples included personal experiences with pet medications, while others were not relevant to study objectives. Two of seven veterinarian comments (27%) did not fit into a theme; one provided clarification on the way a veterinarian chose to respond to a previous item, while another discussed some specific medications that they compound in their practice.

Table 3. Emerging themes from veterinarian comments (n=7)

Theme	n (%)
Community pharmacists lack knowledge of veterinary medications without additional education	3 (42.8)
Our veterinary office uses another pharmacy for our compounding needs	2 (28.6)
Other	2 (28.6)

DISCUSSION

The body of evidence concerning veterinary compounding services in community pharmacies is limited. To the authors' knowledge, this is the first study to evaluate benefits, barriers, need, and business practices regarding veterinary compounding services in the community pharmacy setting. This study showed that the majority of both clients (72 of 116 [62%]) and veterinarians (eight of 10 [80%]) surveyed agreed or strongly agreed that clients would benefit from community pharmacy veterinary compounding services. This may be correlated to the finding that almost 40% of clients with experience administering medications to pets felt it was difficult. This was congruent with Reynolds and colleagues, who demonstrated that medication administration to pets was difficult for over one-third of clients (75 of 221), with nearly 10% (20 of 221) of clients rating it extremely difficult.[5] Veterinary compounding services have the potential to alleviate these administration challenges by providing flavored medications that pets are more likely to take or

medication dosage forms that are easier for clients to administer. However, the current study showed many veterinarians (12 of 15, 80%) do not provide veterinary compounding services. In this study, veterinarians (10 of 15, 67%) indicated they would prescribe more compounds if they had a trusted compounding resource, representing an opportunity for veterinarians and community pharmacists to work together to optimize patient care.

This study also showed there is a perceived need for veterinary compounding services in the urban area studied, as many clients (48 of 118, 41%) would travel out of their way for the service. In comparison, Yen found that adults in urban areas were willing to travel an average of 17.6 miles to receive routine health care for themselves.[14] While clients may be willing to travel fewer miles for healthcare services for their pets than for themselves, the willingness observed by respondents in the current study to travel 10 miles or more out of their way indicates the service is still valuable to the client.

Clients (78 of 116, 67%) were more likely than veterinarians (six of 15, 40%) to agree or strongly agree that community pharmacists have the knowledge to compound pet medications. Similarly, 83 of 116 clients (72%) agreed or strongly agreed that community pharmacists have the skills to compound pet medications, while seven of 15 (47%) veterinarian respondents agreed or strongly agreed with the same statement. These results indicate an opportunity for pharmacists to better educate veterinarians about their technical compounding abilities, training, and drug information skills. Congruently, a 2014 National Association of Boards of Pharmacy (NABP) resolution states that all pharmacists dispensing veterinary medications should have access to drug information resources and possess competence in caring for veterinary patients.[13] Accordingly, resources such as the Merck Veterinary Manual, Plumb's Veterinary Drug Handbook, and the International Veterinary Information Service (IVIS) are readily available to pharmacists, including those practicing in community pharmacies.[15-17] As discussed by Theberge and Sehgal, incorporating veterinary pharmacotherapy and veterinary drug information resources into pharmacy school curricula will better prepare the next generation of pharmacists to care for veterinary patients.[8] Practicing pharmacists may also become Board Certified in Veterinary Pharmacy; complete veterinary residencies, rotations, and compounding boot camps; and focus their continuing education on veterinary pharmacy. They may also actively participate in professional organizations such as the American College of Veterinary Pharmacists and the International Academy of Compounding Pharmacists. At the current time, pharmacy education alone does not make a pharmacist competent in veterinary pharmacology. Pharmacists serving veterinary patients have a duty to seek out these additional resources and opportunities to provide the best patient care. Increasing community pharmacist access to these resources can improve veterinary patient safety; veterinarian knowledge of a community pharmacist's training or credentials in veterinary pharmacotherapy and veterinary compounding may foster interprofessional trust.[8,11,12] Therefore, properly trained community pharmacists can collaborate with veterinarians to become a trusted compounding resource in the care of their mutual patients.

Due to the availability of human generic medications for pet use, it is often inexpensive for clients to obtain veterinary medications at community pharmacies.[9] Furthermore, community pharmacies often offer more convenient operating hours than veterinary practices and specialized compounding pharmacies. Emerging themes from this study indicate medication cost and convenience are important factors for clients when making healthcare decisions for their pets. Thus, veterinary compounding services provided in community pharmacies can service their need for veterinary compounding services while creating a new cash-only revenue stream for the pharmacy. This study also demonstrated that pharmacists may be able to fulfill a need for veterinarians as well by reaching out to them to provide veterinary compounding services.

There are several limitations associated with this study. First, the study was completed in a limited geographical area, and all study pharmacies are located within an urban area. The study sample lacked ethnic and gender diversity; therefore, it is uncertain if the study results are generalizable to more diverse or to rural populations. Additionally, the survey period was relatively short and the surveys used only had face validity. To the authors' knowledge, no validated instruments exist to measure perceived benefits, barriers, need, and current business practices regarding veterinary compounding services. Targeted clients were identified by searching pharmacy dispensing software for patients designated as pets; if demographic information was not entered correctly for these patients, clients could have been missed or misidentified. Another limitation of this study is that one Likert scale question present on the paper veterinarian survey was inadvertently omitted from the electronic survey; thus, the five veterinarians completing the survey electronically were not able to complete this survey item. The item asked respondents to identify the degree with which they agreed or disagreed with the following statement: "My patients' owners would benefit from having medications compounded by a community pharmacist." Lastly, a low incidence of completed veterinarian surveys limited statistical power.

Future research should elicit more veterinarian insight on benefits, barriers, and need for veterinary compounding services. Suggestions to accomplish this include extending the data collection window, increasing the number of survey offer attempts to each veterinarian, and increasing the targeted veterinarian population. Additionally, surveying veterinarians before and after an education session on pharmacist compounding skills and knowledge of veterinary medications is another area of interest. More research is needed to determine what factors affect clients' travel and spending habits related to veterinary compounds provided in community pharmacies. Community pharmacies could consider conducting future research into the effectiveness and profitability of establishing business partnerships with veterinary practices who do not offer veterinary compounding services. Measurement of veterinary compounding service benefits and barriers following implementation of veterinary

compounding services in a community pharmacy has yet to be studied.

CONCLUSIONS

This study assessed client and veterinarian perceptions of veterinary compounding service benefits, barriers, and need in the community pharmacy setting. Overall, client respondents identified more strengths and opportunities for veterinary compounding services in the community pharmacy setting when compared to veterinarian respondents. Both clients and veterinarians identified a need for veterinary compounding services and agreed their provision in community pharmacies would benefit pets and clients in the community. Properly trained community pharmacists and their technicians have the potential to expand their business by reaching out to veterinarians to provide veterinary compounding services.

CONFLICT OF INTEREST

None.

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None.

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Original Research

Potentially inappropriate medication use among older patients attending a geriatric centre in south-west Nigeria

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Abstract

Objectives: To determine the prevalence and describe factors associated with the use of potentially inappropriate medication (PIM) among older patients.

Methods: Cross sectional study of 400 older patients selected systematically at the geriatric centre, University College Hospital, Ibadan between July and September 2016. With the aid of semi-structured questionnaires, information on the socio-demographic characteristics, lifestyle habits, healthcare utilisation and morbidities was obtained. The Beer's criteria 2015 update was used to identify the PIMs. Predictors of PIMs were determined using multivariate analyses at alpha 0.05.

Results: Age was 70.2 (SD=5.9) years and 240 (60%) were females. General prescription pattern showed antihypertensives (34.7%) as the commonest medications used. The point prevalence of PIMs use was 31%. In all, 10 PIMs were used by the respondents. The majority (81.5%) were using one PIM, while (17.7%) used two PIMs and (0.8%) 3 PIMs. NSAIDs (72.6%) were the commonest PIMs identified, followed by the benzodiazepines (24.2%). Respondents had an average of 1.9 morbidities, and mulitmorbidity found in 60.5%. Logistic regression analysis showed self-rated health assessed as better compared with age-mates [OR =1.718 (1.080–2.725)] and being physically active [OR =1.879 (1.026–3.436)] as the most significantly associated with PIMs use.

Conclusions: The use of PIMs among older patients in our setting was high with NSAIDs being the most frequently used medications. An interdisciplinary approach, of medication review by pharmacists', working with physicians may improve prescribing practices among older persons. Therefore, it is necessary to create public health awareness on the use of PIMs among older persons.

Keywords

Inappropriate Prescribing; Professional Practice; Aged; Potentially Inappropriate Medication List; Prevalence; Cross-Sectional Studies; Multivariate Analysis; Nigeria

INTRODUCTION

The older persons represent a majority of the world's population, with approximately two-thirds found in developing countries.[1] Potential inappropriate medications (PIMs), in old age is defined as drugs with higher risk of intolerance related to adverse pharmacodynamics or pharmacokinetics or drug-disease interactions.[2,3] Inappropriate prescribing in the older population is considered a key public health problem because of its direct relationship to morbidity, mortality and consumption of health resources. Potentially inappropriate medications use was found in 34% older Europeans[4] 70% in African American[5] and 15.7 - 45.6% older Nigerians using the Beers criteria.[6-8]

Prescribing of inappropriate medication is a major cause of morbidity and mortality in Europe and the United States.[4,9,10] The sum of healthcare consumed by people above the age of 65 years is, approximately 2.3 times more than that consumed by those below the age of 65 years in Europe.[11,12] Older patients are more predisposed to significant morbidity and mortality due to inappropriate prescribing than the younger patients for numerous reasons. Contributing factors include changes in pharmacokinetic in older age, drug-drug interactions as a result to multiple prescriptions and mostly poorer health status.[13-15]

Physiological changes that arise with ageing mostly affect the drug distribution, hepatic metabolism, but most significantly renal elimination in old age can potentiate the effects of medications, even at doses considered 'normal' in younger adults.[13-15] The Beers criteria comprise of medications the older persons should avoid regardless of the patient's diagnosis.

In Nigeria, numerous studies have investigated the common prescription pattern among patients attending the general outpatients' department.[6-8] Increasing consideration is being paid to inappropriate medication use in older persons. However, criteria defining the appropriate or inappropriate use of medication in Nigeria are not readily available and are not uniform. Notably, no study has been found on PIMs among the older persons in a geriatric centre in Nigeria, therefore the need for this study.

This study aims to assess the use of potentially inappropriate medications using the Beer's criteria among

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older person patients at the Chief Tony Anenih Geriatric Centre (CTAGC), University College Hospital (UCH), Ibadan, Nigeria.

METHODS

This was a cross-sectional, hospital-based study which was carried out at the Chief Tony Anenih Geriatric Centre (CTAGC), University College Hospital (UCH), Ibadan, Nigeria. The CTAGC is the pioneer geriatric centre in Nigeria which was a purpose-built facility for the care of the older persons. The centre has several specialty units such as ophthalmology, physiotherapy, rheumatology, dietetics, geriatric lifestyle, dentistry, memory, and geriatric psychiatry units. In addition, there are service areas in the CTAGC which include the centre inpatient (ward), outpatient, physiotherapy, dietetics, surgical (theatre), and the medical social work services.

The study population was older persons patients aged 60 years and beyond who attended the CTAGC, UCH outpatient clinic from July 2016 to September 2016. The ages of the respondents were determined by direct recall, for those who could not recall their ages, exploration of their ages was made from the table of historical events by Ajayi-Igun.[16] Older persons who did not consent or were too ill to undergo the study procedure were excluded. The sample size was calculated using the Leslie and Kish formula for single proportion using the assumed prevalence of 50%. In all, 400 older persons were recruited. Systematic random sampling method was employed to recruit every third older patient [Sampling interval k=NT/NS=2.7, where NT is the sampling frame (1080) and NS=sample size (400)].

The respondents were interviewed with a semi-structured questionnaire which was pre-tested on 40 patients to ensure the validity of the questionnaire, no changes was made to the questionnaire after the pre-test. However, the participants were not included in the actual study. Information was obtained on the respondents' demographic characteristics such as their age, sex, ethnicity, marital status and number of children; socio-economic characteristics such as educational level, income, occupation (present and past), living arrangement and lifestyle habits. Past medical history of the respondents including previous outpatients' visits, previous hospitalization, healthcare utilization pattern, past morbidities and pattern of medication use in the past one year prior to this study was similarly obtained.

The International Classification of Primary Care second electronic version (ICPC-2e) was used to categorise the diseases of the respondents into domains. ICPC-2e was developed by the World Organization of Family Doctors.[17] The ICPC-2e assesses diseases related to (i) general and unspecified, (ii) blood and immune mechanism, (iii) digestive system, (iv) eye, (v) ear, (vi) circulatory system, (vii) musculoskeletal system, (viii) psychological system, (ix) neurology, (x) respiratory system, (xi) skin, (xii) endocrine, metabolic and nutritional, (xiii) urinary system, (xiv) female genital, and (xv) male genital system.

The Beer's criteria 2015 update was used to determine the potential inappropriate medications (PIMs). The criteria were developed by the American Geriatric Society (AGS).[18] The medications categorized as PIMs in this study were selected from the list of medications indicated as PIMs by the AGS which include medications that cause interactions with drug and diseases, interactions with drug and syndrome, drugs that may aggravate disease or syndrome and medications to be used with caution in the older persons.[18] Similarly, the medication pattern and intake of the respondents were assessed. The questionnaire was translated to Yoruba language and back translated to English language. The administration of the questionnaire took about 40 minutes.

The study received approval from the University of Ibadan/University College Hospital Institutional Ethical Review Board with IRB No (EC/16/0042) approved on 16th June 2016. Informed consent of each respondent was obtained before examination and administration of questionnaires. All the respondents were treated for their primary complaints before administration of the questionnaire.

At the end of each day, the administered questionnaires were sorted out, crosschecked after each interview and coded serially. SPSS (version 21) was used for data entering, cleansing and analysis. Descriptive statistics was

Table 1. Frequency distribution of classes of medications used by respondents

Drug class	N	%
Antihypertensives	575	34.7
Haematinics	176	11.9
Antiplatelets	154	10.4
Analgesics	151	10.2
Oral Hypoglycaemic agents	117	7.9
Disease modifying anti-rheumatic drugs	113	7.6
Antibiotics	42	2.8
Sedatives	30	2.0
Opiods	28	1.9
Anti-lipids	24	1.6
Proton Pump Inhibitors	17	1.1
Anti-malarials	12	0.8
Anti-depressants	9	0.6
Cholinesterase Inhibitors	8	0.5
Anti-Anginal medications	7	0.5
Bisphosphonates	6	0.4
Antacids	5	0.3
Anti-psychotics	3	0.2
Ophthalmic medications	2	0.1
H2-receptor antagonists	2	0.1
Bronchodilators	2	0.1
Steroids	1	0.1
Total	1484	100

Table 2. Frequency distribution of the potential inappropriate medications

Potential inappropriate medications	N	%
Diclofenac	76	51.3
Bromazepam	30	20.3
Rabeprazole	13	8.8
Amitriptyline	8	5.4
Meloxicam	7	4.7
Ketoprofen	5	3.4
Methyldopa	4	2.7
Ibuprofen	2	1.4
Nitrofurantoin	2	1.4
Prochlorperazine	1	0.6
Total	148	100

Table 3. Association of sociodemographic characteristics with the prevalence of use of potential Inappropriate medications

n (%)	Potential Inappropriate Medications			chi-sq	p-value
	YES = 124	NO = 276	Total = 400		
Age groups (years)				0.48	0.92
60 – 64	24 (34.3)	46 (65.7)	70 (100.0)		
65 – 69	37 (30.3)	85 (69.7)	122 (100.0)		
70 – 74	35 (29.7)	83 (70.3)	83 (100.0)		
≥ 75	28 (31.1)	62 (68.9)	90 (100.0)		
Sex				0.02	0.89
Males	47 (29.4)	113 (70.6)	160 (100.0)		
Females	77 (32.1)	163 (67.9)	240 (100.0)		
Marital status				2.42	0.12
Currently married	102 (29.6)	243 (70.4)	345 (100.0)		
Not currently married	22 (40.0)	33 (60.0)	55 (100.0)		
Educational attainment				2.14	0.14
No formal	16 (23.5)	52 (76.5)	68 (100.0)		
Had formal education	108 (32.5)	224 (67.5)	332 (100.0)		
Occupational status				0.02	0.89
Retired	104 (31.1)	230 (68.9)	334 (100.0)		
Not retired	20 (30.3)	46 (69.7)	66 (100.0)		
Living arrangement				0.06	0.81
Alone	6 (28.6)	15 (71.4)	21 (100.0)		
With others	118 (31.1)	261 (68.9)	379 (100.0)		
Financial support				4.87	0.02
Self	95 (34.4)	181 (65.6)	276 (100.0)		
By others	29 (23.4)	95 (76.6)	124 (100.0)		
Number of children				0.05	0.82
0 – 5	88 (30.7)	199 (69.3)	287 (100.0)		
>5	36 (31.9)	77 (67.9)	113 (100.0)		

used to describe socio-demographic characteristics of the respondents. Appropriate charts were used to illustrate categorical variables. Chi-square statistics was used to assess association between categorical variables and Student's t-test to test association between continuous variables. Logistic regression analysis was carried out to explore independent variables associated with potential inappropriate medications. The dependent variable in logistic regression is binary or dichotomous, containing data coded as Yes or No. The goal of logistic regression is to find the best fitting model to describe the relationship between the binary characteristic of interest. Statistical significance was set at $p<0.05$.

RESULTS

There were 400 respondents (females=240). The mean age was 70.2 (SD=5.9) years (range 60 – 91 years). The males were significantly older than the females 71.2-(SD 6.1) years vs 69.5 (SD=5.7) years (t=2.738, p=0.01). In all, 1484 medications were used by the respondents with antihypertensive 575 (34.7%) being the commonest followed by haematinics 176 (11. 9%). See Table 1.

Using the Beer's criteria, 124 respondents were on PIMs giving a point prevalence of 31%. The majority of the respondents 101 (81.5%) used one PIM, while 22 (17.7%) respondents used two PIMs and 1 (0.8%) respondent used 3 PIMs. In all, 10 PIMs were used by the respondents. NSAIDs (diclofenac, meloxicam, ketoprofen, ibuprofen) were the commonest (90, 72.6%) PIMs identified, followed by the benzodiazepines (30, 24.2%). The frequency distribution is shown in Table 2.

As shown in Table 3, higher proportion of females (32.1%) was using PIMs compared with the males (29.4%) but not statistically significant proportion. PIMs use was common among respondents who were not currently married, had formal education, retired from occupation, living with others and had more than 5 children alive. PIMs use was significantly associated with being self-supporting financially (p=0.02).

Higher proportion of respondents who rated their health status better than their age-counterparts significantly used PIMs as compared with those who rated their health status same as their age-counterparts (35.9% vs 23.2%, p=0.01). Similarly, higher proportions of respondents who were physically active (33.9%) significantly used PIMs compared with those who were not physically active (19.8%, p<0.001), as shown in Table 4.

Table 5 describes the diseases of the respondents classified according to ICPC- 2 domains by the prevalence of PIMs. In all, 748 diseases were identified among the respondents giving an average of 1.9 diseases per respondent. Multi-morbidities defined as having more than 2 diseases was found in 242 (60.5%) of the respondents. Highest proportion of PIMs was used by respondents who had diseases in the neurological domain, while none of the respondents with diseases in the skin, ear and female genital domains used PIMs. There was no statistical association between the diseases classified according to ICPC- 2 domains and PIMs.

Table 6 shows the logistic regression analysis carried out on variables which showed significant association with PIMs. Respondents whose self-rated health was assessed as better than those of their age-counterparts (OR=1.718; 95%CI= 1.080 – 2.725, p=0.022) and as being physically active (OR=1.879; 95%CI= 1.026 – 3.436, p=0.041) were found to be most significantly associated with PIMs.

Table 4. Association of healthcare pattern and lifestyle habits with the prevalence of use of potential inappropriate medications

n (%)	Potential Inappropriate Medications			chi-sq	p-value
	YES = 124	NO = 276	Total = 400		
First Admission				3.09	0.21
Never	73 (34.4)	140 (65.7)	213 (100.0)		
Before 60	30 (25.0)	90 (75.0)	120 (100.0)		
After 60	21 ((31.3)	46 (68.7)	67 (100.0)		
Self-rate health				0.01	0.96
Good	118 (31.0)	263 (69.0)	381 (100.0)		
Poor	6 (31.6)	13 (68.4)	19 (100.0)		
Health comparison with age-mate				7.15	0.01
Better	88 (35.9)	157 (64.1)	245 (100.0)		
Same	36 (23.2)	119 (76.8)	155 (100.0)		
Alcohol				0.74	0.69
Yes	1 (20.0)	4 (80.0)	5 (100.0)		
No	123 (31.1)	272 (68.9)	395 (100.0)		
Tobacco				0.02	0.89
Yes	2 (28.6)	5 (71.4)	7 (100.0)		
No	84 (21.4)	309 (78.6)	393 (100.0)		
Physical activities				42.06	<0.001
Active	108 (33.9)	211 (66.1)	319 (100.0)		
Not Active	16 (19.8)	65 (80.2)	81 (100.0)		
Herbal medicine				0.01	0.98
Yes	28 (31.1)	62 (68.9)	90 (100.0)		
No	96 (31.0)	214 (69.0)	310 (100.0)		
Multi-morbidities				0.79	0.37
Yes	71 (29.3)	171 (70.7)	242 (100.0)		
No	53 (33.5)	105 (66.5)	158 (100.0)		
Body mass Index				5.33	0.15
Underweight	2 (13.3)	13 (86.7)	15 (100.0)		
Normal	25 (27.2)	67 (72.8)	92 (100.0)		
Overweight	42 (33.6)	83 (66.4)	125 (100.0)		
Obese	44 (37.9)	72 (62.1)	116 (00.0)		

DISCUSSION

The data revealed high prevalence of PIM in the older persons attending the geriatric centre with NSAIDs as the most frequent PIM identified. Prescribing pattern and ICPC-2 indicates cardiovascular and musculoskeletal diseases as most prevalent among the older people in this study.

Almost 72% of the PIM detected involve NSAIDS (diclofenac, meloxicam, ketoprofen, ibuprofen) followed by benzodiazepines accounting for about 24%. The large-scale use of NSAIDs could be linked to the treatment of musculoskeletal disorders such as osteoarthritis in the older persons, however cardiovascular, gastrointestinal, central nervous system or renal risks remain a serious concern for patient safety. In contrast, the NSAIDs used in some studies in Europe were described to be lower, as acetaminophen or opoids signified the chosen analgesic pathway.[19,20] This might be suggestive of the necessity for reevaluation of the implemented pain management strategies. Benzodiazepines use in the older persons has been identified in many studies as a common potential problem.[21,22] The benzodiazepines are commonly prescribed medications as anxiolytic or as sleep aid among older persons.[22,23] Long term use of these medications are contraindicated in older persons and considered as potentially inappropriate medications in Beer's criteria

Table 5. Potential inappropriate medications use according to diseases of the respondents classified according to ICPC-2 domains.

Diseases classified according to ICPC- 2 domains	Potential Inappropriate Medications			p-value
	Yes = 124 n (%)	No = 276 n (%)	Total = 400 N (%)	
Cardiovascular	91 (29.2)	221(70.8)	312 (100.0)	0.14
Musculoskeletal	49 (30.6)	111 (69.4)	160 (100.0)	0.89
Endocrine, Metabolic & Nutrition	16 (26.7)	44 (73.3)	60 (100.0)	0.43
Neurological	19 (40.4)	28 (59.6)	47 (100.0)	0.14
Eye	13 (27.7)	34 (72.3)	47 (100.0)	0.60
Digestive	12 (40.0)	18 (60.0)	30 (100.0)	0.27
Respiratory	8 (28.6)	20 (71.4)	28 (100.0)	0.77
Psychological	5 (20.0)	20 (80.0)	25 (100.0)	0.22
General and Unspecified	3 (23.1)	10 (76.9)	13 (100.0)	0.53†
Urological	2 (15.4)	11 (84.6)	13 (100.0)	0.22†
Blood and Immune mechanism	4 (40.0)	6 (60.0)	10 (100.0)	0. 53†
Skin	0 (0.0)	1 (100.0)	1 (100.0)	0.50†
Ear	0 (0.0)	1 (100.0)	1 (100.0)	0.50†
Female genital	0 (0.0)	1 (100.0)	1 (100.0)	0.50†
† Fisher's Exact Test				

Table 6. Logistic regression analysis of factors associated with polypharmacy

Variables	beta	p-value	OR	95%CI for OR	
				Lower	Upper
Self-supporting financially	0.127	0.604	1.136	0.702	1.838
Rated health better than age-mates'	0.541	0.022*	1.718	1.080	2.725
Physically active	0.630	0.041*	1.879	1.026	3.436
Constant	0.082	0.810	1.085		

owing to the danger of continued sedation, confusion, psychomotor impairment, falls and physical dependence.[21] The outcomes of this study correlates with those from Europe and United States of America.[21,22]

The mean age of the respondents was about 70 years similar to that documented in other studies.[6,24] The commonest morbidity identified was from cardiovascular system with 34.7% of the patients having hypertension. Comparable studies carried out in different centers in Burkina Faso and Tunisia also stated hypertension as the foremost source of morbidity affecting 82% and 52% of the participants.[25,26] Not surprisingly antihypertensives were the most frequent medications used by the respondents. This was followed by haematinics (11.9%), antiplatelets (10.4%), analgesics (10.2%), oral hypoglycaemic (7.9%) and Disease modifying anti-rheumatic drugs (7.6%). This reflected the high prevalence of cardiovascular and mucoskeletal conditions among older people in Nigeria. As reported by Fadare *et al*. in Nigeria, 30.6% of the prescribed medications were antihypertensive[6], a result similar with other Nigeria findings on medications use in hypertension.[27] Similarly, among older persons Indians, 40.3% of the prescribed medications were antihypertensives.[28] This finding is suggestive of high prevalence of non-communicable diseases among older persons in developing countries.

Inappropriate medication prescribing is a common, major global health issue in older people. This study indicated that PIM frequency amongst the older persons is 31% and of these patients 81.5% used at least one PIM. The PIM prevalence found was comparable to the range mentioned in various European and Nigerian documentation using Beer's criteria.[6,21,29] Moreover, comparison of findings may not be appropriate because diverse set of criteria are applied and in different study environments. Many European countries prescriptions, has found deficiencies in Beers criteria, thus, this led to the establishment of other criteria such as the Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert Doctors to Right Treatment (START).[30,31]

Logistic regression analysis showed that older persons who rated their health better than their age-counterparts and those who were physically active had 1.7 times and 1.9 times risk of using PIMs respectively. Given that the most commonly used PIMs were NSAIDs, one could assume that the pain-free effects of the NSAIDs had positive effects on the self-rated health and activities of the older persons. However, further studies are needed to explore this finding.

The strength of this study includes the use of Beer's criteria in detecting the prevalence of PIMs and the findings of the study will contribute valuable evidence to the literature regarding the prescribing of PIMs to the older persons in this setting. One of the limitations of this study is that it was carried out in the only geriatric centre in Nigeria and this might affect our findings and cannot be generalized to the older patients across Nigeria. The limitation of Beers criteria stands, since this was developed for the USA. It can be noted that some of the medications recorded on the criteria may not have similar antagonistic effects on different population.

Clinical Implications

Our findings indicate that overall prevalence of PIM using Beers criteria was 31%. As PIM is associated with adverse health outcomes, healthcare providers should aim to reduce their prevalence. A systematic review concluded that various interventions including pharmacist interventions, clinical decision support systems and multi-disciplinary approaches can reduce inappropriate prescribing.[32] Screening tools such as Beers criteria have demonstrated to be very valuable in identifying PIM and can be used in intervention studies to improve medication appropriateness and reduce the risk of inappropriate prescribing in older persons, which ultimately should improve other relevant patient outcomes.

CONCLUSIONS

This study has shown the prevalence and factors associated with PIMs and patterns of diseases prevalent in geriatric patients, and have also provided useful baseline data. It showed the high prevalence of PIMs use among the older persons with its attendant public health impact. Assuming the older persons population and the possibilities of PIM, it is necessary to establish and endorse simple applicable, evidence-based national criteria which can be applied in an effective way. With regards the older persons "less is more" hence, safer pharmacological alternatives as well as non-pharmacological strategies might be a good substitute. Drug use studies of this type may eventually help in improving the quality of healthcare services given to the geriatric patients.

CONFLICT OF INTEREST

None.

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Original Research

Evaluation of a prompt card for community pharmacists performing consultations with patients on anticoagulation – lessons learned

Isabelle ARNET, Michael HOLDEN, Sotiris ANTONIOU, on behalf of the iPACT group (International Pharmacists for Anticoagulation Care Taskforce).
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Abstract

Objectives: To evaluate a prompt card (i.e., a post-card sized tool that lists counselling prompt information) with 5 key elements and 3 open key questions to ask patients in community pharmacies.

Methods: Community pharmacists practicing in England and accredited to perform consultations used the prompt card during a formal consultation with emphasis on patients receiving oral anticoagulation. Main outcome measure was the number of performed consultations with pharmacists' thoughts and feedbacks in writing.

Results: During 8 weeks, 19 pharmacists (mean age: 36.6 (SD=9) years; 7 women; accredited an average of 12.9 (SD=9.8) years) performed 1,034 consultations and used the prompt card 104 times during anticoagulation consultations. Overall the prompt card was judged practical and relevant by the 16 pharmacists who used it (100%), especially because it outlines what a good consultation should comprise. The key elements offered a logical framework to guide the overall approach when undertaking a consultation. The two questions, "Why do you want to use this medicine?" and "Why would you not want to use this medicine?" generated negative responses from the patient and pharmacists, respectively.

Conclusions: Our prompt card with key questions summarizing all the points that should be addressed in a consultation supported effective communication during patient-pharmacist interaction. Two questions need rephrasing and a further question is needed to determine how patients are using their medicines.

Keywords

Counseling; Community Pharmacy Services; Pharmacies; Anticoagulants; Pharmacists; Pamphlets; Professional-Patient Relations; Patient Education as Topic; United Kingdom

INTRODUCTION

Community pharmacists have a broad ranging remit and face various challenges in their everyday role. They contribute to patients' care by dispensing medicines safely and in a timely manner, in order to optimise medicines use and improve health outcomes.[1] Pharmacists offer in their daily practice a comprehensive package of services and support to patients. This is mostly achieved through *ad hoc* conversations or more formal consultations. Counselling remains a challenge as within a short period of time, the pharmacist should take an appropriate history and provide relevant advice. Both nationally and internationally, the role and responsibilities of community pharmacists have been changing to use specialised knowledge and clinical tasks[2] for the purpose of optimising patients' use of medicines. The recent change of paradigm from a paternalistic way of giving advice to a passive and silent patient, toward empowering and involving them into the treatment, requires new skills. The implementation of so-called pharmaceutical cognitive services[3] is independent of pharmacy systems and health care structures across countries.

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A prerequisite to pharmaceutical cognitive services is an effective dialogue during patient-pharmacist interaction. A lot has been published to instil Good Communication Practice into healthcare professionals[4-6] that mostly ends up with precepts such as a patient-centred approach[4], individualised medicine advice[7], tailored to the person's context and experiences[7], and delivered in a personalised way.[8] However, how to transform the skill into a verbal interaction with the patient represents the core competency. The importance of how a question is asked has been recognised since years.[9]

A framework has been developed[10] to guide pharmacists during medication-related consultation. It can be used as semi-structured interview guide to obtain and give information in a two-way communication.[11] However, during daily routine, prompt cards and reminders are often preferred[9] because they indicate how questions should be asked or they represent basic information that should be captured in any case. Further, they might represent an essential approach when performing counselling, independently of the degree of experience of the pharmacists. To our knowledge, content of pharmacist-led counselling is poorly investigated[12] and communication tools used by the pharmacists are unknown. We developed a prompt card and asked participants to use it 10% of their consultations with patients on anticoagulants because these are high risk medicines, and new products have come onto the market (non-vitamin K oral anticoagulants,

NOACs) for which a high adherence is needed to reduce patient risk.[13]

The aim of this study is to evaluate in practice a pharmacist's prompt card developed to support effective patient consultation, with an emphasis on anticoagulated patients. The participants were purposively selected and commissioned for the market research from a group of pharmacists by MH Associates who undertook the study. Pharmacists consented to give their personal views and considerations regarding routine counselling of patients. No patient-specific data was collected hence ethics approval was not required.

METHODS

Development of the instruments used

The prompt card (see Figure 1) was developed as a double-sided, post-card format tool. One side aims at giving a sense of responsibility to the pharmacist through background statements that remind them of the advantages of empowering patients to take their medicine. Slogans and 4 general statements were adapted from published recommendations.[11,14,15]

On the other side, 5 key elements (left half of the card) remind to start a consultation by introducing oneself; to indicate the length and purpose of the consultation; to establish what the patient would like from the consultation; to gain consent to record and share information with their doctor; to take a holistic approach to the patient's lifestyle and social circumstances. These elements were adapted from postgraduate education program on consultation skills.[16]

Three formulated key questions (right half of the card) were developed to lead the pharmacist to understand the patient's knowledge ("Why do you think you have to use this medicine?"), motivation ("Why do you want to use this

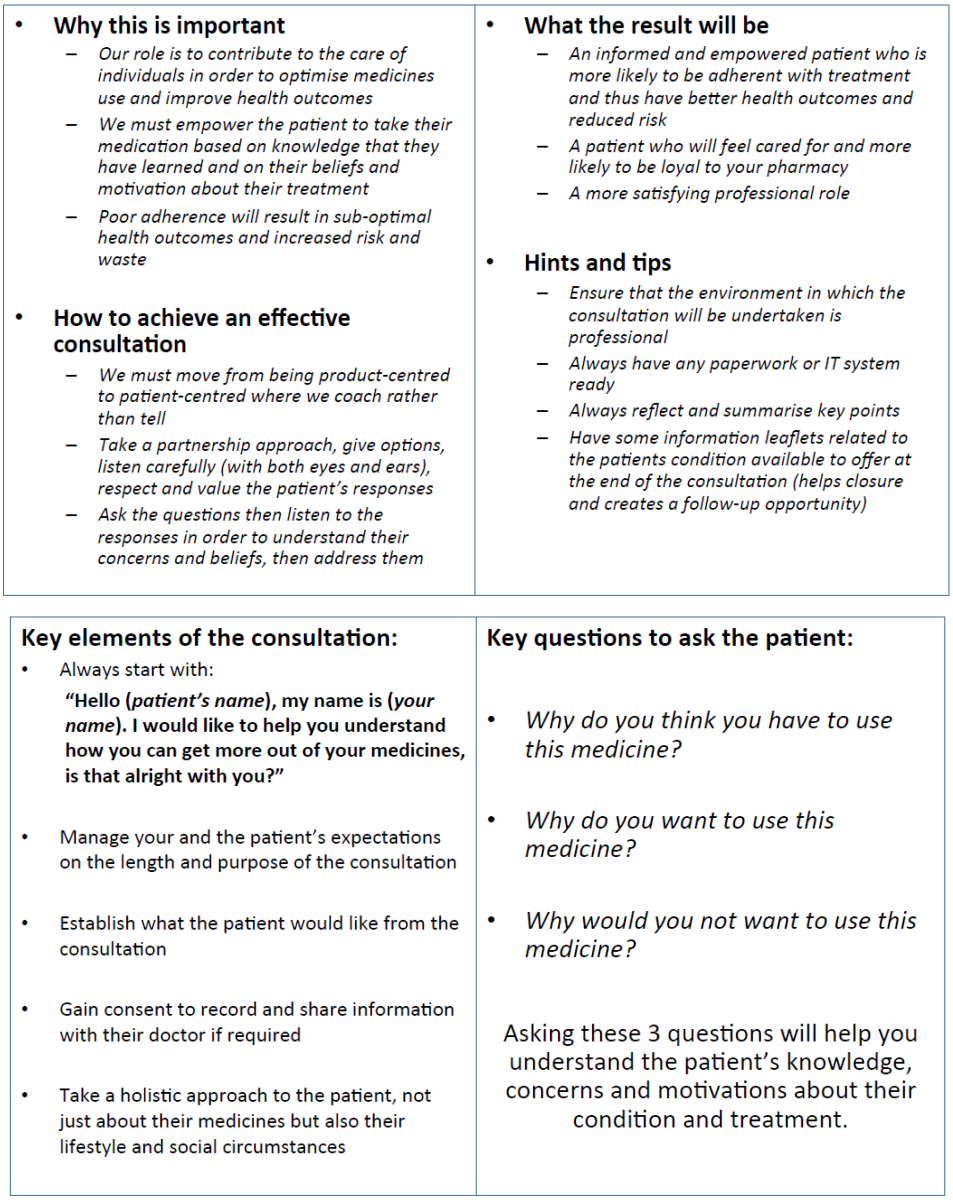


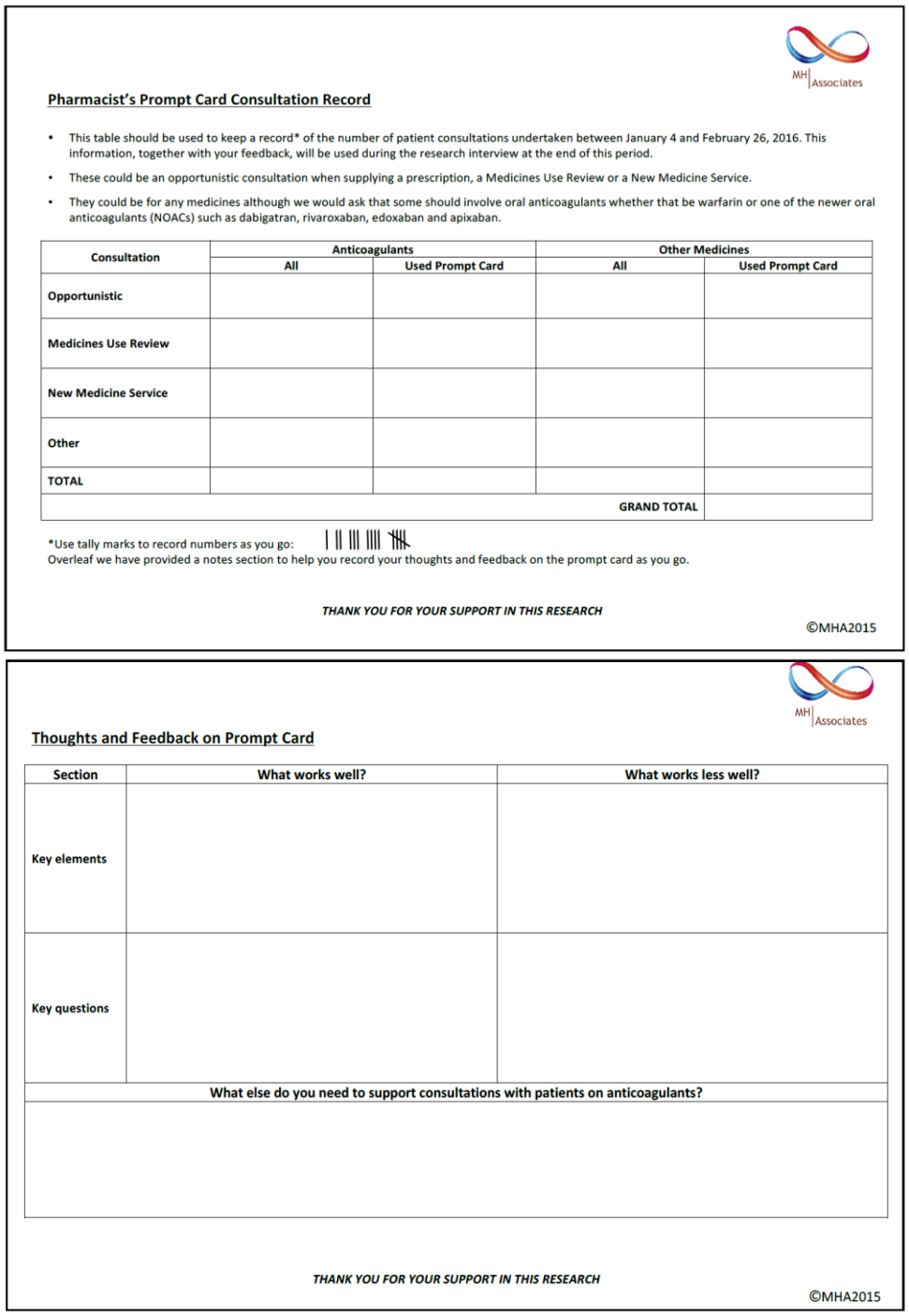
Figure 1. Prompt card, front and back side.

medicine?"), and concerns ("Why would you not want to use this medicine?") about their condition and treatment. These elements were developed based on the concept of "Start with why" to change human behaviour[17] and have never been used in the past. The key questions address the critical phases of initiation and persistence of therapy[18] and not the implementation (such as intake with food; twice daily 12h apart; on an empty stomach etc.).

A consultation record card was developed and given to the participating pharmacists (see Figure 2). Thoughts and feedbacks concerning the key elements and the key questions could be noted on the back of the card.

Study design and setting

This was an exploratory study performed in community pharmacies in North of England. Independent community pharmacists who were already engaged in delivering Medicine Use Review (MUR) and New Medicine Service (NMS) were invited by a personal letter to participate in the research aimed to test and validate the prompt card. They were provided with prompt cards and consultation record cards, and were asked to use the prompt card in consultations during the period 4th January 2016 to 26th February 2016. Patients' inclusion criteria were left at the pharmacists' discretion but should justify an opportunistic consultation (i.e., when supplying a prescription), a NMS or



Pharmacist's Prompt Card Consultation Record

- This table should be used to keep a record* of the number of patient consultations undertaken between January 4 and February 26, 2016. This information, together with your feedback, will be used during the research interview at the end of this period.
- These could be an opportunistic consultation when supplying a prescription, a Medicines Use Review or a New Medicine Service.
- They could be for any medicines although we would ask that some should involve oral anticoagulants whether that be warfarin or one of the newer oral anticoagulants (NOACs) such as dabigatran, rivaroxaban, edoxaban and apixaban.

Consultation	Anticoagulants		Other Medicines	
	All	Used Prompt Card	All	Used Prompt Card
Opportunistic				
Medicines Use Review				
New Medicine Service				
Other				
TOTAL				
			GRAND TOTAL	

*Use tally marks to record numbers as you go: | || ||| |||| 𝍸

Overleaf we have provided a notes section to help you record your thoughts and feedback on the prompt card as you go.

THANK YOU FOR YOUR SUPPORT IN THIS RESEARCH

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Thoughts and Feedback on Prompt Card

Section	What works well?	What works less well?
Key elements		
Key questions		
What else do you need to support consultations with patients on anticoagulants?		

THANK YOU FOR YOUR SUPPORT IN THIS RESEARCH

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Figure 2. Consultation card, front and back side.

a MUR, for any medication. One in tenth consultations should involve any oral anticoagulant (warfarin, dabigatran, rivaroxaban, edoxaban and apixaban). Pharmacists were asked to record the total number of consultations and to note the number of times the prompt card was used.

Telephone interviews were conducted with the pharmacists during the period 4th March to 16th March 2016 using a professional market researcher. A qualitative in-depth methodology was used. In brief, loosely structured interviews of 30 minutes duration in the form of a guided conversation with a pre-determined set of questions were carried out to explore subjective viewpoints, personal experiences and any learning with elements of the prompt card. Follow-up questions were allowed to further clarify a participant's answer, if needed. Participants were asked to rate usefulness of the prompt card on a 7-point Likert scale, with 1 being not at all useful and 7 being extremely useful.

Data analysis

We used a mixed-methods approach with sequential strategy where the quantitative phase (i.e., use of the prompt card during counselling) informed the following qualitative phase (i.e., telephone interviews). For descriptive statistics, we reported percentage and mean values with standard deviation and range, where appropriate. Qualitative data from the telephone interviews and written statements from the consultation record cards were coded and summarised in thematic categories and subcategories using deductive content analysis.[19]

RESULTS

Of the 30 pharmacists invited to participate, 20 accepted and 19 completed the study (66% response). They were on average 36.6 (SD=9.0) years old, mainly men (63.2%) and pharmacy managers (68.4%). They were qualified pharmacists of 12.9 (SD=9.8) years of experience on average (range: 2-34 years) and performed MURs since an average of 7.3 (SD=3.1) years (range 2-10 years), with a post-graduate qualification for eight of them (clinical diploma (7), one independent prescriber). All worked >20 hours in independent pharmacies (13 medium sized, 4 large and 2 small sized) and located in suburban areas (7), health centres (6) or high street (6).

Over the 8-weeks study period, a total of 1,034 consultations were performed, mostly MURs (62.2%), of which 12.8% were anticoagulant consultations. Any reminder was used 497 times, the prompt card was used 104 times during anticoagulation counselling (10%; see Table 1). Three pharmacists did not use the study prompt card and one pharmacist exclusively performed brief *ad hoc* consultations. All pharmacists were interviewed.

Overall views on the prompt card

There was agreement that the card acts as a useful reminder to cover all points that should be addressed in a consultation ("*It makes sure that patients say what they need to, and that you provide all the information that is necessary*"). The main key advantages were the concise form, the completeness ("*Makes sure cover all bits you should*") and the value of the questions ("*Not something that we always ask*"). Even when pharmacists have significant experience with consultations and may have developed their own style, the card helped to keep consultations focused and on track ("*old dog new tricks*", "*Helps to keep / bring back to key focus of conversation*"). There was a feeling that the card would be more valuable for less experienced pharmacists and those with less confidence engaging in conversations with patients ("*For those that don't want to / find it hard to talk to patients*"; "*It will be particularly useful to newly qualified pharmacists who are looking for something to get themselves into the way of doing stuff*"). However, there was some resistance to having to read off a prompt card in a face to face consultation ("*You could look like you don't have the knowledge if you keep looking down at the prompt card*"; "*The idea of a card is reasonably useful if I've got a telephone conversation taking place*").

Background statements

The information included in this section was commented on positively ("*Empowering the patient, patient centred care, these are buzzwords that the NHS is using at the moment. It's very helpful*"; "*I would be surprised if people don't know this, but they might not practice it*"). However, there was mention that some additional education or information is needed about how best utilise and to implement the card approach ("*It says manage your and the patients expectations about the consultation – how?*"). However, there was some acknowledgement that with experience of using the card, pharmacists would become familiar with the approach and be able to adapt the concept to individual patient and consultation scenarios ("*Once you have used it long enough you would probably be able to do it out of memory*").

Five key elements

1. Start: The personal introduction was recognised as extremely important to start the consultation to let the patient know who the pharmacist is, and that the pharmacist is aware of the patient's name. It puts the patient at ease and begins to build rapport ("*This is*

Table 1. Number and type of consultations performed by the 19 community pharmacists enrolled in the study, with number of prompt cards used during anticoagulant consultation.

Consultation type	MUR	NMS	opportunistic	other	Total
Number (%)	643	308	60	23	1,034
anticoagulant	57 (8.9%)	50 (16.2%)	23 (38.3%)	2 (8.7%)	132 (12.8%)
other medication	586 (91.1)	258 (83.8%)	37 (61.7%)	21 (91.3%)	902 (87.2%)
Use of a reminder	318	140	35	4	497 (48%)
prompt card during anticoagulant consultation	49 (15.4%)	37 (26.4%)	16 (45.7%)	2 (50%)	104 (10%)
other reminder	269 (84.6%)	103 (73.6%)	19 (54.3%)	2 (50%)	393 (38%)

MUR: medicines use review; NMS: new medicine service; opportunistic: when supplying a prescription; other: shorter consultation within a different contract.

empowering the patient and asking patient's permission, involving them rather than just giving all the advice whether they like it or not"; "*To be honest, 'is this alright with you?' is a fantastic way of gaining agreement that this consultation is worthwhile and can be carried out*"). Participants did not use the phrase "*I would like you to get more out of your medicines*" but adapted the introduction to fit the purpose of the consultation. For example, if they were undertaking an MUR, they would explain briefly what that covered ("*Hello I'm… we are just going to run through your medicines to see how you are taking them and to see if you have any problems*"). There was consensus that the introduction should explain the purpose of the consultation, certainly for consultations where patients are being taken into the consultation room. Patients can become concerned when the pharmacist proactively asks to speak to them, so there is need to provide reassurance that there is nothing to worry about.

2. Length and purpose: Participants indicated that it was relevant to provide the patient with some idea about how long the consultation was likely to last, especially because patients do not want to spend a long time in a consultation. For several participants, it was a revelation ("*The 2nd point is brilliant, it gives them an idea of how long a consultation is going to take so they don't go over time as well, the staff don't interrupt me, they now know it will be 5 to 10 minutes, and they can tell patients that are waiting how long I will be*"). Informing patients increases their willingness to participate in any pharmacist initiated consultations ("*I guess it encourages them to think it's worthwhile without taking too much time*").

3. Establish what patients want: This question was more relevant if a patient initiated a consultation, since most patients do not specifically want something out of the consultation. There was a general feeling that the question provided more an opportunity for patients to contribute their views about their medicines, ask questions about their conditions, and discuss any other health related issues ("*It can be a bit rude saying what do you want today, it's more about how can I help and listening to them*"). There was feeling that this element needs additional explanation and practical examples of how to incorporate it into a consultation ("*I find it better to run through things and then to ask them if there is anything else they would like to ask or talk about*").

4. Doctor consent: There was overall agreement that this is part of the process when undertaking an MUR or NMS consultation. Pharmacists would require this in *ad hoc* consultations should it become appropriate ("*Today I was speaking to a gentleman and I asked 'would you like me to write to your GP to do that', and he said 'yes please'. I told him that I needed his permission to speak to the GP on his behalf*"). The only debate was that some pharmacists gain consent at the beginning of a consultation whereas others do it at the end. There was consensus on explaining why the pharmacists would need this.

5. Holistic approach: Although relevant holistic topics (diet, lifestyle, weight, smoking cessation) are addressed in MUR/NMS consultations, participants agreed that it is massively important to broaden out the conversation in order to optimise the value of the consultations ("*The patient is getting a better experience because they are being treated as a whole person rather than just a list of medications*"). There was agreement that taking a holistic approach has many benefits including patient centeredness, adding to good reputation, and getting better connection with the patient. The only downside mentioned in terms of taking a holistic approach, was lack of time ("*It would be lovely to be able to do all the healthcare advice but it's not always top of the agenda*").

Three key questions

The participants agreed that the open questions were useful and would work well. They felt they would be able to adapt the questioning in terms of how the conversation was going during the consultation, and add additional questions. In this regard, many felt there was a need to include a specific question about "*how patients are taking their medicines*" on the prompt card. This would enable the pharmacists to understand if medicines were being taken correctly and if not, to provide information and rationale for adhering consistently to the recommended regimen ("*You want to build up a picture about how they feel about their medicines and how they are taking them to ensure they are getting the best use*").

1. Why use medicine: The participants effectively used this question in their consultations, and found it relevant and valuable ("*Good opener*"). Overall, the phrasing worked well ("*You get a genuine answer about what they think they are taking their medicines for*"). The general sense was that the question provides a logical and user friendly way for pharmacists to gain an understanding about patient's knowledge of their medicine. ("*That's important in terms of the modern approach to patients, it's patient led. Rather than just being told to take this tablet, it's more about the patient understanding why*"). The response from the patient then enables the pharmacist to correct any misunderstandings, and also to provide additional information about the medicine ("*We can clarify more why they should be taking it*"). One participant felt the question may work less well in an MUR situation as it would be repetitive when asking for every medicine the patient is taking.

2. Why want to use medicine: The participants commented on this question negatively, and most abandoned using it during the trial period. Fundamentally, it added no value to consultations ("*Most people just said it's because the doctor has told me to use it*"). When asked for suggestions of what would be more relevant to include in a consultation, most pharmacists focused on a question to determine what benefits a patient expected to gain from taking their medicine ("*What do you think are the personal benefits of taking that medicine?*").

3. Why not want to use medicine: Although participants understood what was attempting to elicit from patients in terms of any concerns about their medicines, many were not comfortable using the wording of the question. This question generated negative responses, and could lead to patients questioning the value or safety of their medicine ("*This leads into problems with medication, side effects, tablets not working, stigma, image*"). However, there was a view that getting information around any problems or

concerns is important during a consultation. It allows pharmacists to provide reassurance or offer solutions, with the ultimate goal being to stress how important it is to take medicines as prescribed ("*You can then question them further and find out what is worrying them and then see if you can actually improve their outcomes and try to sort it out for them*").

Rating usefulness and potential use of the prompt card

The prompt card was estimated as quite useful with most pharmacists rating either 4 or 5 (median 4.5; range 2-7). The most valuable reasons cited were "*a good aide memoire*", "*reinforces what should be doing*", and "*sets out best way to undertake consultation*". The less useful reasons cited were "*don't want to hold / read off the card*".

Use of the prompt card with anticoagulated patients

As an MUR and NMS target group, anticoagulated patients are clearly important. The pharmacists did not mention any specific difficulties when using the prompt cards with patients taking anticoagulants. One participant emphasised the absence of concordance on the card, and if this was deliberate, as this was part of his consultation with anticoagulant patients. The participants commented that communication skills specific to anticoagulant patients would be useful, mainly for the most experienced pharmacists as refresher ("*How about a consultation technique specific to anticoagulant patients? A checklist of what you need to consider and what you need to look out for*"). Importantly, there was significant discussion about the need for patient focused information and leaflets, with some feeling that these would be useful tools for pharmacists to have access to, and would potentially reinforce key points about anticoagulants for patients ("*The newer anticoagulants haven't been out that long, so I'm kind of OK with those, but obviously if anything changes we need to be kept up to date*").

DISCUSSION

Adoption of the new skills required for the dispensing of cognitive pharmaceutical services (e.g., "*Take a partnership approach*") has been slow[20], and barriers concern predominantly the communication.[21] In this context, to raise the pharmacists' awareness by means of describing the new skills seems necessary and was approved by our participants. Even though the recruited pharmacists were accredited and used to perform consultations, the background statements on one side of our prompt card were clearly judged relevant.

The prompt card acted as a checklist and reassured that they did not miss any key point during the consultation. Moreover, the explicit questions were highly appreciated since one barrier to counselling is often the lack of knowledge of which questions to ask patients[9] or using self-developed questions that had been judged adequate over time, however doubts raised about whether a different phrasing might be better. Thus, our study highlighted the accuracy of 5 key elements. The specific phrasing for starting the consultation "*Hello, my name is... I would like to* [define the purpose of the consultation] *and help you understand your medicines, is that alright with you?*" was highly appreciated. Even if the introduction to consultation has been promulgated for years as a way to start consultations with patients, for example with the framework Situation – Background – Assessment – Recommendation (SBAR), using pre-formulated wordings may sometimes be challenging. Thus, our starting question seems to create rapport and obtain first active approval from the patient.

Although developed as open questions, only the 1st key question ("*Why do you think you have to use this medicine?*") worked very well to open the discussion, and to gain an understanding about patient's knowledge of their medicine in a friendly manner. The aim of the 2nd question, i.e., to assess a patient's perceived necessity to use the medicine ("*Why do you want to use this medicine?*") was not recognised by the pharmacists or the patients, probably because the underlying concept is not obviously phrased. The aim of the 3rd question, i.e., to assess a patient's perceived concerns to use the medicine ("*Why would you not want to use this medicine?*") was recognised by the pharmacists, but the phrasing was misunderstood by patients as appealing to potential issues with the medicine, instead of personal behavioural statements. Both questions need rephrasing, probably with the explicit use of the terms 'necessity' and 'concerns' to target personal statements.

One of the barriers to use the prompt card was that reading sentences from a card made the pharmacists feel uncomfortable. However, studies about pharmacists looking into a computer placed at the point of sale (e.g., while seeking for information or entering data in a system) demonstrated that this action did not negatively affected the relationship between patient and the health care professional.[22] When paperwork for personal notes or information leaflets are present in the counselling room, the presence of the prompt card can be discrete and unnoticed by the patient.

We acknowledge some limitations. First, we did not assess how the pharmacists perceived that the communication based on the prompt card adds to (or differ from) the way they usually communicate. However, the specific elements of the prompt card have been assessed and a revised version can now be designed, whose effect on the pharmacist's communication can be tested. Second, the quality of the present study depends on the motivation (quantitative phase) and the answers (qualitative phase) of the participants. The data show consistency and saturation, but different results might have been obtained with different participants. Nevertheless, the purposive sampling of accredited and highly motivated pharmacists should have restricted this limitation.

CONCLUSIONS

Our prompt card offers a logical framework to guide the overall approach when undertaking a consultation. It proposes explicit phrasing (e.g., "*is that alright with you?*") and is indicated during the phases of introduction and data collection / problem identification. However, of the 8 proposed elements and questions, two need rephrasing and an additional question is needed to determine how

patients are using their medicines. We will develop and test a revised version of the prompt card.

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CONFLICT OF INTEREST

On behalf of the authors, I have read and understood the disclosure form on declaration of interests and declare that we have no competing interests.

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Original Research

Benzodiazepine and z-hypnotic prescribing from acute psychiatric inpatient discharge to long-term care in the community

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Abstract

Background: Benzodiazepine and z-hypnotic prescribing has slowly decreased over the past 20 years, however long-term chronic prescribing still occurs and is at odds with prescribing guidance.

Objectives: To identify the pattern of benzodiazepine and z-hypnotic prescribing in psychiatric inpatients at discharge and 12 months post-discharge.

Methods: Retrospective observational longitudinal cohort study of patients admitted to two adult psychiatric wards between June and November 2012 (inclusive) who were discharged with a prescription for a benzodiazepine or z-hypnotic drug. Routinely collected prescription data available from NHS Scotland Prescribing Information System was used to identify and follow community prescribing of benzodiazepine and z-hypnotics for a 12 month period post-discharge. Data were entered in Excel® and further analysed using SPSS 23. Ethical approval was not required for this service evaluation however Caldicott Guardian approval was sought and granted.

Results: Eighty patients were admitted during the study period however only those patients with a single admission were included for analysis (n=74). Thirty per cent (22/74) of patients were prescribed a benzodiazepine or z-hypnotics at discharge; 14 of whom received 'long-term' benzodiazepine and z-hypnotics i.e. continued use over the 12 month period. Seven patients received a combination of anxiolytics and hypnotics (e.g., diazepam plus temazepam or zopiclone). Long-term use was associated with a non-significant increase in median benzodiazepine or z-hypnotic dose, expressed as diazepam equivalents.

Conclusions: One in three patients were prescribed a benzodiazepine or z-hypnotics at discharge with 1 in 5 receiving continuous long-term treatment (prescriptions) for 12 months post-discharge. As chronic long-term B-Z prescribing and use still remains an issue, future strategies using routine patient-level prescribing data may support prescribers to review and minimise inappropriate long-term prescribing.

Keywords

Benzodiazepines; Patient Discharge; Practice Patterns, Physicians'; Psychiatric Department, Hospital; Psychiatry; Retrospective Studies; United Kingdom

INTRODUCTION

Benzodiazepine and z-hypnotic (B-Z) prescribing remains an issue across different care settings in North America, Australasia and Europe.[1-3] Whilst there has been some reduction in the use of specific benzodiazepines, it appears to be at the expense of z-hypnotics, whose usage has increased.[4] Much of the B-Z prescribing results in long-term chronic use[1,2] which is contrary to good practice, guidance, and terms of license.[5] B-Zs demonstrate marginal benefits for short-term relief of insomnia and some anxiety disorders[6] which are traits common in most psychiatric disorders and so may warrant short-term or 'as required' use in acute settings. However, issues with tolerance, dependence and adverse effects including cognitive impairment, depression and paradoxical effects i.e. disinhibition, anxiety and impulsivity, can limit their usefulness.[7] More recently, studies have reported increased mortality associated with B-Z use in various populations including those with psychiatric illness.[8,9]

Information regarding B-Z prescribing upon discharge from inpatient psychiatric services is limited, although a few studies have reported that 36%, 37% and 50% of patients in New Zealand[10] and the UK[11,12] received B-Zs on discharge. More importantly, information is lacking regarding their prescribing post-discharge which may contribute to potentially inappropriate long-term prescribing in primary care. At a practical level, routine patient-level prescribing information required to follow a patient's journey from hospital to community care is often lacking or incomplete in most health care systems. However, recent developments in Scotland in the collection and processing of routine patient-level primary care prescription dispensing data can now make this possible.[13] This paper reports on a study which set out to identify the pattern of B-Z prescribing in psychiatric inpatients at discharge and 12

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months post-discharge using routine patient-level prescribing and dispensing information.

METHODS

Ethical opinion was sought from the West of Scotland Research Ethics Service on the use of anonymised patient-level data for the study. The advice received was that the study was considered to be service evaluation and hence did not require research ethics approval. Nevertheless, Caldicott Guardian approval was sought and granted by the NHS Greater Glasgow and Clyde Prescription Data Governance Group.

A retrospective observational longitudinal cohort study design was applied. All patients admitted between June and November 2012, to two acute adult wards in the same psychiatric hospital, in the southwest region of the health board area were eligible for inclusion. Individual patient-level data including: Community Health Index (CHI) number; age; gender; residential postcode to allow mapping of Scottish Index of Multiple Deprivation (SIMD) codes[14]; primary psychiatric diagnosis and admission status (informal or detained) were collected using a standardised data collection form. Patients with multiple admissions during the study period were excluded, as it was assumed these individuals were 'more unwell/complicated' and so any B-Z prescribed would not necessarily be representative of 'routine practice'.

In Scotland, healthcare is delivered by a tax funded National Health Service (NHS) and service users are assigned a CHI number. The CHI number acts as a unique identifier containing details of gender and date of birth.[15] The CHI number enables linkage to other national datasets which use the CHI number as their point of reference such as the national Prescribing Information System (PIS). The PIS contains information pertaining to all NHS prescriptions that have been dispensed in the community i.e. primary care.[13] The overwhelming majority of which are prescribed by the patient's general practitioner (GP), with a minority of prescriptions being written by non-medical prescribers (e.g. nurses and pharmacists), Out of Hours and speciality outpatient services and dispensed in community. The CHI number was used to identify patients who had received a prescription, in primary care, for a B-Zs during within 12 months after discharge. The prescriptions included the patients CHI number and medication details: drug name, dosage form, strength, quantity dispensed, dosage instructions and date dispensed.

Patient-level admission data and B-Z prescribing data were matched for the 12 months following discharge. Details of any B-Z dispensed at months 1 to 12 post-discharge including the name of the medication and the total daily dose were collected from PIS. Where dosage instructions were unavailable or ambiguous e.g. 'as directed' or 'as required', the average daily dose was estimated by dividing the total prescription dose by 28 days e.g. 14 temazepam 10mg tablets (one as required) is 140mg/28 and would be recorded as a total daily dose of 5mg temazepam. As the majority of 'as required' and 'as directed' prescriptions were being dispensed monthly (e.g. zopiclone 7.5 mg tablets, 14 tablets, dispensed each month) and all regular prescriptions were supplied as 28 day prescriptions.

To enable comparison of individual patient-level total daily doses at various times post-discharge, diazepam dose equivalents were calculated for the different B-Zs in line with previous guidance.[16,17] Since most clinical guidelines and product licenses' recommend restricting B-Z use to 2-4 weeks[5,6], long-term or inappropriate use was defined as 'receiving the medication for more than 4 weeks'. All data was anonymised prior to analysis.

Data were entered in Excel and further analysed using SPSS v.23. Where appropriate, due to small cell sizes containing data counts <5, data were aggregated into 'quarters' for the 12 months post-discharge and were defined as: quarter 1=month 1, 2 and 3, quarter 2=month 4, 5 and 6, etc. Where appropriate the Chi-square test or Mann-Whtney U test were used. Since the diazepam dose equivalents did not exhibit normal distribution, the Mann-Whitney U test was used to assess statistical difference between discharge doses and quarter 4 doses for all patients prescribed B-Zs.

RESULTS

Eighty patients were admitted during the study period, six of whom had multiple admissions and were thus excluded. The remaining 74 patients had a mean age of 40 years (range 18-77 years), 45 of whom (61%) were male with just over half (54%, n=40), according to the SIMD score, living in the 20% most deprived areas of Scotland. The most

Table 1.Patient characteristics and demographics at discharge

Patient sample n=74	B-Z prescribed n=22 (30%)	B-Z not prescribed n=52 (70%)	
Gender			
Male n=45 (%)	14 (64)	31 (60)	
Female n=29 (%)	8 (36)	21 (40)	chi-sq=0, df 1, p=1
Median age years (range)	39 (26 to 62)	41 (18 to 77)	Mann-Whitney U test p=0.511
SIMD most deprived quintile (%)	12 (55)	52 (54)	chi-sq =0.04, df 1, p=0.814
Primary Psychiatric diagnosis			
Schizophrenia F20	7	18	
Mood disorder F30	5	11	
Personality disorder F60	5	9	chi-sq =0.4, df 3, p=0.940
Other: anxiety disorder, substance misuse, unknown	5	14	
Admission status (%)			
Informal	15 (68)	36 (69)	chi-sq =0.03, df 1, p=0.862
Detained	7 (32)	16 (31)	

B-Z: Benzodiazepine or z-hypnotic. Primary diagnosis grouped as per International Statistical Classification of Diseases and Related Health Problems 10th (ICD-10) Revision coding.[37]

common primary diagnosis was schizophrenia (n=25), followed by mood disorder (n=16), personality disorder (n=14), substance misuse (n=10) and anxiety disorder (n=7). Fourteen patients (19%) had multiple psychiatric co-morbidities. Twenty-three patients (31%) were detained under Mental Health Act legislation on admission.

Twenty-two patients (30%) were prescribed B-Z medication at discharge, five (7%) of whom received a combination of an anxiolytic and a hypnotic, e.g. diazepam plus temazepam or zopiclone, with males more commonly prescribed B-Zs (Odds Ratio 1.19, 95% CI 0.42 to 3.32). No significant differences in demographics were found between patients prescribed B-Zs and those not prescribed B-Zs at discharge (Table 1). The most commonly prescribed B-Zs were diazepam (n=11), zopiclone (n=8) and nitrazepam (n=3), with z-hypnotics more commonly prescribed than benzodiazepine-hypnotics. The median total daily dose expressed as diazepam equivalents was 8mg (range 2.5mg to 50mg). Four patients, not discharged on B-Zs, started treatment within three months of discharge and remained on long-term treatment.

B-Z prescribing for 12 months post-discharge

Of the 22 patients discharged on B-Zs, six patients did not receive any further B-Zs prescriptions. Of the remaining 16 patients (73%, 9 males and 7 females) who continued to receive repeat B-Z prescriptions post-discharge, 14 individuals received 'long-term' treatment including 9 patients receiving B-Zs continuously for 12 months; 3 patients for 12 months with a single 4 week break in their supply, 1 patient for 10 months and another for 7 months. Only two patients received less than a 4 weeks supply post-discharge. Three patients who were not originally discharged on B-Zs started and remained on long-term treatment: two for 12 months and one for 6 months continuously.

Seven of the 16 patients were dispensed diazepam in combination with either nitrazepam, temazepam or a z-hypnotic. Four of these individuals were prescribed these as 'regular' doses with the remainder using them on an 'as required' basis. Another 9 patients from the original cohort were found to have started a B-Z within the 12 months post-discharge period. Five of whom received short-term irregular treatment but 4 people received regular (long-term) prescriptions of a single B-Zs.

For all 25 patients who received B-Zs in the 12 months post-discharge, 275 B-Z prescriptions had been dispensed. The most frequent was diazepam (n=123, 45%, median total daily dose of 15mg, range 2mg to 50mg), followed by zopiclone (n=46, 17%, 7.5mg, 3.75mg to 15mg), nitrazepam (n=39, 14%, 10mg, 2.5mg to 20mg), zolpidem (n=28, 10%, 10mg, 5mg to 10mg), temazepam (n=21, 8%, 20mg, 20mg to 60mg) and lorazepam/lormetazepam (n=18, 7%). The most common primary diagnosis amongst this cohort was schizophrenia (n=7), personality disorder (n=5) and mood disorders (n=5). The remainder were diagnosed with either an anxiety disorder, substance misuse or had an 'unknown' diagnosis.

B-Z long-term use

Of the 14 patients discharged on B-Zs who subsequently received long-term regular prescriptions there was a statistically non-significant (Mann-Whitney U test, p=0.519) increase in median doses (expressed as diazepam equivalents) from 10mg at discharge to 15.8mg at 12 months, Figure 1. For all patients (n=18) who received long-

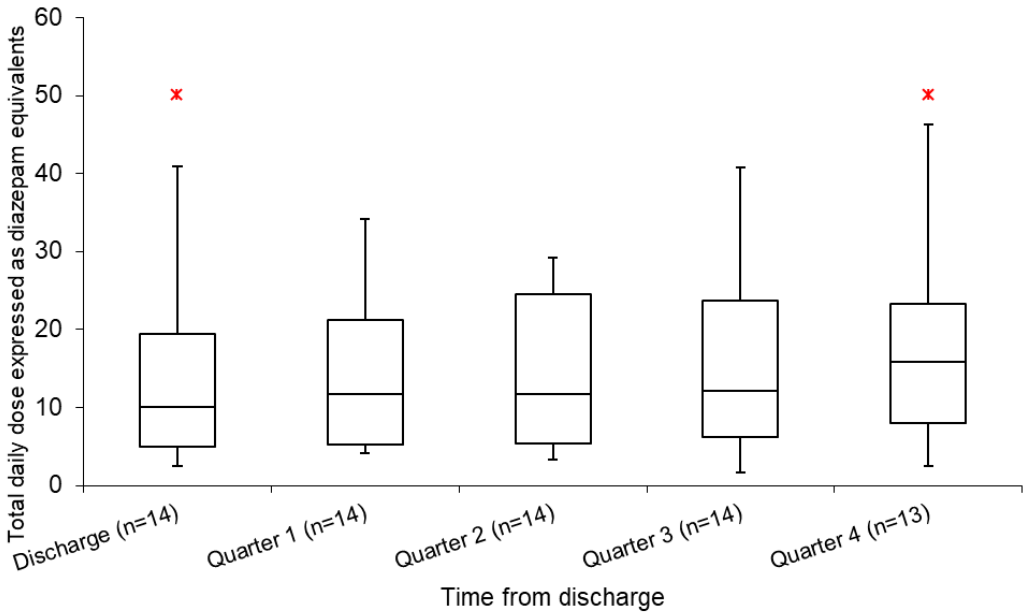

Figure 1, Box plot of total daily doses (expressed as diazepam equivalents) for patients prescribed Benzodiazepines or z-hypnotics at discharged and long-trem.
Quarter 4, n=13 patients as one patient did not receive Benzodiazepines after 7 months of continuous treatment. Mann-Whitney U test p=0.519 discharge versus quarter 4.

term B-Zs including those not prescribed at discharged, the most common primary diagnoses were schizophrenia (33%) followed by depression (22%) and personality disorder (22%). While the median dose for this group increased from 10mg at discharge to 14.6mg at 12 months, Figure 2.

DISCUSSION

One in three patients in this cohort were prescribed B-Zs at discharge. This is comparable to other studies[10,12], but significantly lower than a previous UK study.[11] One in five patients were also found to receive continuous, long-term, B-Zs prescriptions 12 months post-discharge. Most clinicians are aware of the problems associated with chronic B-Z use, and that courses should be limited to a maximum of 2-4 weeks[5], stopping or reducing chronic prescribing in this instance may be more challenging. This may be partly due to patient or carer expectations of continuing treatment, or GPs having reservations in reducing or stopping B-Zs as they were initiated by specialist mental health services. GPs may also lack training or the psychiatrists support in managing the reduction and withdrawal of long-term B-Zs.[18]

B-Z tolerance can develop quickly, particularly if there is dose escalation, and our study is the first to our knowledge to demonstrate small escalations in median doses over time. One factor acknowledged by others as contributing to dose escalation is concomitant use of 2 or more B-Zs. This was observed in a small proportion of our patients and was higher than that reported amongst a Spanish sample.[19] Diazepam was the most commonly prescribed B-Z, with one patient's dose being above the licensed maximum daily dose of 30mg at discharge and at three months post-discharge.[5] The median discharge B-Z dose, expressed as diazepam equivalents, of 10 mg daily is nearly half that previously reported[12] although the dose range was similar to that reported by Summers and Brown.[11] Some differences will be due to patient characteristics including severity and nature of illness or prescriber characteristics which can be influenced by local practice and policy[20], such as z-hypnotic use in preference to benzodiazepine-hypnotics, e.g. temazepam, due to the potential for misuse and drug-related deaths.[21,22]

The majority of those prescribed B-Zs had a diagnosis of schizophrenia, followed by mood disorders and personality disorder, as with other studies[10-12], although Summers and Brown more commonly reported alcohol dependence as the main indication.[11] The long-term use of B-Zs in people with schizophrenia may be to address suboptimal antipsychotic response or an attempt to achieve an antipsychotic sparing effect.[23] However, the evidence supporting such strategies is lacking[24], and more worryingly, B-Z use is associated with increased mortality for people with schizophrenia.[9] For those with mood disorders, selective serotonin reuptake inhibitors (SSRIs) use has been associated with greater longer-term B-Z use, and in part may be due to SSRIs exacerbating insomnia and agitation, especially at higher doses.[25,26] A possible reason for long-term B-Z use in personality disorder could be the challenging nature of the patients who present with a range of behaviours. Nevertheless, B-Zs can provoke aggressive behaviour and increase the risk of suicide

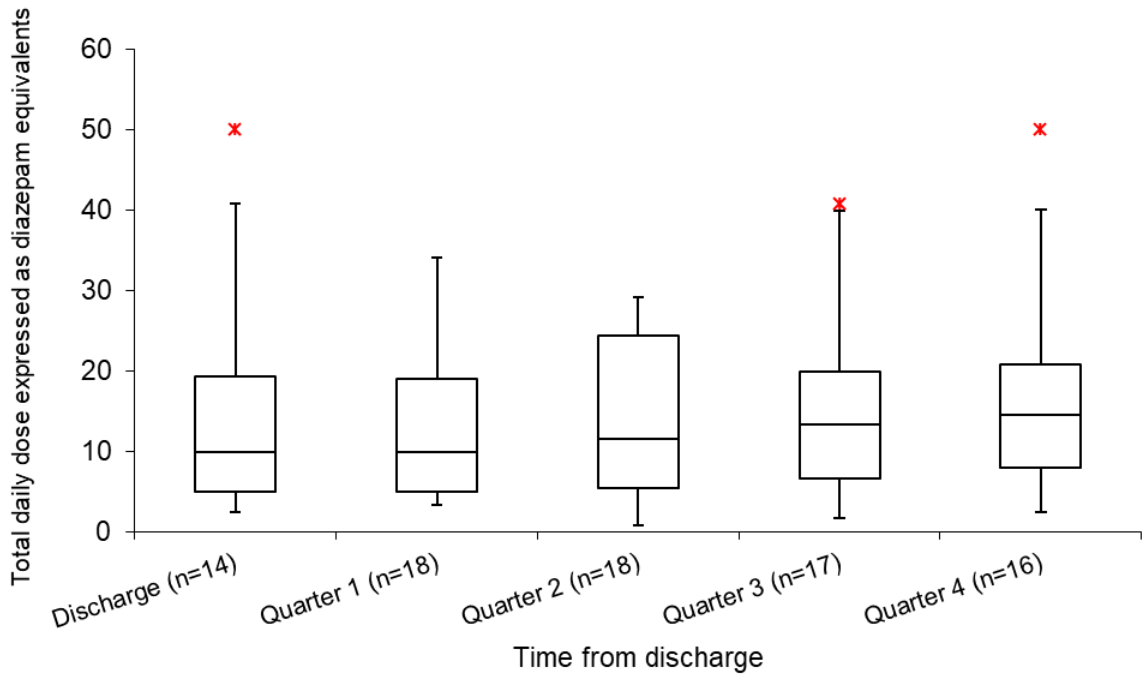

Figure 2. Box plot of total daily doses (expressed as diazepam equivalents) for all patients receiving long-term Benzodiazepines or z-hypnotics post-discharge.
Number of patients receiving long-term Benzodiazepine or z-hypnotics varied during the 12 months. Mann-Whitney U test p=0.498, discharge versus quarter 4.

amongst people with personality disorder.[27] Another problem is that concomitant B-Z use can reduce the efficacy of some psychological therapies, particularly for anxiety.[28] Alternatives such as sedating antipsychotics are not without their own substantial cardiometabolic risks and require more intensive physical health monitoring.[29,30]

The main strength of this study is that it uses routine patient-level primary care prescribing data for dispensed prescriptions containing the CHI number, allowing primary and secondary care data to be 'linked'. This enables relatively easy longitudinal assessment of long-term routine prescribing, without the demands of significant resource implications which previously made this work very challenging and prohibitive prior to PIS data being available. Another strength was that we did not solely rely on the manual collection of prescribing data and the inherent problems associated with that type of data collection.

The main limitations, as with other studies, is that we were unable to assess concordance and compliance with the prescription directions and actual drug use, including possible self-medication with non-prescribed B-Zs[31,32], as well as patient, carer, ward staffing, and prescriber factors which are known to be associated with variations in B-Z prescribing. The lack of post-discharge information such as: if prescribers discussed, attempted or supported patients with B-Z reductions; or if patients' experienced crises which did not require admission but did require extra 'as required' doses which may have inadvertently continued, all contribute to potential limitations affecting the depth and totality of the analysis. Finally, some may consider findings to be limited in their generalisablity; however, this study's findings may be of interest to those working in primary and secondary care serving populations with similar demographics.

As already acknowledged, a challenge for practice is ensuring good communication between specialist services and general practice[33,34] to help minimise inappropriate long-term B-Z prescribing and avoidable drug-related harms. In recent years, pharmacists working within general practices have been supporting GPs to review patients receiving B-Zs; including those attending mental health services, and where appropriate support joined up working.[35] This study demonstrates the utility of routine patient-level PIS prescribing data and 'linked data' in identifying such prescribing issues within specific patient groups at a local level. The use of PIS data will enable national, regional, and local services to target resources to achieve reductions in inappropriate prescribing of various medicines, including psychotropics in line with clinical guidance and policies. It can also be used to enable clinicians to identify high-priority patients for regular medication review in line with national polypharmacy guidance supporting the reduction in inappropriate medicines and associated avoidable drug risks, as well as assessing the impact of regional and national prescribing strategies and interventions.[36] The ability to 'link' PIS patient-level data with other datasets at local, regional and national levels opens up significant potential for pharmacists and non-pharmacist led pharmacovigilance and pharmacoepidemolgical studies, as well as evaluating changes in routine practice at a local, regional or national level. However, patient-level PIS data could also be used to support and enable secondary care specialists to review and reflect on prescribing as general practitioners and practice pharmacists currently do.

CONCLUSIONS

One in three patients were prescribed B-Zs at discharge with 1 in 5 receiving continuous long-term B-Z prescriptions 12 months post-discharge. For those receiving regular long-term benzodiazepine and z-hypnotics prescriptions there was a small non-statistically significant increase in median prescribed dose during the 12 months post-discharge. As chronic long-term B-Z prescribing and use still remains an issue, future strategies using routine patient-level prescribing data may support prescribers to review and minimise inappropriate long-term prescribing.

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CONFLICT OF INTEREST

None.

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Original Research

Pain management in hospitals: patients' satisfaction and related barriers

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Abstract

Background: Suboptimal pain control has been frequently reported in healthcare settings and documented to negatively impact patients' health. Patients' perception regarding pain management may influence their satisfaction regarding treatment.

Objectives: This study focuses on the assessment of patients' satisfaction regarding pain therapy and defining patient-related barriers for its implication.

Methods: A cross-sectional study was conducted in two tertiary care hospitals from April till July 2017. A face-to face interview questionnaire was filled regarding pain scores and patients' attitudes regarding pain management. Both medical and post-surgical adult patients with all types of pain were eligible to participate. A descriptive analysis of patient satisfaction and perceptions regarding pain management was done.

Results: Results from 183 participants with a mean age of 49 (SD=17.33) revealed that pain was their main reason for hospitalization (71.6% of the cases). Numeric pain scores were recorded only in 14.2% of the patient medical files. Pain intensity documentation by healthcare professionals was found in 41.5% of the cases, and 7.7% of the patients had to wait for more than 30 minutes before getting the pain medication. Around 85% of the patients were satisfied with their pain management. Patients' barriers to effective pain therapy were mainly fear of adverse effects, addiction, and additional costs ($p<0.05$).

Conclusions: Pain remains a prevalent problem that requires more efforts for improvement. Our study can effectively serve as a start for larger studies where barriers to pain management can be assessed as an independent variable affecting pain management practice.

Keywords

Pain; Attitude to Health; Pain Management; Patient Satisfaction; Inpatients; Surveys and Questionnaires; Lebanon

INTRODUCTION

Patient's right to involvement in all aspects of his/her pain management is promoted by governing organizations and healthcare institutions.[1-3] Patients' satisfaction with treatment is crucial to measure performance and success of the healthcare setting.[2] In fact, patients expect to receive optimal pain management resulting in fewer adverse effects.[4] Despite pain-related position statements and the recommendation of the American Pain Society that pain should be assessed by health care providers (HCPs) as a 'fifth vital sign'[5-7], under-treatment of pain remains a global concern. Although the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the American Society of Anesthesiologists addressed patients' rights to have effective pain management[1,2], insufficient knowledge of pain management still leads to inadequate pain evaluation which might adversely affect patients' quality of life, physical and psychological wellbeing.[3,4,8] Suboptimal pain control has been frequently reported in acute care settings to negatively impact patients' health and reduce patient satisfaction.[9,10]

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In the Middle East, the literature pertaining to the adequacy of pain management is still inaccurate and only few observational studies addressed the management of pain in Lebanese hospitals with a focus on the different patient-related barriers to adequate pain management.[11,12] Despite the emphasis of the National Committee for Pain and Palliative Care to set standards for the improvement of pain management in Lebanon, many patients still suffer from pain during hospitalization.[13,14] For instance, a Lebanese study conducted by Ramia *et al.* found that documentation of pain intensity was not completed for more than 90% of surveyed patients[15] which constituted a major problem for adequate pain assessment. Similarly, multiple studies on pain management showed that documentation of pain was not consistently done which deprived the patients from proper treatment.[16-20] Thus, understanding patient's satisfaction as well as defining the barriers inhibiting such an appropriate assessment needs further investigation.

Accordingly, this study aims at 1) assessing patients' description of pain intensity and characteristics; and 2) evaluating overall patients' satisfaction regarding pain management. Secondary objectives were 1) describing if pain assessment and evaluation were practiced and documented by HCPs according to patients' statements, 2) assessing patients' attitudes and perceptions towards their pain management during hospitalization and their barriers prohibiting adequate therapy and 3) identifying predictive factors that affect patients' satisfaction regarding pain management.

METHODS

Study design and setting

A prospective, descriptive, cross-sectional study was conducted from April till July 2017 in two private tertiary-care centers. Patients' surveys were used to describe patients' pain intensity as well as their attitudes and beliefs prohibiting its adequate management. Other information such as the methods of pain assessment and their documentation by HCPs were also obtained from patient medical charts, physician orders and nurses' progress notes.

Study population

The study targeted all inpatient adults with pain of any origin during their hospital stay. Eligible patients were alert adults who have been hospitalized for at least 24 hours and prescribed at least one analgesic. Patients were distributed among four different hospital units: Internal Medicine (IM), Obstetrics and Gynecology, Coronary Care Unit (CCU) and orthopedics unit. Excluded patients were pediatrics (<18 years old) or older adults (>85 years old) with cognitive impairment. Patients admitted to the emergency room (ER), or discharged within 24 hours or less, and those who were missing a complete medical record were also excluded from the study.

Tool for data collection

Face-to-face questionnaires, divided into two sections, one for the description of pain and patients' satisfaction and another for patient's perceptions regarding pain therapy, were developed in English and then translated to Arabic. It consisted of 8 data collection pages, with most of the questions requiring a "yes" or "no" answer. The first set of questions regarding pain score and intensity was developed in congruence with the American Pain Society Patient Outcome Questionnaire (APS-POQ) (Internal reliability: alpha Cronbach's score of 0.89) and modified to align with the study requirements.[21,22]

Patient-related barriers were incorporated from the Barriers Questionnaire-13 (BQ-13) (Internal reliability: alpha Cronbach's score of 0.86) obtained from the study conducted by Boyd-Seal *et al*.[23]

Participating patients were asked to voluntarily fill out the questionnaires that included the following sections: 1) Demographic features including age, gender, educational status, living place, income, health insurance and marital status; 2) pain intensity measured with the items "least" and "most" severe based on numerical rating scales (NRS) with answer options ranging from 0 to 10, where 0 reflects no pain and 10 worst pain possible; 3) pain interference with activities (walking, sitting, and standing) and sleep (turning, repositioning in bed, difficulty falling asleep and difficulty staying asleep); and 4) overall patient satisfaction measured using a 4-point Likert scale including strongly dissatisfied, dissatisfied, satisfied, and strongly satisfied that was assessed after 48 hours from the initiation of the first prescribed analgesic. Patient satisfaction categories were then divided into two groups: strongly dissatisfied or satisfied and satisfied or strongly satisfied.

Pain evaluation by HCPs section included 1) patient's recall if pain intensity was communicated with any HCP; 2) the existence of documentation of pain scores in patients' medical files; 3) patient's education regarding therapy; 4) timely delivery of intervention; and 5) follow-up of any HCP with the patients. As for the attitudes of patients regarding pain management, barriers to adequate pain management such as fear of addiction/tolerance, fear of side effects, fear of additional costs and injections were recorded. Barriers such as communication problems, and fear of distracting a physician were also reported. Social and cultural opinions such as sparing medications for severe illnesses, the association of step-up therapy with poor prognosis, the belief that ''good'' patients do not complain about pain were subsequently noted. Patient's opinions categories were grouped as "Do not believe" or "believe".

Concerning the health status of each patient, the investigators referred to the patient's charts, physician orders, and nurses' progress notes in order to record the reason of hospitalization, co-morbidities, home medications and smoking history as well as allergies. Pain categories were later classified as: mild (NRS score of 1–3), moderate (NRS score of 4–6), and severe (NRS score of 7–10) as per World Health Organization (WHO) pain ladder.[5,24]

The study was completed in accordance with the Ethics Code set and approved by the Medical Directory of the hospital. Participation was voluntary and oral consents were taken from each study participant. This study was performed in accordance with the ethics standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Data collection

Eligible patients for inclusion were identified by a pain medication order arriving to the hospital pharmacy. Interviewers and the chief pharmacist of each hospital were making sure that medications such as acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed for pain rather than fever reduction. That was done by referring to nurses and progress notes or physician orders and by checking the vital signs of each patient especially the temperature. Any temperature below 38ºC was not considered to be a fever.[25] When in doubt or in the case of borderline temperatures; interviewers asked the nurses of each medical department about the reason of each analgesic administration and referred always to the patient to ask about pain status and for their willingness to answer the questionnaire. Prescribed pain medications and the occurrence of any side effect were also recorded from patient's medical records and progress notes. A follow-up after 48 hours from the initiation of pain therapy was done to track therapy changes, and assess helpfulness of pain treatment as well as patient satisfaction and perceptions.

Statistical analysis

Completed questionnaires were analyzed using SPSS version 22.0. Descriptive statistics were used to describe patients' characteristics. Means and standard deviations were calculated for continuous variables. Pain characteristics, including severity, method of pain assessment, patterns of pain, non-pharmacologic and

pharmacological therapies were summarized. Relationship between categorical variables such appropriateness of therapy and its relationship with patients' satisfaction were examined using Pearson's Chi^2. Fisher's exact test was used when a condition of any expected cell count in a 4x4 table is less than 5. An alpha level of ≤5% was used to detect statistical significance. A forward stepwise likelihood ratio logistic regression was then conducted for multivariable analysis to identify the predictive factors associated with patients' satisfaction. The dependent variable was satisfaction of the patients and variables that showed significant results in the univariate analysis ($p<0.001$) were considered the independent variables. Such a restrictive criterion was considered because of the small sample size of the study. The Hosmer-Lemeshow goodness-of-fit test was used to assess the overall fit of the model, and adjusted odds ratios (aOR) were calculated.

RESULTS

Baseline characteristics

A total of 200 patients were eligible to participate in the study. 82 were selected from the first hospital and 118 from the second hospital. Of them, 183 (91.5%) patients met the inclusion criteria and completed the questionnaire whereas 17 (8.5%) were excluded. The most common reason for exclusion was lack of follow-up due to hospitalization of less than 48 hours (Figure 1). The mean age was 49 (SD=17.335) [range 19-85]. There was a similar distribution of the gender groups (57.4% females, 42.6% males). Patients were distributed as follows: 127 (69.4%) from IM, 15 (8.2%) from CCU, 29 (15.8%) from obstetrics and 12 (6.6%) were from the orthopedics unit. 53.9% of the patients underwent surgeries (obstetrical, orthopedics, or any type of surgery such as gastric sleeve, appendectomy, etc.). The majority of patients were covered by national social security fund (NSSF) (54.6%) or private insurances (13.1%) or both (8.2%). Around 64% were admitted with health coverage of a second medical class versus 21.9% were from the first class and 13.1% from the third class. 125 patients (68.2%) were given analgesics before admission. The mostly prescribed home analgesics were acetaminophen (53%), ketoprofen (4.9%), ibuprofen (3.8%), diclofenac (3.8%), and tramadol (2.7%) either on regular basis or as required. More baseline characteristics are listed in Table 1.

Primary Endpoints

Around three-quarters (71.6%) of the sample reported that pain was their main reason for hospitalization while pain was determined after an operational procedure in 98 cases (54%). When asked to describe their pain intensity on NRS with answer options ranging from 0 to 10, where 0 reflects no pain and 10 worst pain possible, the majority of the patients described their pain as severe (85.2%, n=156) at its highest intensity whereas only three patients (1.8%) described it as severe at its least. they varied in their description of pain and reported pain of different intensities: mild (69.2%) and moderate (29%). When at its highest, the pain intensity was again broadly reported as mild (2.2%, n=4) and moderate (12%, n=22).

After 48 hours of follow-up, new pain scores were recorded: the majority (59.4%) reported to have mild pain (n=110), 35.5% (n=66) reported to have moderate pain and only two (1.2%) as severe. Most of the patients reported that pain interfered severely with some of the daily activities: 84 (46%) determined that pain severely interfered with their ability to turn, sit and reposition in bed whereas 80 (43.7%) reported that pain interfered moderately with such activities. A similar number reported that they could not do activities out of bed such as eating, walking and sitting (49.1% as severe versus 41.5% as moderate). Similarly, pain interfered moderately with the ability of patients to fall asleep (41.5%) and stay asleep (40.4%).

Results from the first day of admission revealed that 82 patients (44.8%) were prescribed one medication, 89 (48.6%) two, nine patients (4.9%) three and one participant only (0.5%) four different pain medications, while two patients (1.1%) were not given any pain medication at all. Adjunct therapy, such as gabapentin was given to one patient whereas hyoscine butylbromide was prescribed for eight patients (4.4%) and phloroglucinol for six patients

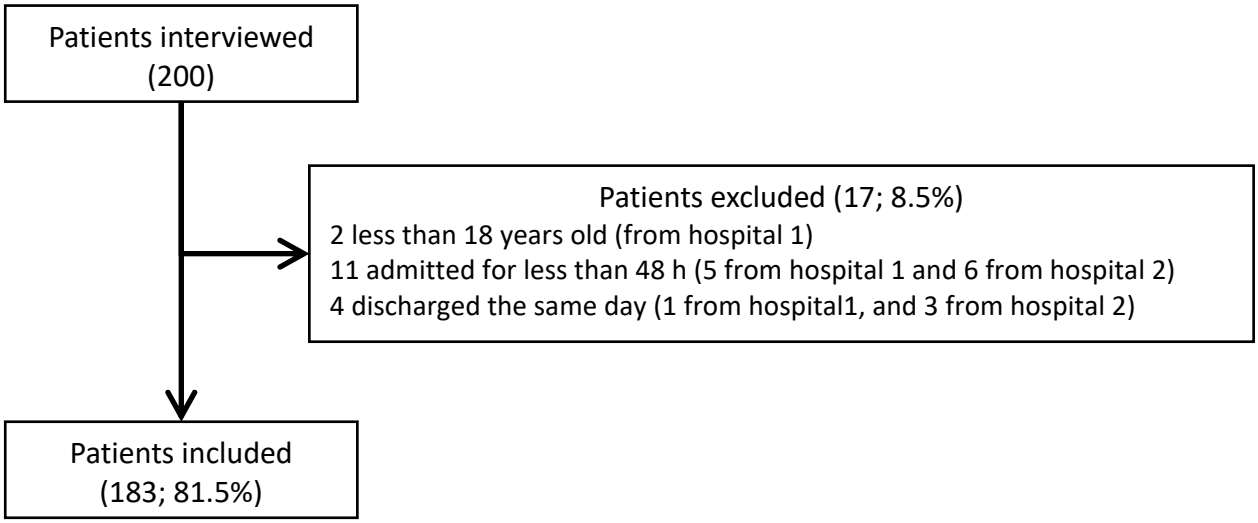

Figure 1. Patient inclusion procedure.

Table 1. Patients' demographic characteristics.	
	N (%)
Gender	
Male	74 (40.4)
Female	109 (59.6)
Age	
19-30	35 (19.1)
31-40	30 (16.4)
41-50	22 (12.0)
>50	96 (52.5)
Health coverage	
Self-payer	23 (12.6)
NSSF and/or insurance	139 (76.0)
MOH coverage	12 (6.6)
Others	9 (4.9)
Medical class	
First	40 (21.9)
Second	117 (63.9)
Third	24 (13.1)
Highest level of education	
Not completed	68 (37.2)
High school degree	73 (39.9)
University degree	42 (23.0)
Income Status	
Poor	22 (12.0)
Fair	57 (31.1)
Good	17 (9.3)
Marital Status	
Single	34 (18.6)
Married or divorced	139 (76.0)
Widowed	10 (5.5)
Unit	
IM	127 (69.4)
Obstetrics	29 (15.8)
CCU	15 (8.2)
Orthopedics	12 (6.6)
Surgery	
No	83 (45.4)
Yes	97 (53.0)
Smokers	78 (42.6)
Allergies	
NSAIDs	4 (7.0)
Acetaminophen	2 (1.1)
NSSF= National Social Security Fund; MOH= Ministry of Health; IM= Internal Medicine; CCU= Cardiac Care Unit; NSAIDs= Non-Steroidal Anti-inflammatory Drugs.	

(3.3%). Acetaminophen, ketoprofen and meperidine were the most frequently reported drug used (95.1%, 34.4%, and 15.3% respectively). Side effects were detected in 34 participants (18.6%). Common side effects were constipation (6%, n=11), nausea/vomiting (4.9%, n=9), heartburn (4.4%, n=8), and dizziness (4.4%, n=8). As for the non-pharmacologic methods for pain relief, they were practiced by 37 patients (20.2%). The most commonly used were distraction (6.6%, n=12), bed rest (6%, n=11), deep breathing (5.5%, n=10), and exercises like walking (4.4%, n=8). Of noteworthy findings, these methods were useful in alleviating pain only in 7.1% of cases. More details about pain characteristics are listed in Table 2.

Results have shown that pain scores significantly decreased from an average of 8.34 (SD=1.884) on the first day of treatment to 3.24 (SD=1.611) after 48 hours of follow-up ($p<0.001$). In general, the majority of patients reported to be satisfied (68.3%, n=125) and 30 patients strongly satisfied (16.4%) regarding pain management therapy. Only 28 patients (15.3%) were either dissatisfied or strongly

Table 2. Disease characteristics and pain severity and assessment	
	N (%)
Worst pain severity	
Mild to moderate [a]	26 (14.2)
Severe [b]	156 (85.2)
Scale used to measure pain	
Verbal	23 (12.6)
Numeric	3 (1.6)
Pattern of pain	
Continuous	58 (31.7)
Comes and goes	113 (61.7)
Gets worse in the evening	8 (4.4)
Pain makes the patient feel	
Anxious	82 (44.8)
Depressed	41 (22.4)
Frightened	56 (30.6)
Insomnia	53 (29.0)
Weak	45 (24.6)
Nausea and vomiting	53 (29.0)
Pain severely interferes with [c]	
Turning and repositioning in bed	84 (46.0)
Daily activities out of bed	90 (49.1)
Falling asleep	69 (37.7)
Staying asleep	64 (35.0)
Breathing	49 (26.8)
[a]Pain score of 0 to 6; [b]Pain score of 7 to 10 (according to the World Health Organization's three-step ladder for pain management); [c]Scores of 7 to 10	

dissatisfied. When comparing between categories of pain severity, it was shown that 25 patients (16.2%) with mild to moderate pain were satisfied or strongly satisfied versus 129 (83.8%) with severe pain. Again, only one patient with mild to moderate pain was either dissatisfied or strongly dissatisfied when compared to 27 patients (96.4%) with severe pain. This trend failed to show any statistical significance (p=0.078).

Secondary endpoints

Several unfavorable management practices related to pain assessment and management were reported in both medical and surgical services. These included the following findings: (1) pain status not being discussed with a HCP prior to analgesic administration [76 patients (41.5%) were properly assessed versus 39.9% (n=73) not sufficiently assessed and 11.5% (n=21) not assessed at all]; (2) pain score was not recorded on medical files (54.6%, n=100); (3) patients not being provided with sufficient education regarding the importance of pain reporting and management (53.6%, n=98) nor followed-up appropriately in the next 48 hours (75.4%, n= 138); (4) patients having to wait for more than 30 minutes before getting the pain medication when requested (7.7%, n=14); and (5) patients asked about pain medications but were not given (10.9%, n=20). Among the cases in which pain assessment was done before initiation of pain treatment, pain score was recorded only in 14.2% of the medical files with the NRS being the most frequently used scale (12.6%). Nurses were the most involved HCPs to report pain since 16.9% of pain cases were assessed by nurses solely versus 2.7% by physicians.

When asked about their perceptions regarding pain management in hospitals, patients' opinions were classified as follows: (1) with regards to addiction, 69 patients (37.7%) either agree or strongly agree about its influence on pain assessment; (2) when it comes to fear of the side

Table 3. Sociodemographic predictive factors associated with patient's satisfaction with pain management

	Strongly dissatisfied or dissatisfied	Strongly satisfied or satisfied	p-value
Gender			0.311
Male	14 (18.9%)	60(81.1%)	
Female	14 (12.8%)	95 (87.2%)	
Age	87 (69.6%)	38 (30.4%)	0.035
19-65	19 (12.7%)	131 (87.3%)	
>65	9 (27.3%)	24 (72.7%)	
Health coverage			0.685*
Self-payer	4(17.4%)	19 (82.6%)	
NSSF or/and insurance	20 (14.4%)	119 (85.6%)	
MOH coverage	3(25.0%)	9 (75.0%)	
Others	1 (11.1%)	8 (88.9%)	
First class coverage			0.515
No	21 (14.6%)	123 (85.4%)	
Yes	7 (18.9%)	30 (81.1%)	
Highest level of education			0.24
Not completed	9 (13.2%)	59 (86.8%)	
High school degree	15 (20.5%)	58 (79.5%)	
University degree	4 (9.5%)	38 (90.5%)	
Income status			0.82*
Poor	3 (13.6%)	19 (86.4%)	
Fair	7 (12.3%)	50 (87.7%)	
Good	1 (5.9%)	16 (94.1%)	
Marital status			0.28
Single	4 (11.8%)	30 (88.2%)	
Married or divorced	24 (17.3%)	115 (22.7%)	
Widowed	0 (0.0%)	10 (100.0%)	

*Fisher's exact test

effects, 58 (31.7%) reported that they are afraid of them such as constipation (15.8%), drowsiness (10.9%), confusion (8.2%) and nausea (13.6%); (3) 91 patients (49.7%) were afraid from receiving more injections and 62 (33.9%) were afraid from additional costs; (4) regarding cultural beliefs, 78 patients (42.6%) report that pain medication should be saved for more severe pain, 103 (56.3%) are afraid that step-up therapy may be associated with more severe illnesses, and 57 (31.1%) are convinced that good people should avoid talking about pain; (5) regarding the HCP-patient relationship, 71 (38.8%) agree that complaining may distract the physician on focusing on the main health problem whereas 101 (55.2%) report that miscommunication between the HCP and the patient may lead to inadequate assessment.

Results detailing the socio-demographic factors and their association with patients' satisfaction are presented in Table 3. Both genders were equally satisfied (81.1% males vs. 87.2% females, p=0.263). Patient satisfaction failed also to show any statistically significant difference between those who had first class coverage or not (p=0.515). However, being an elderly which is defined by an age over 65 years was associated with more dissatisfaction when compared to a younger age group (27.3% versus 12.7%; p=0.035).

Patients who had proper pain assessment were more satisfied when compared to those who were not properly assessed (27.1% versus 20.1%, p<0.001). A total of 137 patients (91.3%) who think that their pain treatment was helpful were significantly satisfied (p<0.001). Those who did not receive timely medication administration (<30 minutes) and those who asked for pain medication but were not provided were more dissatisfied (71.4% versus 10.9% and 65.0% versus 7.7% respectively; p<0.001). More details about pain assessment conditions and their relationship with patient satisfaction are listed in Table 4.

As for patients' perceptions, fear of addiction and side effects such as constipation or drowsiness were significantly associated with patient dissatisfaction (p<0.001). Again, 66.1% and 76.9% of those who were afraid of additional costs and injections were considered satisfied or strongly satisfied when compared to those who were not afraid [90 (97.8%) and 74 (91.4%); p<0.001 and p=0.001 respectively]. Moreover, only 64.2% who believed that complaining about pain may lead to distraction of the HCP were satisfied versus 96.8% with no such belief (p<0.001). The same trend was shown with the patients who believed that good communication between the patient and the HCP is important for appropriate pain management (p<0.001).

Multivariable analysis

A multivariable analysis for patients 'satisfaction with all variables with p<0.001 was done: (1) Patients perceptions and opinions such as fear of addiction, additional costs and side effects, in addition to lack of communication between HCPs and the patients as well as fear of distracting HCPs by complaining about pain were also taken into consideration. (2) Pain assessment methods such as proper assessment of pain by a HCP, waiting more than 30 minutes before receiving pain medications and asking for analgesics but not being provided. The stepwise forward approach was adopted. Five models were obtained; the Omnibus Tests of Model Coefficients was found significant (<0.001) suggesting that the model is fit and suitable to the data. The Hosmer and Lemeshow goodness-of-fit test was found to be non-significant (0.175) emphasizing that the model is fir with its data. The overall percentage from the classification table was 95.8% suggesting that the entered

Table 4. Pain management predictive factors associated with patient's satisfaction

	Strongly dissatisfied or dissatisfied	Strongly satisfied or satisfied	p-value
Fear of addiction			<0.001
No	4 (4.3%)	89 (95.7%)	
Yes	21 (30.4%)	48 (69.6%)	
Fear of side effects			<0.001
No	6 (5.8%)	97 (94.2%)	
Yes	22 (37.9%)	36 (62.1%)	
Fear of constipation			0.002
No	14 (11.4%)	109 (88.6%)	
Yes	10 (34.5%)	19 (65.5%)	
Fear of drowsiness			0.044
No	23 (17.3%)	110 (82.7%)	
Yes	0 (0.0%)	20 (0.0%)	
Fear of additional costs			<0.001
No	2 (2.2%)	90 (97.8%)	
Yes	21 (33.9%)	41 (66.1%)	
Fear of more injections			0.01
No	7 (8.6%)	74 (91.4%)	
Yes	21 (23.1%)	70 (76.9%)	
Do you think miscommunication with a HCP may be a cause of pain mismanagement?			<0.001
No	1 (1.4%)	71(98.6%)	
Yes	26 (25.7%)	75 (74.3%)	
Do you think that complaining about pain may distract the HCP from the main problem?			<0.001
No	3 (3.2%)	90 (96.8%)	
Yes	24 (33.8%)	47 (64.2%)	
Do you think that good people avoid talking about their pain?			0.953
No	19 (15.4%)	104 (84.6%)	
Yes	9 (15.8%)	48 (84.2%)	
Do you think that pain builds the character?			0.787
No	21(15.8%)	112 (84.2%)	
Yes	4 (13.8%)	25 (86.2%)	
Do you think that pain medications should be spared for more severe diseases?			0.072
No	10 (10.6%)	84 (89.4%)	
Yes	16 (20.5%)	62 (79.5%)	
Do you think that pain is a type of punishment?			0.768
No	17 (16.5%)	86 (83.5%)	
Yes	11 (14.9%)	63 (85.1%)	
Was your pain properly assessed prior to pain medication administration?			<0.001
No	8(38.1%)	13 (61.9%)	
Insufficiently	3(4.1%)	70(95.9%)	
Yes	15 (19.7%)	61 (80.3%)	
What was the longest time you had to wait to get a pain medication?			<0.001
<30 min	17(10.9%)	(89.1%)	
>30min	10 (71.4%)	4 (28.6%)	
Did any HCP follow-up on your pain?			0.249
No	10 (11.6%)	75 (88.4%)	
Inconsistently	11 (22.4%)	38 (77.6%)	
Yes	7 (15.6%)	38 (84.4%)	
Did a HCP educate you about pain treatment?			0.767
No	16 (15.2%)	89 (84.8%)	
Yes	12 (16.9%)	59 (83.1%)	
Did you ask about pain medication but were not given?			<0.001
No	11(7.7%)	131(92.3%)	
Yes	13 (65.0%)	7 (35.0%)	
Do you think that pain management was helpful?			<0.001
No	15 (60.0%)	10 (40.0%)	
Yes	13 (8.7%)	137 (91.3%)	

variables could explain more than 50% of the variability of the dependent variable. The Nagelkerke R square was 0.762 indicating that 76.2% of the variation of patient satisfaction is due to the variation of the independent variables included. Results of both significant and non-significant variables in the equation are presented in Table 5. Results have shown that patients' satisfaction significantly decreased because of some prejudgments such as patients' fear of side effects (aOR=0.098) and additional treatment costs (aOR=0.007). When it comes to the involvement of HCPs in the therapy, it was shown that satisfaction significantly decreased when the patient had to wait for more than 30 minutes before getting the analgesic (aOR=0.006) or if he/she asked for additional therapy but were was not given (aOR=0.024). Proper pain assessment and asking about pain intensity by a HCP significantly increased patient's satisfaction (aOR=30.403).

Table 5. Multivariable analysis for the predictors of patient satisfaction			
Independent variables in logistic regression model	**ORa**	**95%CI**	**p-value**
Did you ask for pain medication but were not given?	0.024	0.003 – 0.208	0.001
Was your pain properly assessed prior to pain medication administration?	30.403	1.587 – 82.603	0.23
Did you have to wait more than 30 minutes before receiving a pain medication?	0.006	0.000 – 0.291	0.009
Fear of side effects	0.098	0.011 – 0.848	0.035
Fear of additional costs	0.007	0.000 – 0.375	0.015
(Dependent variable is patient satisfaction). ORa= Adjusted odds ratio; CI= Confidence interval			

DISCUSSION

Our results have shown that pain was prevalent and consistently experienced by hospitalized patients in varying intensities (71.6%). These results are comparable with many other studies which demonstrated that pain is present in more than 40% of hospitalized patients.[26] Around 86% of the patients in our study were categorized to have severe pain on their first day of hospitalization. This is in congruence with the definition of pain by the International Association for the Study of Pain whereby 'pain' is referred to as an emotional experience that is highly subjective.[27]

An intervention-necessitating finding in our current study is the lack of documentation of pain scores in 54.6% of surveyed patients. When compared to Zeitoun *et al*., it was shown that 49.1% of the patients who were interviewed were undertreated based on the subjective pain scales they were provided, which deprived them from proper treatment.[19] Moreover, in the study conducted by Ramia *et al*., documentation of pain was not consistently done for the majority of patients.[15]

On the other hand, inadequate follow-up by a HCP was one of the major concerns of this study. In fact, only 24.6% of the hospitalized cases were followed up during the first 48 hours whereas the majority of them did not receive proper follow-up or were inconsistently followed up. These results are consistent with Zeitoun *et al*. in which it was shown that 22% of the patients had adequate follow-up.[19]

As for the patients' opinions and perceptions regarding therapy, their satisfaction was highly dependent on adequate pain assessment by HCPs and their involvement in therapy. Fear of side effects and treatment costs were barriers that affected patients' satisfaction negatively. This lack of patients' knowledge and involvement in pain treatment was also identified by the First National Pain Medicine Summit as one of the top barriers to receiving adequate patient care.[28] Similarly, Ramia *et al*. reported that an average of 92% of surveyed patients were either satisfied or strongly satisfied with their pain management and identified patient satisfaction to be higher when doctors and nurses were more involved in pain intensity assessment and immediate provision of treatment.[15] Our findings are also supported by Bourdillon *et al*. and Thorson *et al*. reporting that pain assessment prior to administration of pain medications as well as timely administration of analgesics leads to better pain relief.[29-30].

This study provided optimistic data that 84.7% of the patients were either satisfied or strongly satisfied; this is in congruence with previous literature on patient engagement and satisfaction with care[31-33] and which can be explained by the fact that only 7.7% of the patients had to wait for more than 30 minutes before getting the pain medication when requested and only 10.9% of them did not get any additional analgesic for their increasing pain. Moreover, almost half of the recruited participants were provided with sufficient education regarding their pain status and therapy. Accordingly, such favorable practices involving patient engagement in the care process could explain our positive findings of patient satisfaction despite the substantial pain that was still being experienced.

Another finding in our study was the statistically significant association of older age with dissatisfaction in regards to pain management; this can be explained by the fact that elderly have lower pain threshold and tend to have more medical and cognitive problems that may affect negatively their satisfaction. In addition, older adults are more likely to experience adverse reactions from pharmacologic agents which might modify the treatment. This finding, supported by Cavalieri was also addressed in published literature where it has been speculated that pain perception may be different in older adults because of an atypical presentation of diseases. It was stated that physicians need to be skillful in pain assessment and knowledgeable of both pharmacologic and non-pharmacologic approaches to providing optimal analgesia.[34]

To our knowledge, this study is among the few epidemiological studies conducted in the region to assess patients' satisfaction regarding pain management and evaluate the obstacles that may affect their satisfaction. Moreover, this is the first study to statistically evaluate patients' related barriers to adequate pain control during hospital stay. It addressed an essential clinical problem that remains suboptimally managed. In fact, Daher *et al*. identified potential impediments to adequate pain control in Lebanon including national policy (restrictive laws and regulations that govern the medical use of opioids) and barriers in the provision of health services[11], but only mentioned some of the patient-related concerns without statistical evaluation. Furthermore, in the study conducted by Nasser *et al.*, the aim was to evaluate physicians' assessments of their own competency in pain management and identify physician-related barriers to effective pain control[20] whereas barriers to adequate pain management from patients' perspective were not mentioned. In addition, this study's tool for data collection is based on a validated questionnaire which significantly high Cronbach alpha scores to evaluate pain management during hospitalization. However, some limitations must be underlined. First of all, many participants might not recall previous medical actions and decisions regarding their pain which might introduce a recall bias; in this case, investigators were encouraged to collect missing information from patient medical charts, physician orders and nurses' progress notes. Another limitation is the presence of many interviewers with face-to-face questionnaires which may lead to interviewer bias. For this

sake, prior training and the use of a single translated version of questionnaire were applied to limit this type of bias. Moreover, the existence of contraindications or precautions that may influence the choice of pharmacologic medications and the preference of one drug over another may play the role of confounding factors that may also affect negatively the external validity of our study. To add, many underlying conditions such as chronic co-morbidities or other mental or psychiatric disorders like depression or anxiety may reduce patients' satisfaction regarding pain treatment which might affect negatively the generalizabiltiy of the results. Aside from being a descriptive, non-interventional study with voluntary convenience sampling method at a limited number of sites, a follow-up of pain was done after 48 hours from the beginning of pain therapy which strengthens our findings.

CONCLUSIONS

Despite the growing evidence on pain management, pain is still a prevalent problem that needs more attention and evaluation. Identified patient barriers that hamper pain management must be overcome and active patient participation in their care might be an effective way to improve pain management. Thus, institutions should place their money and effort on continually evaluating the quality of pain management, educating both the patients and health care professionals and stressing on adherence to clinical guidelines which are paramount for effective pain management. A prompt evaluation of pain should be warranted as soon as possible in order to limit patients' suffering.

Our findings may help build the national database on pain management from the perspective of the patients and help regional authorities to better understand their patient needs and improve the implementation of acute pain management services.

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CONFLICT OF INTEREST

We declare that the corresponding is full-time employee at the Lebanese Order of Pharmacists, Drug Information Center Department. Katia Iskandar is the chief pharmacist of the Lebanese Canadian Hospital and a professor at the Lebanese University and Beirut Arab University. Pascale Salameh is a full-time Professor at the Lebanese University and the chair (non-profit position) of the scientific committee at the Lebanese Order of Pharmacists. We have no other conflict of interest to declare.

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Original Research

Knowledge, practice and attitudes regarding antibiotics use among Lebanese dentists

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Abstract

Objectives: Explore antibiotic use, assess conformity with evidence-practice guidelines, and describe knowledge and attitudinal factors among Lebanese dentists.

Methods: National cross-sectional telephonic survey, using a standardized questionnaire addressing demographic, educational and professional data, usual antibiotics prophylactic and curative prescription pattern and influential factors, knowledge concerning antibiotics use in selected patient-populations, and attitude regarding antimicrobial resistance. Analyses used descriptive statistics, and bivariate analysis to observe predictors of higher knowledge.

Results: the overall response rate for the study was around 21%. 322 dentists participated. On average, 17.51% of consultations resulted in antibiotic use; previous antibiotic experience mostly influenced prescriptions (81.3%). Referral of pregnant and lactating women and cardiac patients, when antibiotics are needed, was high (26.9%, 28.5% and 79.4%, respectively). Macrolides were the dominant first-line antibiotics in penicillin allergy (47.4%). Penicillins were most common for pregnant and lactating women. Penicillins (95.0%), 2g (63.9%), and 1 hour pre-procedure (34%) were the main components of prophylaxis for cardiac patients. Prophylactic and curative use varied widely; few dentists exhibited guideline-conform prescriptions. Mean knowledge scores of prophylaxis for cardiac and non-cardiac patients, and antibiotics' side effects were predominantly poor (46.75±14.82, 39.21±33.09 and 20.27±18.77, respectively over 100). Practicing outside Beirut, undergraduate qualification in Lebanon, and post-graduate qualification predicted higher knowledge. 75.9% acknowledged the contribution of dentistry-based prescribing to antibiotic resistance and 94.7% knew at least one cause of resistance.

Conclusions: Dentists show positive attitude towards antimicrobial resistance. Yet, they lack uniformity in antibiotic stewardship. Poor knowledge and guideline-incongruent prophylactic and therapeutic prescribing are observed. Development of targeted interventions is needed to promote judicious antibiotic use within Lebanese dentistry.

Keywords

Antibiotic Prophylaxis; Health Knowledge, Attitudes, Practice; Inappropriate Prescribing; Professional Practice; Guideline Adherence; Penicillins; Streptomyces; Dentists; Surveys and Questionnaires; Lebanon

INTRODUCTION

Antimicrobial resistance is a serious threat to human life, posing catastrophic public health and economic burdens.[1] Since the mid-1990s, dentistry-based antimicrobial prescribing emerged as one potential driver of the global phenomenon of antibiotic resistance.[2] Clearly, the use of antibiotics as an adjunct to local treatment is the most appropriate method of managing oral infections.[3,4] However, its inappropriate prescription would not provide sufficient benefit yet, it runs the risk of causing side effects ranging from gastrointestinal disturbances to fatal anaphylactic shock and emergence of resistant bacteria, and yields greater health.[5,6] Thus, dentistry-based antibiotic prescribing for prophylactic and therapeutic conditions is dictated by defined criteria, and dentists are urged to judiciously prescribe antibiotics.[4,7-10] However, the increasing and inappropriate use of antibiotic by dental professionals remain an international finding.[11-17]

Knowledge and attitudinal factors are pivotal in explaining this evidence-practice gap.[18] Specifically, in the Middle East, dentists are prone to prescribe on patient's demand, especially when short of time. Antibiotics are abused to prevent postoperative infections or as a consequence of the lack of aseptic clinical techniques.[19] Conflicting data from the region show that in some countries in spite of good knowledge of local and international guidelines, and awareness of the importance of the judicious use of antimicrobials, dentists tend to use antibacterials for inappropriate indications.[15,20] Studies have shown patterns of overprescribing among dentists where broader spectrum antibiotics, longer durations and higher doses are given.[21-26] In Lebanon, information on antibiotic stewardship in dentistry is scarce. The only available evidence is in acute and chronic dento-alveolar abscess and emanate from a small study conducted in Beirut. It reports results parallel with the international literature: inappropriate use in terms of dosage, duration and frequency is evident, with amoxicillin being the primary prescribed agent.[27]

Monitoring trends in antibiotic prescriptions by dentists and elucidating pertaining knowledge and attitudinal factors may reveal previously unrecognized opportunities to curb prescribing, and might identify areas of concern in a

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service or where there is a potential for improvement and optimize antibiotic treatments and stem the emergence and spread of resistance.[5,18] A national survey was conducted among Lebanese dentists to explore antibiotic use and its concordance with guidelines, and to describe pertaining knowledge and attitudinal factors.

METHODS

An observational cross-sectional telephone-based survey was performed between July and September 2017. The study participants were chosen from the list of Lebanese dentists registered at the Lebanese Order of Dentists. Out of 4432 registered dentists, complete data were obtained for 3222 dentists. Dentists were then sorted according to their region of practice and gathered into subgroups based on the corresponding governorate. They were distributed as follows: 20% from Beirut, 55% from Mount Lebanon, 13% from South Lebanon (including Nabatiyeh), 11% from Bekaa, and 1% from North Lebanon.

The study sample was drawn to respect the same distribution of dentists per governorate. A minimum sample size of 322 participants (10% of the list of dentists with complete data) was considered sufficient to fulfill the study's main objective.

A systematic random sampling was then adopted, and dentists with an odd number in the list {1, 3, 5, 7, etc.} were orderly called until reaching the required number of participants from each region. In total, we had to make 1530 phone calls to be able to reach 460 dentists, among whom 322 gave their oral consent to participate in the study (1070 calls resulted in the following: "dentist absent" or "dentist busy" or "no answer"). The telephonic interview lasted between 10 and 15 minutes.

A standardized questionnaire was designed in English as well as in French. Translations were supervised by professional translators. The questionnaire was pre-tested with 10 dentists for validity and acceptability. Validity was examined by evaluating whether the questions were comprehensive. Acceptability was evaluated by asking the dentists how they found answering the questionnaire and if they wanted to omit or add questions. Confidentiality of the respondent was ensured. The first section of the questionnaire included questions regarding demographic data, specialty, education details, level of experience, working place, attendance of continuing education sessions, average activity. In the second section, dentists were asked to indicate their usual prescription pattern of antibiotics and factors that influence their behavior. The third section was composed of table with a list of different non-invasive and invasive dental procedures and a question about their routine prophylactic or curative prescription of antibiotics (type, dose, duration, route of administration) in general population and in high risk of infection patients (immune-suppressed and with high risk of infective endocarditis). The final section included their knowledge concerning antibiotics, high risky patients, recommendations and their own role in antimicrobial resistance.

The Lebanese University ethics committee waived the need for approval since the study was observational, anonymous and respected the individuals' confidentiality.

Statistical Analysis

Data were collected and all analyses were performed using SPSS version 20. Descriptive analysis was generated. Means and standard deviations were used for quantitative variables while percentages were shown for qualitative variables.

Knowledge questions were isolated and scored. One (1) mark was given for every correct response and zero (0) for an incorrect response. Responses of "Do not know" were counted as incorrect, and no points were given. The total knowledge score was the sum of all correct answers. For dentists who provided answers to all questions, mean knowledge score (%) was calculated and divided into three categories: poor (<60%), intermediate (60-80%) and good (>80%) level.

The antibiotic prescriptions in different dental procedures were compared to recommended guidelines[5-9] in order to evaluate their appropriateness (indication, type, dose, frequency and duration). Finally, a bivariate analysis was computed to observe the relations between the knowledge of dentists and their demographic and professional characteristics; i.e. Independent Samples T-Test to explore the association between knowledge scores and independent variables having two mutually exclusive groups, and One-Way ANOVA to explore the association between knowledge scores and independent variables having 3 or more mutually exclusive groups.

RESULTS

322 dentists completed the interview. Their mean age was 44.87 years (9.60; range: 24-67), and 67.1% of them were males. The professional characteristics of participants are provided in Table 1. Reported antibiotic prescribing frequency varied widely among the respondents: on average, 8.8 (11.73) systemic courses were prescribed weekly, and overall 17.51% (18.32%) of dental consultations resulted in the prescription of an antibiotic.

Table 2 details antibiotic prescribing practices. It should also be noted there was a wide range of antibiotics prescribed as a first choice for people who are allergic to penicillin, as well as for both pregnant and lactating women, with varying spectrums of activity. To note that macrolides were the most common first-line antibiotics prescribed to patients allergic to penicillin (47.4%). Interestingly, 5.9% of dentists reported penicillin agents as their first choice. In addition, cetirizine was recommended by one respondent as a first choice antibiotic for a patient allergic to penicillin. Amoxicillin and amoxicillin/clavulanate (Penicillins) were the most common antibiotics prescribed for pregnant and lactating women, followed by macrolides. More than one-quarter of respondents reported referring these women to their gynecologists, when antibiotic prescription is needed (26.9% and 28.5%, respectively). Also, referral of cardiac patients, when necessary, was high (79.4%). 86.9% of the sample always enquired whether their patients are taking antibiotics before proceeding to

Table 1. Professional Characteristics of Participating Dentists

	N	%
Main Consultation Region (n=322)		
Mount-Lebanon	177	55.0
Beirut	65	20.2
South (including Nabatiyeh)	42	13.1
Bekaa	35	10.9
North	3	0.9
Primary dental qualification (n=318)*		
Lebanon	192	60.4
Other countries	126	39.6
Years in practice (n=314)*		
< 1-5 years	21	6.7
5-10 years	43	13.7
> 10 years	250	79.6
Specialty (n=309)*		
General practitioner	134	43.4
Oral surgeon	33	10.7
Endodontic	30	9.7
Implant surgeon	28	9.1
Pediatric dentist	22	7.1
Orthodontist	21	6.8
Restorative Dentist	12	3.9
Prosthodontics	15	4.9
Periodontics	9	2.9
Other	5	1.6
Postgraduate qualification (n=315)*		
None	134	42.5
Master's degree	114	36.2
University Diploma	49	15.6
PhD	18	5.7
Country where postgraduate qualification was obtained (n=169)*		
Lebanon	132	78.1
Western Europe	23	13.6
Eastern Europe	8	4.7
USA	5	3.0
Egypt	1	0.6
Practice setting (n=322)		
Private Clinic	308	95.7
Private Hospital	1	0.3
Public Hospital	1	0.3
Mixt	12	3.7
Continuing education source (n=314)*		
None	13	4.1
National conferences	154	49.0
National and international conferences and continuing education lectures	99	31.5
International conferences	33	10.5
Continuing education lectures	15	4.8
Guidelines followed for prescribing prophylaxis regimens for infective endocarditis among susceptible patients (n=315)*		
Do not know	103	32.7
Guidelines provided during dental qualification years	84	26.7
American Health Association (AHA)	73	23.2
Agence Française de Sécurité Sanitaire des Produits de Santé (Afssaps)	33	10.5
National Institute for Clinical Excellence (NICE) and the British Society for Antimicrobial Chemotherapy (BSAC)	21	6.7
Other	1	0.3
Attending at least 1 lecture relating to the use of antibiotics in dental medicine during the past 5 years (n=316)*	154	48.7
Reading at least 1 journal article relating to the use of antibiotics in dental medicine during the past 5 years (n=314)*	157	50.0

	Min	Max	Median	IQR	Mean	SD
Number of patients per week (n=233)	10	240	48.00	30.00	53.71	35.81
Number of prescribed systemic antibiotics courses per week (n=260)	0	100	5.00	7.00	8.80	11.73
Frequency of antibiotic prescription per dental consultation (%) (n=274)	0	100	10.00	12.50	17.51	18.32

*Valid percentages are reported, Min: minimum; Max: maximum; IQR: interquartile range; SD: standard deviation

Table 2. Attitude of participating dentists toward antibiotic prescribing

		N	%
First choice antibiotic prescribed to patients allergic to penicillin (n=289)*	Spiramycin + Metronidazole	86	29.8
	Spiramycin	69	23.9
	Unspecified Macrolides	35	12.1
	Clindamycin	34	11.8
	Clarithromycin	33	11.4
	Amoxicillin	11	3.8
	Cephalosporin	10	3.5
	Amoxicillin + Clavulanic acid	6	2.1
	Metronidazole	2	0.7
	Cetirizine	1	0.3
	Ciprofloxacin	1	0.3
	Sulphamides + Diamonopyrimidine	1	0.3
First choice antibiotic prescribed to a pregnant woman (n=275)*	Amoxicillin + Clavulanic acid	86	31.3
	Spiramycin	53	19.2
	Amoxicillin	44	16.0
	Spiramycine + Metronidazole	8	2.9
	Clindamycin	4	1.5
	Azithromycin	2	0.7
	Cephalosporin	2	0.7
	Aminosides	1	0.4
	Penicillines or Spiramycine + Metronidazole	1	0.4
	Referral to gynecologist	74	26.9
First choice antibiotic prescribed to a breastfeeding woman (n=274)*	Amoxicillin + Clavulanic acid	85	31.1
	Spiramycin	51	18.6
	Amoxicillin	42	15.3
	Spiramycine + Metronidazole	9	3.3
	Clindamycin	5	1.8
	Cephalosporin	2	0.7
	Gentamycin	1	0.4
	Penicillines or Spiramycine + Metronidazole	1	0.4
	Referral to gynecologist	78	28.5
Frequency of referring cardiac patients to their physician when necessary (n=321)*	Always	255	79.4
	Sometimes	58	18.1
	Never	8	2.5
Enquire if the patient is currently taking an antibiotic before proceeding to consultation (n=320)*	Always	278	86.9
	Often	24	7.5
	Sometimes	14	4.4
	Never	4	1.3
Attitude regarding a patient who has already taken antibiotics before consultation (n=154)*	Continue antibiotic course	85	55.2
	Action depends on the antibiotic	32	20.8
	Change the antibiotic	19	12.3
	Action depends on time (change if antibiotic taken during last month)	8	5.2
	Discontinue antibiotic course	7	4.5
	Continue antibiotic course and add vitamins	2	1.3
	Increase the dose	1	0.6
Feeling pressure from patients to prescribe antibiotics (n=319)*	Always	27	8.5
	Often	43	13.5
	Sometimes	72	22.6
	Never	177	55.0
Factor(s) mostly influencing antibiotics prescribing behavior (n=321)*†	Previous antibiotic experience	261	81.3
	Comorbidities of the patient	174	54.2
	Socio-economic status of the patient	103	32.1
	Price of the antibiotic	101	31.5
	Samples availability	44	13.7
	Medical representative visits	37	11.5

*Valid percentages are reported; †Percentages may add up to more than 100%, due to multiple possible answers

the consultation. Continuing antibiotic course was the dominant action when a patient was found to be already taking antibiotics (55.2%). Only 5.2% of dentists reported changing the antibiotic if given during the past month. Nearly half (45.0%) of participating dentists reported being, to varying extent, pressured by patients to prescribe antibiotics. Factors governing antibiotic prescribing were primarily physician-related (previous antibiotic experience: 81.3%), followed by patient-related factors (presence of comorbidities: 54.2%). It also should be noted that the socio-economic status (32.1%) and price of the antibiotic (31.5%) were approximately one third of the factors that influenced antibiotic prescribing behavior. Other less influencing factors were the availability of the samples and medical representatives (13.7% and 11.5%, respectively).

Table 3 describes prophylactic antibiotic prescription patterns of sampled dentists. The vast majority of dentists refrained from prescribing antibiotics for restoration (96.7%), prosthesis (96.4%), crown (93.8%) and local anesthesia (91.6%). Systematic antibiotic prescription was mostly considered for implant (55.7%), bone graft (48.3%) and surgical extraction (mandibular tooth: 46.9%, maxillary tooth: 47.1%). Prescription for patients at high risk for infection was more common for braces (33.3%) and scaling (28.2%). Great divergences were noted for bone graft, implant, teeth extraction and gerectomy. Conformity with evidence-practice guidelines was inconsistent; it was high for restoration and interim care (96.7% each), prosthesis (96.4%), crown (93.8%) and local anesthesia (91.6%), where antibiotics are not indicated. Agreement with guidelines was especially low for procedures where prophylactic antibiotics should be prescribed for high-risk patients, such as implant (2.6%), intraligamentary local anesthesia (4.2%), tumor resection (4.6%), frenectomy (8.8%), gingivectomy (9.2%) and Crown lengthening (10.4%). Among those who prescribed prophylactic antibiotics correctly when indicated, conformity with evidence-practice guidelines

Table 3. Prophylactic and Curative Antibiotic Prescribing Practices of Participating Dentists and Conformity with Evidence-Practice Guidelines

N (%)	No	Yes all patients	Yes High-risk patients‡	Indication	Conformity with evidence-practice guidelines*		
					Type	Dose	Duration
					Among those who provided a correct answer to indication		
Reported prophylactic antibiotic prescribing*†							
Bone graft (n=180)	84 (46.7)	87 (48.3)	9 (5)	87 (48.3)	67 (77.0)	54 (62.1)	3 (3.4)
Braces (n=30)	20 (66.7)	0 (0)	10 (33.3)	20 (66.7)	NA		
Crown (n=306)	287 (93.8)	0 (0)	19 (6.2)	287 (93.8)	NA		
Crown lengthening (n=240)	165 (68.8)	50 (20.8)	25 (10.4)	25 (10.4)	2 (8.0)	1 (4.0)	0 (0)
Extraction mandibular tooth (n=294)	103 (35)	138 (46.9)	53 (18)	138 (46.9)	84 (60.9)	38 (27.5)	4 (2.9)
Extraction maxillary tooth (n=293)	106 (36.2)	138 (47.1)	49 (16.7)	138 (47.1)	91 (65.9)	49 (35.5)	4 (2.9)
Flap surgery (n=166)	101 (60.8)	49 (29.5)	16 (9.6)	101 (60.8)	NA		
Frenectomy (n=249)	188 (75.5)	39 (15.7)	22 (8.8)	22 (8.8)	4 (18.2)	2 (9.1)	1 (4.5)
Germectomy (n=209)	107 (51.2)	80 (38.3)	22 (10.5)	80 (38.3)	51 (63.8)	26 (32.5)	2 (2.5)
Gingivectomy (n=293)	225 (76.8)	41 (14)	27 (9.2)	27 (9.2)	4 (14.8)	2 (7.4)	1 (3.7)
Implant (n=228)	95 (41.7)	127 (55.7)	6 (2.6)	6 (2.6)	2 (33.3)	1 (16.7)	1 (16.7)
Interim care (n=306)	296 (96.7)	0 (0)	10 (3.3)	296 (96.7)	NA		
Intraligamentary local anesthesia (n=311)	298 (95.8)	3 (1)	13 (4.2)	13 (4.2)	2 (15.4)	2 (15.4)	0 (0)
Local anesthesia (n=311)	285 (91.6)	13 (4.2)	13 (4.2)	285 (91.6)	NA		
Necrotic tooth (n=299)	188 (62.9)	84 (28.1)	27 (9)	188 (62.9)	NA		
Prosthesis (n=306)	295 (96.4)	0 (0)	11 (3.6)	296 (96.4)	NA		
Restoration (n=306)	296 (96.7)	0 (0)	10 (3.3)	296 (96.7)	NA		
Scaling (n=309)	215 (69.6)	7 (2.3)	87 (28.2)	215 (69.6)	NA		
Simple extraction (n=305)	209 (68.5)	46 (15.1)	50 (16.4)	50 (16.4)	23 (46.0)	17 (34.0)	1 (2.0)
Tumor resection (n=151)	126 (83.4)	18 (11.9)	7 (4.6)	7 (4.6)	0 (0)	0 (0)	0 (0)
Reported curative antibiotic prescribing*‡							
Agressive periodontitis (n=268)	77 (28.7)	176 (65.7)	15 (5.6)	176 (65.7)	90 (51.1)	47 (26.7)	60 (34.1)
Apical abscess (n=306)	97 (31.7)	192 (62.7)	17 (5.6)	17 (5.6)	9 (52.9)	0 (0)	1 (5.9)
Bacterial stomatitis (n=142)	104 (73.2)	38 (26.8)	0 (0)	38 (26.8)	24 (63.2)	21 (55.3)	17 (44.7)
Cellulitis (n=253)	53 (20.9)	174 (68.8)	26 (10.3)	174 (68.8)	122 (70.1)	0 (0)	67 (38.5)
Chronic periodontitis (n=289)	213 (73.7)	55 (19)	21 (7.3)	213 (73.7)	NA		
Combined lesion (n=293)	173 (59)	117 (39.9)	3 (1)	173 (59)	NA		
Fistula (n=285)	137 (48.1)	127 (44.6)	21 (7.4)	127 (44.6)	77 (60.6)	39 (30.7)	58 (45.7)
Gingivitis (n=297)	246 (82.8)	37 (12.5)	14 (4.7)	246 (82.2)	NA		
Maxillary sinusitis (n=159)	104 (65.4)	48 (30.2)	7 (4.4)	48 (30.3)	36 (75.0)	15 (31.3)	18 (37.5)
Osteomyelitis (n=170)	68 (40)	90 (52.9)	12 (7.1)	90 (52.9)	78 (86.7)	61 (67.8)	35 (38.9)
Periapical abscess (n=305)	77 (25.2)	203 (66.6)	25 (8.2)	25 (8.2)	8 (32)	0 (0)	1 (4.0)
Periimplantitis (n=170)	100 (58.8)	51 (30)	19 (11.2)	19 (11.2)	0 (0)	0 (0)	0 (0)
Periodontal abscess (n=284)	75 (26.4)	192 (67.6)	17 (6)	17 (6)	8 (47.1)	4 (23.5)	4 (23.5)
Pulpitis (n=305)	269 (88.2)	27 (8.9)	9 (3)	269 (88.2)	NA		
Salivary gland infection (n=136)	113 (83.1)	23 (16.9)	0 (0)	23 (16.9)	20 (87)	18 (78.3)	9 (39.1)
Tooth decay (n=311)	304 (97.7)	5 (1.6)	2 (0.6)	304 (97.7)	NA		

NA: not applicable. †Dentists describing cases as referred or rarely seen were excluded; *Valid percentages are reported; ‡Selected patients with cardiac conditions; compromised immunity; shunts, indwelling vascular catheters, medical devices; and prosthetic joints (5-9).

Table 4. Percentage of prophylactic antibiotics regimens for cardiac patients (n=103)	
types of prophylactic antibiotics	
Amoxicillin	52.5
Amoxicillin and Clavulanic acid	36.4
Unspecified penicillin	6.1
Spyramicin	3.0
Amoxicilin or Spyramicin	1.0
Depends on the case	1.0
doses of prophylactic antibiotics	
2 g	63.9
3 g	9.8
Flash dose	8.2
50 mg/Kg	4.9
1-2 g	3.3
2-3 g	3.3
Other	6.6
timing of antibiotics prophylaxis	
1 hour before procedure	34.0
1 hour before and after procedure	10.6
1 hour before and 6 hours after procedure	7.4
1 hour before and 7 days after procedure	6.4
2 hours before procedure	6.4
1 day before procedure	4.3
2 days before procedure	3.2
3 days before procedure	3.2
Other	24.5
*Valid percentages are reported	

regarding the type of antibiotics ranged between 0 and 77%; whereas that of dose ranged between 0 and 62.1%, and that of duration between 0 and 16.7%. Overall, there was a significant divergence from the guidelines for several indications for both patient who were and are not at risk.

Table 3 also shows curative antibiotic prescription patterns of participants; answers were inconsistent for the majority of conditions. Non-prescription was most common in case of tooth decay (97.7%), pulpitis (88.2%), salivary gland infection (83.1%) and gingivitis (82.8%). Around two-thirds of the dentists reported prescribing antibiotics for all cases diagnosed with cellulitis (68.8%), periodontal abscess (67.7%), periapical abscess (66.6%), aggressive periodontitis (65.7%) and apical abscess (62.7%). Discrepancies were mainly noted for fistula, aggressive periodontitis, apical abscess and maxillary sinusitis. It is important to note that 11.9% of respondents prescribe antibiotics for pulpitis and 17.8% of participants prescribe antibiotics for gingivitis, which is unnecessary prescribing. Also for conditions such as cellulitis (20.9%) and salivary gland infections (83.1%), there were a significant proportion of dentists for both conditions who do not prescribe antibiotics when they are actually indicated. The lowest conformities were observed for apical abscess (5.6%), periodontal abscess (6%) and periapical abscess (8.2%), where curative antibiotics are indicated only for high risk patients. Among dentists who provided a correct answer to indication, the prescribed types of antibiotics were adequate for cases with salivary gland infection (87%) and osteomyelitis (86.7%), and were all inadequate for periimplantitis. When curative antibiotics where prescribed correctly when indicated, conformity with evidence-practice guidelines regarding the type of antibiotics ranged between 0 and 87%; whereas that of dose ranged between 0 and 78.3%, and that of duration between 0 and 45.7%.

As displayed in Table 4, penicillins were the dominant type (95.0%) of prophylactic antibiotics for cardiac patients. Answers were greatly scattered, especially for the dose and timing. Doses ranged between 1.87g up to 5g, with 63.9% prescribing 2g. Timing of antibiotic prophylaxis ranged between 3 days before the procedure, up to 7 days afterwards. The most common timing was 1 hour before procedure (34.0%), followed by 1 hour before and after the procedure (10.6%).

Table 5. Knowledge of antibiotic prescribing of participating dentists		
	N	**%**
*Prophylactic prescription of antibiotics for cardiac conditions (correct answers)**		
Prosthetic cardiac valves (n=140)	135	96.4
Rheumatic heart disease (n=131)	26	19.8
Mitral valve prolapsed with valvular regurgitation (n=124)	16	12.9
Previous infective endocarditis (n=127)	102	80.3
Previous coronary artery bypass graft surgery (n=140)	70	50.0
Hypertrophic cardiomyopathy (n=147)	84	26.1
Intravascular cardiac pacemakers (n=147)	49	33.3
Myocardial infarct in the last 6 months (n=125)	26	20.8
Cardiac transplantation recipients who develop cardiac valvulopathy (n=131)	65	49.6
Unrepaired cyanotic heart disease (n=134)	57	42.5
Recently placed coronary stents (n=144)	30	20.8
Atrial septal defect after 6 months of repair (n=134)	59	44.0
Ventricular septal defect with repair (n=140)	56	40.0
Patent ductus arteriosus (n=140)	56	40.0
Cardiac catheterization without stents (less than 1 year) (n=183)	61	43.9
*Prophylactic prescription of antibiotics for other conditions (in case of invasive procedure) (correct answers)**		
Human immunodeficiency virus (n=155)	90	58.1
Neutropenia (n=132)	51	38.6
Cancer chemotherapy (n=136)	81	59.6
Diabetes (n=245)	188	76.7
Hematopoietic stem cell or solid organ transplantation (n=133)	56	42.1
Bisphosphonate therapy (n=173)	62	35.8
Chronic steroid usage (n=172)	91	52.9
Asplenism or status post splenectomy (n=175)	69	39.4
Patients with prosthetic joints (n=173)	16	9.2
*Valid percentages are reported		

Table 6. Mean Knowledge Scores (%) by Sociodemographic and Professional Characteristics

	Prophylaxis for cardiac conditions (n=76)	Prophylaxis for non-cardiac conditions (n=85)	Side effects of antibiotics (n=322)
Overall score	46.75 (14.82)	39.21 (33.09)	20.27 (18.77)
Age in years			
24-34	53.33 (12.34)	39.35 (35.13)	23.80 (17.77)
35-50	43.95 (15.27)	43.46 (31.23)	19.23 (18.46)
>50	45.83 (15.21)	34.78 (33.55)	19.95 (19.95)
p-value	0.13	0.62	0.30
Gender			
Male	46.02 (15.35)	40.50 (33.36)	19.17 (18.65)
Female	50.00 (12.19)	35.74 (32.81)	22.50 (18.90)
p-value	0.36	0.55	0.13
Region			
Beirut	44.10 (7.47)	23.14 (28.73)	13.40 (10.97)
Other	47.30 (15.91)	45.53 (32.75)	22.01 (19.92)
p-value	0.27	0.003	<0.001
Experience years			
< 1-5 years	56.19 (13.80)	37.03 (41.94)	25.85 (15.39)
5-10 years	47.33 (19.98)	40.00 (32.74)	21.26 (18.00)
> 10 years	45.63 (13.89)	39.65 (31.91)	20.00 (19.28)
p-value	0.20	0.97	0.38
Specialty			
General practitioner	47.13 (15.07)	30.82 (31.65)	20.25 (14.47)
Other	46.26 (14.71)	44.03 (33.22)	20.28 (21.35)
p-value	0.80	0.07	0.98
Undergraduate qualification			
In Lebanon	52.72 (13.37)	45.89 (31.91)	21.94 (19.87)
Outside Lebanon	42.17 (14.38)	32.73 (33.43)	18.14 (16.89)
p-value	0.002	0.07	0.06
Post-graduate qualification			
No	47.23 (15.07)	30.82 (31.65)	20.25 (14.47)
Yes	46.45 (14.90)	46.18 (32.91)	20.59 (21.52)
p-value	0.84	0.04	0.86
Continuing education			
No	46.66 (11.54)	24.07 (32.52)	18.68 (10.72)
Yes	47.04 (15.26)	43.07 (32.91)	20.45 (19.09)
p-value	0.96	0.17	0.58
Number of patients per week			
0-50	46.23 (18.13)	44.14 (34.19)	21.88 (19.98)
51-100	49.16 (12.38)	48.41 (31.60)	27.60 (21.85)
>100	42.85 (14.32)	68.88 (27.66)	19.64 (11.51)
p-value	0.67	0.29	0.13
Frequency of antibiotic prescription per dental consultation (%)			
0-10	45.71 (15.05)	40.54 (34.36)	21.36 (17.17)
>10	49.85 (16.43)	41.58 (32.71)	21.65 (20.82)
p-value	0.30	0.89	0.90

Regarding cardiac conditions, the highest knowledge was for prosthetic cardiac valves (96.4%), followed by previous infective endocarditis (80.3%) (Table 5). The adequacy of answers greatly decreased for all other conditions. The worst knowledge was observed for mitral valve prolapsed with valvular regurgitation (12.9%) and rheumatic heart disease (19.8%). The mean score of dentists who provided answers to all questions in this section (n=76) was 46.75 (14.82). None of them had good knowledge about prophylactic prescription of antibiotics for cardiac conditions; two-thirds (67.1%) had poor knowledge, and one-third (32.9%) had intermediate knowledge. Regarding non-cardiac conditions, less than half of respondents could adequately identify prophylactic antibiotic prescription, except for the cases of diabetes (76.7%), cancer chemotherapy (59.6%), infection with the human immunodeficiency virus (58.1%) and chronic steroid usage (52.9%). Knowledge pertaining to prophylactic antibiotic prescription for patients with prosthetic joints was the worst (9.2%). For dentists who provided answers to all questions in this section (n=85), the average knowledge score was 39.21 (33.09). The participants had predominantly poor knowledge (67.1%); 14.1% had intermediate knowledge and only 18.8% showed good knowledge.

In total, 50.3% of sampled dentists could correctly identify at least one side effect of amoxicillin/co-amoxiclav. This rate sharply declined for other antibiotics, and was almost null for cephalosporin (3.7%). The mean knowledge score about side effects of antibiotics was 20.27 (18.77). Almost all dentists (97.5%) had poor knowledge; only 4 (1.2%) had intermediate knowledge and 4 others (1.2%) exhibited good knowledge.

As shown in Table 6, in the bivariate analysis, demographic and professional characteristics did not influence knowledge scores; with the exception of dentists in Beirut being less knowledgeable of prophylactic prescription for non-cardiac patients and antibiotic side effects than those working in other regions. Moreover, dentists receiving their

undergraduate qualification in Lebanon had greater knowledge scores about prophylactic prescription for cardiac patients than the others, and those with a post-graduate qualification had higher knowledge of prophylactic prescription for non-cardiac patients than their peers.

Finally, 75.9% of respondents were aware of the contribution of dentistry-based antibiotic prescribing to the problem of antibiotic resistance at the national level and 94.7% knew at least one cause of antibiotic resistance.

DISCUSSION

Given the potential contribution of dentistry-based antibiotic misuse to the epidemic of antimicrobial resistance, this study was the first effort to describe current knowledge, attitude and practices related to antibiotics, and to assess the extent to which prophylactic and therapeutic prescribing conforms to guidelines among dentists across Lebanon. In order to reach the desired sample size (322 dentists), the survey targeted 1,530 dentists, of whom, 460 were accessible, revealing a participation rate of 21% out of all targeted dentists, and a response rate of 70% among those who were accessible. This is in line with previous similar national studies conducted among dentists in other countries.[13,17,28]

Although, within the population studied, the reported rate of antibiotic prescribing was relatively high (17.51%) compared to other studies in Australia, Belgium and the United Kingdom[12,29,30]; and while participants lacked uniformity in antibiotic prescribing knowledge and practices, unindicated, inappropriate and extended uses were obvious, suggesting guideline-incongruent prophylactic and therapeutic prescribing. The problematic prescribing in Lebanon is further evidence to the international concern of dentistry-based antibiotic misuse[11-17,28], and provides additional argumentation justifying the solicitation of national efforts to promote judicious antibiotic use across the profession. Several factors noted in our sample emerge as potential contributors to these findings, including poor knowledge of evidence-practice regimens, limited exposure to scientific updates relating to the use of antibiotics, in addition to pressure of non-medical factors, such as patient requests for antibiotics prescription and influence of pharmaceutical industry. Various non-clinical pressures are in agreement with studies from other countries.[11,12,31,32] Our sample exhibited several conform prescribing behaviors, such as mainly using macrolides as first-line antibiotics for patients allergic to penicillins.[33] This behavior was in line with data from Belgium[12], yet differed from data reported from other countries, where clindamycin and erythromycin were the most prescribed antibiotics in the United Arab Emirates and United Kingdom[13,15] and in Iran[16], respectively. Several factors might explain this finding, among them is the comparative safety and tolerance of macrolides and the concern from the higher rates of fatal and nonfatal adverse drug reactions associated with C. *difficile* infections with clindamycin use[34] in one hand, and the unavailability of erythromycin in oral form in Lebanon, on the other hand. Yet, several deviant practices related to this condition were observed, such as the use of penicillins for these patients, or even substituting antibiotics by anti-histaminic or even not recognizing that amoxicillin and amoxicillin/clavulanic acid are both from the penicillin group. These behaviors-denoting poor knowledge of basic antibiotic pharmacology-might engender serious side effects, some of which could be life-threatening. Similarly, as previously noted in Lebanon[35], the use of penicillins as primary antibiotics for pregnant and lactating women was evident. Yet, a substantial proportion of dentists adopted metronidazole as their first choice for these women. First-line use of this agent is not supported by evidence, especially during the first semester of gestation and during lactation, rather, it is typically indicated for second-line use.[34] Although few in numbers, alarming practices emerged in this patient population, such as the use of spiramycin, aminosides and gentamycin in first-line.

On the other hand, our sample showed evidence of factors fostering antimicrobial resistance. First, antibiotic prescribing was found to be biased toward broad spectrum agents, i.e. association amoxicillin with clavulanic acid, association spiramycin with metronidazole and metronidazole, which were used in numerous instances, even when not clinically required. This finding is universal among dental practitioners.[12,14,15,17,20] Second, a high proportion of dentists inquired whether the patient is using antibiotics before consultation; however the vast majority resorted to systematically changing the antibiotic to combat a potential or present infection and only few patients followed the recommendation of changing the antibiotic if taken in the previous month.[34] Third, massive doses ranging up to 5g and long duration extending to 8 days of prophylaxis were prescribed for cardiac patients-clearly exceeding the recommended dose and duration of use.[34] Fourth, a considerable proportion of physicians adopted routine prescription to all patients, even when not indicated, such as in flap surgery, implant and necrotic tooth; and this misuse was accentuated in antibiotic therapy, such as with cases diagnosed with combined lesion, periapical and periodontal abscess and periimplantitis. Additionally, among physicians who practiced indicated prescribing, optimal adherence to guidelines (type, dose and duration of antibiotic use) was practically inexistent in prophylaxis; it was slightly better for therapeutic use. It is worthy to note that most deficiencies revolved around over and extended use, rather than the type of antibiotics. Finally, the lowest conformity to guidelines was found where antibiotics are indicated for high risk patients only. Potentially, the practitioners might not be confident in identifying high risk patients requiring antibiotics, and resorted the routine prescribing as a preventive mechanism.

As found in other countries[15,16,35], knowledge related to conditions where prophylaxis is indicated varied widely amongst participating dentists, was on average far from being optimal, and showed to be specifically low when it comes to non-cardiac conditions. The high referral rate witnessed in our sample, might partially contribute to this finding in a vicious circle. Potentially, dentists are deferring providing care to at-risk patients due to deficiency in their medical knowledge - as noted among other physicians[36], thus losing motivation to continuously upgrade their knowledge and skills to take in charge these patients. In

parallel, knowledge about the side effects of antibiotic showed to be the poorest. Addressing this issue is of utmost importance, taking into account the fatal and nonfatal adverse reactions associated antibiotic use. We were able to identify few inconsistent factors associated with higher knowledge: practicing outside Beirut area, receiving their undergraduate qualification in Lebanon, and having a post-graduate qualification.

This study raises many questions to be explored in future endeavors. First, as found in previous publications[15,18,20], the majority of dentists were aware of the contribution of dentistry-based antibiotic prescribing to the problem of antibiotic resistance at the national level, and the vast majority of them acknowledged either over, extended and/or misuse of antibiotics as causes of antimicrobial resistance. It was noted that in our sample more importance was accorded to preventing and treating infections rather than preventing antimicrobial resistance. In fact, qualitative data from the United Kingdom indicate that while dentists are aware of the theoretical contribution of dentistry-based prescribing to the emergence of resistance, they perceive it to be far less incriminated than the contribution of their medical col¬leagues.[18] This might partly explain the conflicting results emanating from our study. Second, our sample exhibited high referral of pregnant and lactating women, as well as cardiac patients to specialist physicians, when antibiotic prescription is needed. This behavior possibly denotes the limited knowledge, capacity or time of participants to take in charge these critical conditions, or could be regarded as part of the multidisciplinary approach to patient care. Available data do not permit us to generate a conclusion. The study relied on self-reported practices and the answers were not verified against patient records. Participants might have provided more professionally desirable answers, probably resulting in an underestimation of the true prescribing levels. Future studies should consider auditing patient records to provide documented data and ensure accuracy. Another limitation of this study is the absence of published national treatment guidelines of antibiotics prescription in dental practice and the use of international guidelines to assess conformity which may have created some underestimation of the conformity. Moreover, telephone interviews may have underestimated the real percentage of antibiotic prescription. Finally, we used a systematic random sample which also limits the selection bias. In spite of this, the low response rate may affect the external validity.

CONCLUSIONS

To conclude, while this study pioneers in revealing antibiotic-related knowledge, attitude and practices of dentists in Lebanon, following studies must further investigate the determinants of poor knowledge, attitudinal barriers and inappropriate prescribing, and future research is therefore required to identify practitioners most at-risk of prescribing antibiotics when they are unlikely to be of clinical benefit.

It is now vital that Lebanese professional dental bodies strengthen the knowledge of dentists, and support and encourage judicious antibiotic prophylactic and therapeutic antibiotic prescribing across the profession. Effective interventions could use pharmacist-delivered academic detailing[37] as well as clinical audit[38] with the issuing of national guidelines and an educational component[39], among others.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Original Research

Management of allergic rhinitis in the community pharmacy: identifying the reasons behind medication self-selection

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Abstract

Background: Community pharmacists have a key role to play in the management of allergic rhinitis (AR). Their role is especially important because the majority of medications used to treat AR are available for purchase over-the-counter (OTC), allowing patients to self-select their own medications and bypass the pharmacists. Patients' self-selection often results in suboptimal treatment selection, undertreated AR and poor clinical outcomes. In order for pharmacists to optimise the care for AR patients in the pharmacy, pharmacists need to be able to identify patient cohorts who self-select and are at high risk of mismanagement.

Objectives: This study aimed to compare the demographics, clinical characteristics and medication selected, between pharmacy customers who choose to self-select and those who speak with a pharmacist when purchasing medication for their AR in a community pharmacy and identify factors associated with AR patients' medication(s) self-selection behaviour.

Methods: A cross-sectional observational study was conducted in a convenience sample of community pharmacies from the Sydney metropolitan area. Demographics, pattern of AR symptoms, their impact on quality of life (QOL) and medication(s) selected, were collected. Logistic regressions were used to identify factors associated with participants' medication self-selection behaviour.

Results: Of the 296 recruited participants, 202 were identified with AR; 67.8% were female, 54.5% were >40 years of age, 64.9% had a doctor's diagnosis of AR, and 69.3% self-selected medication(s). Participants with AR who self-select were 4 times more likely to experience moderate-severe wheeze (OR 4.047, 95% CI 1.155-14.188) and almost 0.4 times less likely to experience an impact of AR symptoms on their QOL (OR 0.369, 95% CI 0.188-0.727).

Conclusions: The factors associated with AR patients' self-selecting medication(s) are the presence of wheeze and the absence of impact on their QOL due to AR symptoms. By identifying this cohort of patients, our study highlights an opportunity for pharmacists to engage these patients and encourage discussion about their AR and asthma management.

Keywords

Rhinitis, Allergic, Seasonal; Self Medication; Quality of Life; Community Pharmacy Services; Professional Role; Pharmacies; Surveys and Questionnaires; Multivariate Analysis; Australia

INTRODUCTION

Community pharmacists have a key role in managing allergic rhinitis (AR), which is a chronic respiratory condition increasing in prevalence.[1] It is classically characterised by nasal itching, sneezing, anterior/posterior rhinorrhoea and nasal congestion, however ocular symptoms may present (itchy or watery eyes) as well as itchy throat/palate.2 AR currently affects up to 30% of the world's population[1,3], with 19% of Australians self-reporting AR.[4] The socioeconomic burden of AR in Australia has been measured to be up to AUD9.4 billion, due to absenteeism from the work place, reduce productivity at work and treatment cost.[1,5]

When left undertreated, AR can impact on the day-to-day activities of individuals with the condition[1,2] or predispose the development or worsening asthma.[6-10] Despite having up to 90% of patients dually affected by AR and asthma[11], the majority under-recognise the impact of their AR symptoms and its impact on asthma control.[12] In fact, a high proportion of patients who have uncontrolled asthma, experience more severe AR symptoms when compared to patients with well controlled asthma.[12] The importance of optimal treatment for AR increases for patients with both AR and asthma, as uncontrolled AR increases asthma-related risk.[13] With optimal AR treatment, patients with coexisting AR and asthma have a lower risk for asthma related events.[9,14]

Early detection and optimal management of AR allows patients to minimise the impact of AR on the patient. Diagnosis of AR is often a challenge for Health Care Professionals (HCPs) because patients underreport their AR symptoms and HCPs are not always equipped with

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resources to make the correct diagnosis of AR. Optimal management of AR is further compromised with patients' bypassing the HCPs altogether[15,16], with 70% self-selecting medication for their AR symptoms.[12,16-18] Patients' self-selection is suboptimal with only 15% selecting appropriate over-the-counter (OTC) medications[19] from community pharmacies.[15,16] The most commonly used medications are oral antihistamines, which are not deemed to be the most effective medication for moderate-severe AR symptoms.[16,20] Therefore, despite the high dependence on medications, AR sufferers remain undertreated.[12,19,21]

With an increasing number of OTC medications being available from Australian community pharmacies[15] and online, the choice of medication becomes more complicated. The availability of AR treatments OTC in Australia has occurred ahead of other countries, with implications for self-medication patterns in rhinitis (and other disease states). While pharmacists are ideally placed to meet the needs of AR patients, however research has suggested that pharmacists are not being consulted by patients who visits the pharmacy, they are not taking advice from pharmacists for their AR.[16,19,22] Pharmacists play a crucial role in optimising the management of AR by regularly updating patients with the latest knowledge on AR management and ensure that they are managing their AR with appropriate medications. This is because it has been shown that patients lack medical knowledge about their condition and treatment, which has led to many misconceptions about AR medications.[23] Currently, many are in search for medications that are more effective for their condition[20,23,24], and pharmacist can the make most of this opportunity to engage with this cohort of patients.

Clearly, if the management of AR is to improve, it is critical that AR patients seek advice from pharmacists when in the community pharmacy, in a timely and regular manner. Currently, little is understood about why patients choose to self-manage, bypassing pharmacists. In order for pharmacists to optimise the management of AR, it is important to identify patient cohorts who self-select and are at high risk of mismanagement. Therefore, this study aimed to (i) compare the demographics, clinical characteristics and medication(s) selected between pharmacy customers who choose to self-select and those who interact with a pharmacist when purchasing AR medication(s) within the community pharmacy setting and to (ii) identify factors associated with AR patients' medication self-selection behaviour.

METHODS

Study design

This research took the form of a cross-sectional observational study conducted on a sample of pharmacy customers purchasing medications to treat AR symptom(s) from community pharmacies. The study was approved by the University of Sydney Human Research Ethics Committee (Ref No. 2015/527).

Community pharmacies within the Sydney metropolitan area who expressed an interest in research or pharmacy services were engaged to participate in this research. A researcher stood in the pharmacy and approached all pharmacy customers who choose to self-select off the shelf from the pharmacy and those who spoke to the pharmacist in regard to a product request, a symptom request or a doctor's prescription. These pharmacy customers were only included in the study if they were purchasing a product for AR-related symptoms, i.e. sneezing, rhinorrhoea, nasal congestion, itchiness in the nose, ears or palate, itchy/watery eyes and wheeze. The sample size was calculated to ensure that data were collected from a representative sample, based on an estimated proportion of 0.5 (50%) of people with AR self-selecting medication in a pharmacy.[20] A sample of 200 AR participants was required.[25]

The pharmacy customers were invited to participate if they fulfilled the following inclusion criteria: independently self-selected OTC medication(s) to treat AR-related symptoms (i.e. sneezing, rhinorrhoea, nasal congestion, itchiness in the nose, ears or palate, itchy/watery eyes and wheeze) or interacted with a pharmacist for OTC and/or prescribed medication(s) for these symptoms. Pharmacy customers who selected medication(s) on behalf of others (parents of children less than 18 years old and partners) were also included if they were instructed to purchase a particular product by others and could complete the data collection process and did not violate the following exclusion criteria. The exclusion criteria included unable to complete the data collection process or expressed disinterest in participation (Figure 1). Pharmacy customers, younger than 18 years old were not approached, as adolescents are not old enough to give their own consent in participating in this study, but parents who accompanied them in the pharmacy were eligible to participate and answer on their behalf. Also, pharmacy customers who were purchasing on behalf of their partner were eligible, as in real life, people with AR trivialise their condition and people with AR may find it more convenient for others to purchase their AR medication for them. All participants gave verbal consent to participate prior to data collection.

Participants were classified as having AR, NAR, or 'other'. Classification was based on doctor's diagnosis self-reported by participants or where a previous diagnosis was not present, determined by the expert panel of clinicians, pharmacists and researchers who applied the criteria for the diagnosis of AR according to the ARIA guidelines[26], which is based on triggers, and symptoms reported. The triggers were reported in response to the question: "What brings on/makes your symptoms worse?" and "Is there, if any, a particular time of the year that these symptom(s) occur?".[16]

Variables

Data were collected using a researcher administered survey (online appendix). This included demographic characteristics, pattern of AR symptoms, their impact on quality of life (QOL), triggering factors and medication(s) selected (class of medications and reason for the selection). The survey was developed based on the empirical data and the framework of the international guidelines – Allergic Rhinitis and the Impact on Asthma (ARIA).[26] The questions in the survey were based on patients' symptoms and medication management of AR and the practicality for pharmacists to assess and manage patients with AR in the

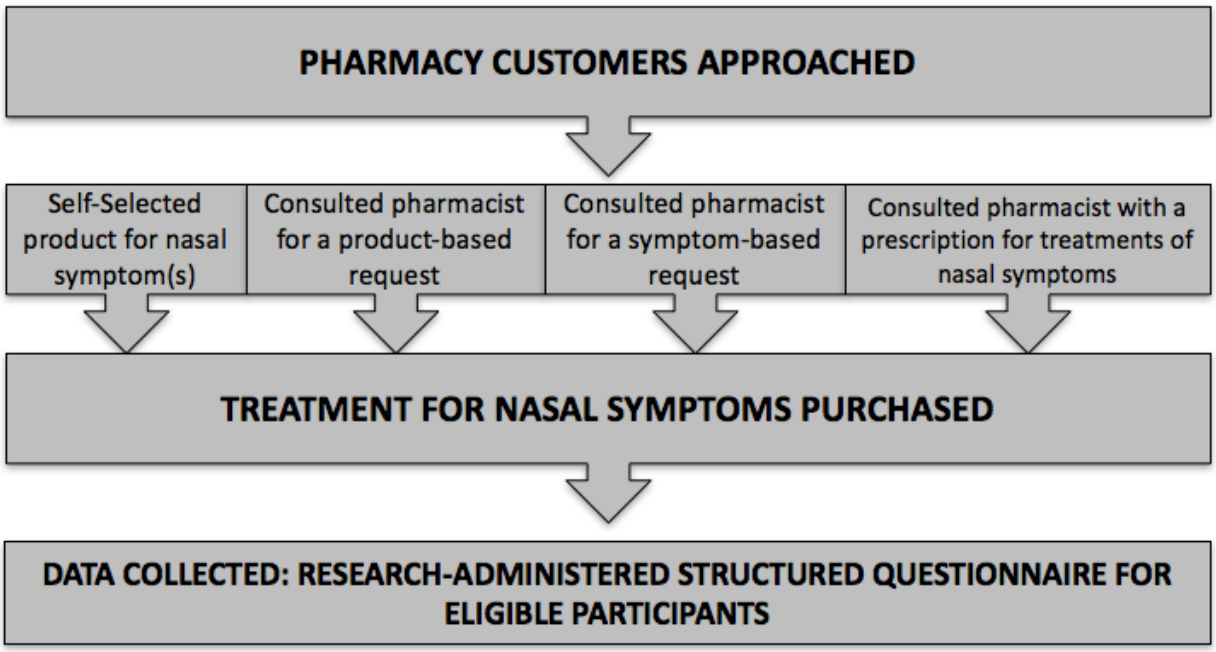

Figure 1. Study Design Overview

pharmacy.[27] The survey was designed to facilitate quick and easy administration and reviewed by specialist clinical experts, i.e. a respiratory physician and clinical pharmacists. All responses were anonymised, and participants were de-identified.

Bias

Potential bias in this study may have arisen as a result of: convenience sample of pharmacies within a Sydney Metropolitan area; the collection of data during high allergy seasons; inability to collect data from people who have mild AR who are less likely to visit a pharmacy for treatment.

Quantitative variables

ARIA guidelines classify AR according to patients' symptom(s) severity and impact on QOL experienced.[26] There are four categories; mild or moderate-severe intermittent and mild or moderate-severe persistent.[26] Symptoms that occurred less than four days per week or less than four weeks per year were classified intermittent, and symptoms that occurred more than four days per week and more than four weeks per year were classified persistent.[26]

Participants were asked to report the severity of their symptoms in the questionnaire, either none, mild, moderate or severe of their presenting symptoms, in accordance with Total Symptoms Score (TSS).[28] The impact of their QOL on participants' symptoms were also recorded. The impacts are related to whether they experienced an impact on their daily activities, performance at school or at work and/or disturb their sleep. Their symptoms were considered moderate-severe if they report their symptoms to be moderate or severe in the TSS table or if they report the presence of any impact on their QOL. The frequency of their symptom occurrence was also recorded in the questionnaire, as to whether they experienced symptoms less or more than four days per week and/or less or more than four weeks per year,

Statistical analysis

Data were analysed with SPSS version 24TM (SPSS-IBM, Chicago, IL, USA). Descriptive statistics were used, and data were compared between participants who self-selected and those who interacted with the pharmacist. Categorical variables were analysed using the Pearson chi-square test, and continuous variables were analysed using the independent sample t-test. A series of independent variables (participants' demographics, reported moderate-severe symptoms, impact of AR symptoms on QOL, medications selected) were evaluated to see if it was associated with participants' medication self-selection behaviour. These independent variables were statistically examined for suitability for inclusion in the multivariate logistic regression modelling using univariate logistic regression analysis to examine the presence of any binary correlations between participants who self-selected and each independent variable. Multivariate logistic regression analysis was performed on the univariate predictors, with $p<0.05$ used as the threshold for entry into the model, which was a value sufficiently significant to ensure potential interactions were not disregarded.[29] A statistical approach to variable selection was chosen as this was an exploratory study and no prior assumptions of relationships between factors have been established.[29] The goodness of fit of the logistic regression model was confirmed by the Hosmer and Lemeshow test. The final logistic regression model was determined with significance levels set at $p<0.05$.[29]

RESULTS

Data collection occurred in August-September, 2015 and April-July, 2016 (Australian Spring and Autumn respectively) from 8 community pharmacies, 6 hours/day

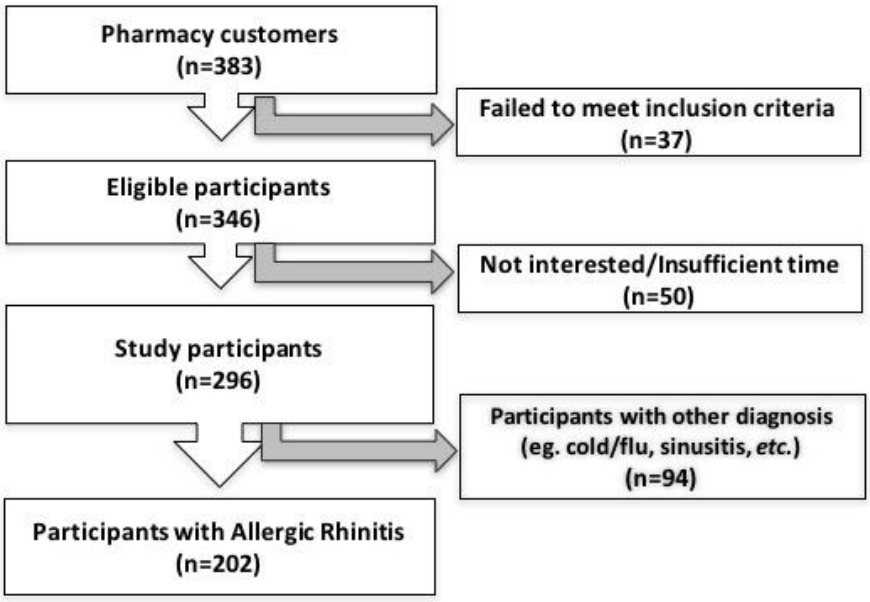

Figure 2. Participants Flowchart

and 4 days in each pharmacy. Each survey took an average of 5 minutes to administer for each participant. A flowchart of participants included and excluded are summarised in Figure 2. The 37 individuals who did not meet the inclusion criteria, were purchasing treatments other than for nasal symptoms or were unable to answer questions relating to the purchase of the product when purchasing for others.

Of the participants with AR, 1.5% (3/202) has mild intermittent, 1.5% (3/202) has mild persistent, 43.5% (88/202) has moderate-severe intermittent and 53.5% (108/202) has moderate-severe persistent.

Table 1 summarises participants' demographic characteristics. Of the 202 participants identified as having AR (Figure 1), 54.5% (110/202) were aged >40 years, 67.8%

Table 1. Demographic, clinical characteristics and medication class selected of total sample and by those who self-selected (n=140) and those who speak with a pharmacist (n=62).

Survey item	All participants (n=202)	Self-Selected		p-value
		Yes (n=140)	No (n=62)	
Gender				
Female	137 (67.8%)	100 (71.4%)	37 (59.7%)	0.105
Male	65 (32.2%)	40 (28.6%)	25 (40.3%)	
Age				
< 18 years old	15 (7.4%)	12 (8.57%)	4 (4.84%)	
18-39 years old	75 (37.1%)	52 (37.1%)	23 (37.1%)	>0.05
> 40 years old	110 (54.5%)	77 (55.0%)	33 (53.2%)	
HCP diagnosed AR	131 (64.9%)	91 (65.0%)	40 (64.5%)	1.000
AR symptoms (moderate-severe)				
Sneezing	128 (63.4%)	86 (61.4%)	42 (67.7%)	0.431
Rhinorrhoea	139 (68.8%)	91 (65.0%)	48 (77.4%)	0.100
Nasal Congestion	129 (63.9%)	84 (60.0%)	45 (72.6%)	0.112
Itchy/Watery Eyes	118 (58.4%)	81 (57.9%)	37 (59.7%)	0.877
Itchy Nose	63 (31.2%)	48 (34.3%)	15 (24.2%)	0.188
Itchy Ears/Palate	45 (22.3%)	33 (23.6%)	12 (19.4%)	0.585
Wheeze	27 (13.4%)	24 (17.1%)	3 (4.8%)	0.023
Frequency of AR symptoms				
Intermittent	91 (45.0%)	62 (44.3%)	29 (46.8%)	0.761
Persistent	111 (55.0%)	78 (55.7%)	33 (53.2%)	
Seasonal*	124 (61.4%)	84 (60.0%)	40 (64.5%)	0.639
Identified at least a trigger that affected their AR symptoms	149 (73.8%)	108 (77.1%)	41 (66.1%)	0.119
AR symptoms impacted on at least one aspect of QOL**	122 (60.4%)	75 (53.6%)	47 (75.8%)	0.003
Class of medications selected				
Oral Antihistamine	115 (56.9%)	82 (58.6%)	33 (53.2%)	0.539
Intranasal Antihistamine	2 (0.5%)	2 (1.4%)	0 (0%)	1.000
Intranasal Corticosteroids	63 (31.2%)	34 (24.3%)	29 (46.8%)	0.003
Intranasal Decongestant	23 (11.4%)	17 (12.1%)	6 (9.7%)	0.811
Oral Decongestant	4 (2.0%)	2 (1.4%)	2 (3.2%)	0.589
Saline	17 (8.4%)	9 (6.4%)	8 (12.9%)	0.168

* Seasonal – participants reported that their symptoms occurred seasonally or all year round in response to the question "Is there, if any, a particular time of the year that these symptom(s) occur?"
** Aspect of QOL includes Impact on daily activities, performance at school or at work, or sleep disturbance.

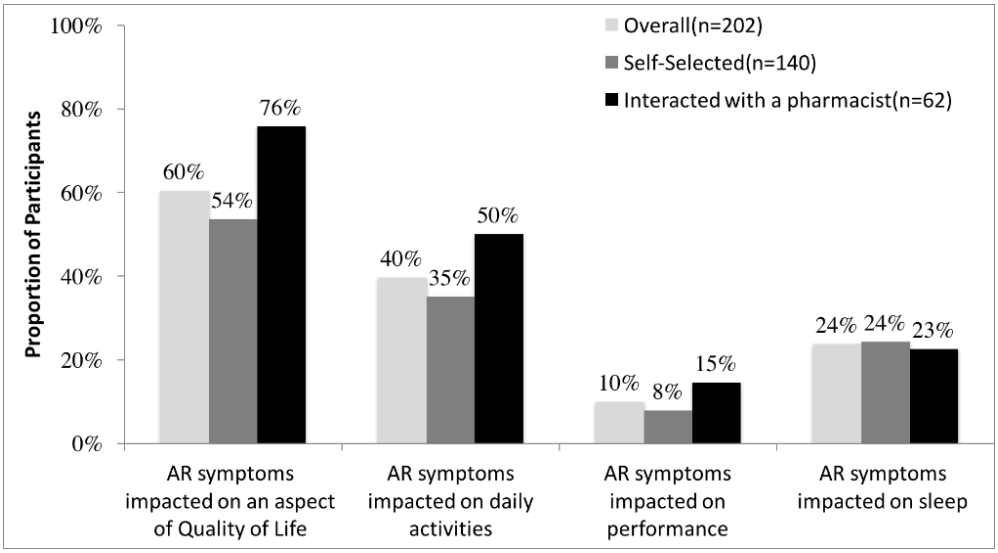

Figure 3. Impact of allergic rhinitis (AR) symptoms on at least one aspect of quality of life (QOL) - daily activities, performance and sleep, and each domain individually of total sample (n=202) and by self-selected (n=140) and interacted with the pharmacist (n=62) groups.

(137/202) were female, 35.1% (71/202) had undiagnosed AR, and 69.3% (140/202) self-selected medication(s) (Table 1). There were no significant differences in age groups, gender and HCP diagnosis of AR between participants who chose to self-select and those who spoke with a pharmacist (Table 1).

Table 1 also summarises participant's clinical characteristics - pattern of symptoms, impact of AR symptoms on QOL, triggering factors, and classes of medications selected for the symptoms experienced. Moderate-severe rhinorrhoea was the most commonly experienced symptom overall, followed by nasal congestion and sneezing. Over two-thirds (136/202) of participants experienced nasal and ocular symptoms in combination with itchiness in the ears/palate, with 32.7% (66/202) experiencing nasal symptoms only. Oral antihistamines and intranasal corticosteroids were the most frequently selected medication classes (Table 1). Figure 3 summarises the impact of AR symptoms on QOL by participants who self-selected and those who interacted with a pharmacist. The majority of the participants in this study could identify at least a trigger (Table 1). Those who self-selected were more likely be experiencing a wheeze, (p=0.023), and less likely to have an impact of AR symptoms on QOL (p=0.003) and/or purchase of intranasal corticosteroids (p=0.003) (Table 1).

Following univariate logistic regression analysis, two independent variables were significantly correlated with medication self-selection; presence of moderate-severe wheeze and AR symptoms impacting on at least one aspect of QOL (Table 2). There was no correlation between these two variables, therefore they were subsequently included for analysis in the multivariate logistic regression model. Classes of medication selected were not included in the model. These variables were statistically significant (chi-squared=15.546, df=2, p<0.001) (Table 2). Participants who self-selected were 4 times more likely to experience moderate-severe wheeze (OR 4.047, 95% CI 1.155-14.188) and almost 0.4 times less likely to experience AR symptoms impacting on their QOL (OR 0.369, 95% CI 0.188-0.727) (Table 2).

DISCUSSION

It is well established that patients commonly and sub-optimally self-select treatment for their AR, whilst continue to live with symptoms which impact on their QOL. This study is the first to explore the factors that are associated with medication self-selection behaviour of patients with AR in a 'real-life' setting viz; primary care and community pharmacy. Currently, the research question in this study has not been addressed to date. Our study revealed that the majority of people with AR self-selected OTC medication(s) in the community pharmacy to treat AR symptoms without speaking to the pharmacist. This study also found significant differences between those who self-selected and those who interacted with the pharmacist. The differences were related to the presence of moderate-severe wheeze and impact of AR symptoms on at least one aspect of QOL. Interestingly, symptom severity was not a driving factor for participants to interact with the pharmacist, although a majority of patients with AR were experiencing moderate-severe symptoms. While significantly higher proportion of participants who interacted with the pharmacist were purchasing intranasal corticosteroids compared to those who self-selected

Table 2. Analysis of factors associated with participants' medication self-selection behaviour.

Analysis	Predictors	B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I.for Exp(B)	
								Lower	Upper
Univariate	Moderate-severe wheeze	1.403	0.633	4.917	1	0.027	4.069	1.177	14.067
	Impacted on Quality of Life	-0.999	0.342	8.555	1	0.003	0.368	0.189	0.719
Multivariate	Moderate-severe wheeze	1.398	0.640	4.772	1	0.029	4.047	1.155	14.188
	Impacted on Quality of Life	-0.996	0.346	8.309	1	0.004	0.369	0.188	0.727

medication(s), this medication class was not included in the logistic regression model as it was an outcome of the pharmacist interaction.

Participants who self-select their own medication were less likely to report an impact of their AR symptoms on their QOL. In this study, 60% of the patients reported having AR symptoms impacting on one or more QOL domains (daily activities, performance at work or school, or sleep disturbance). There was a disconnection between the QOL and the severity of the AR symptoms reported by the participants. This is not an uncommon perception, in fact this has occurred similarly with other diseases such as asthma. Patients with asthma also underperceive the severity of their condition.[30] This suggests the patients can tolerate symptoms but when these symptoms impact on their QOL[16], it begins to impact on their medication management behaviour. This kind of behaviour has been reported in previous literature.[20,21,24,31,32] This might also reflect the concept of symptoms and patients' perception. From the pharmacist's perspective, these findings highlight that 1) patients who self-select are less likely to experience an impact of AR symptoms on their QOL and not speak to the pharmacist but pharmacists cannot assume that these patients have mild disease and are able to manage it without advice; 2) patients' poor perceptions of their AR symptoms are barriers to optimal management of AR16 and pharmacists should not solely rely on patients' perception to guide optimal treatment. Hence, in addressing this problem there are several possibilities/recommendations that we propose: 1) Pharmacists attempt/aim to approach every patient at least initially to assess their condition and follow up about their AR on the patients. 2) Pharmacy staff are encouraged to prompt patients to speak to the pharmacists before leaving the pharmacy. 3) Tools can be available for patients to self-evaluate their symptoms, such as the visual analogue scale, then prompted to speak to the pharmacist when appropriate. These tools are available through ARIA. It could be placed at the shelving where the AR medications are located for patients to evaluate their AR status.

In trying to determine whether participants had coexisting asthma, it was felt that asking the patient whether they experienced wheeze was the most non-judgemental and appropriate approach in this real-life scenario. In this study, the proportion of patients with co-existing wheeze was 13%, which is at the lower end of the range of the published prevalence of asthma amongst AR patients.[2] Participants who self-selected were more likely to be also experiencing moderate-severe wheeze in addition to AR. While this was both an unexpected and counter-intuitive finding, the literature indicates that there are complexities associated with asthma patients who are known to overestimate their asthma control[33] and underestimate the seriousness of their asthma.[34] Possible explanations for this finding could be due to patients' misinterpretation of the term 'wheeze' or because patients with asthma consider their AR a "minor" condition compared to wheeze. However, this study was not able to determine where patients place the importance of their wheeze, but it was able to clearly suggest that they do not associate their AR with their wheeze. It is important for pharmacists to be aware of this finding especially in light of the recent "Thunderstorm Asthma" events resulting in serious exacerbations and even death.[35] Pharmacists should alert patients regarding these co-existing conditions, provide them with education[36,37], and refer them to a general practitioner for a diagnosis, as it is critical that these patients treat their AR and co-existing conditions optimally. Pharmacists should recommend intranasal corticosteroids, as literature has shown that this medication does not only optimally controls AR symptoms but also reduces asthma symptoms.[13]

The majority of treatments for AR are available OTC. Although this allows for patients to purchase these medications OTC, it also provides opportunity for mismanagement of AR to occur. Therefore although 65% of patients with AR have had a diagnosis, it was possible for them to choose incorrect or suboptimal treatment options for their conditions. There are three possibilities for this situation, 1) patients might be recommended a treatment OTC by their doctor, which they may or may not take up or 2) patients might be prescribed a medication but chose to select their own medication OTC or 3) patients with follow up scripts from pharmacy. Nonetheless, while the terms suboptimally treated, undertreated AR and poor clinical outcomes of AR are similar, they are different. Suboptimal treatment selection refers to choosing a treatment that is not necessarily incorrect however it is not the optimal treatment for that patient, under treatment refers to a less than optimal amount of what might be an optimal treatment and poor clinical outcomes is not related to treatment but is describing the clinical feature/presentation.

The strengths of this research are the identification of opportunities for pharmacists to intervene in the current management of AR in the community pharmacy are identified; proper counselling and recommendation of medication selection, especially for patients with co-existing asthma. The limitations of this study are associated with the cross-sectional study design, non-randomised selection of pharmacies and the limited number of patients with mild AR approached.

CONCLUSIONS

In conclusion, the key factors associated with AR patients' self-selecting medication(s) are the presence of moderate-severe wheeze and the absence of AR symptoms impacting on their QOL. This research highlights the need for pharmacists to assist every patient who self-selects OTC medications, because this study has demonstrated that some patients are likely to be experiencing coexisting asthma and maybe underestimating the impact of AR on their QOL. Pharmacists should engage their AR patients and ensure that a proper diagnosis is obtained, an evaluation for coexisting conditions made, impact of the condition on QOL assessed and the most appropriate treatment recommended. Pharmacists plays the important role in AR management and future research should focus on providing evidence for the role of the pharmacist in the management of AR. Pharmacy staff are encouraged to prompt patients to consult pharmacists about their AR before leaving the pharmacy. Tools, available through ARIA, can also be available for patients, at the shelving where AR

medications are located, for patients to self-evaluate their symptoms, such as the visual analogue scale, then prompted to speak to the pharmacist when appropriate.

CONFLICT OF INTEREST

Vicky Kritikos: Received honoraria from AstraZeneca, GlaxoSmithKline and Pfizer.

Kwok Yan: Received honoraria for speaking and consulting from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Meda, Mundipharma and Pfizer.

Peter Smith: Has also been a speaker for Meda, GlaxoSmithKline, Novartis, Mundipharma and AstraZeneca.

David Price: A board membership with Aerocrine, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, and Teva Pharmaceuticals; consultancy agreements with Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, Mundipharma, Napp, Novartis, Pfizer, Teva Pharmaceuticals, and Theravance; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from UK National Health Service, British Lung Foundation, Aerocrine, AKL Research and Development Ltd, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, Pfizer, Respiratory Effectiveness Group, Takeda, Teva Pharmaceuticals, Zentiva, and Theravance; payment for lectures/speaking engagements from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Meda, Merck, Mundipharma, Novartis, Pfizer, Skyepharma, Takeda, and Teva Pharmaceuticals; payment for manuscript preparation from Mundipharma and Teva Pharmaceuticals; payment for the development of educational materials from Novartis and Mundipharma; payment for travel/accommodation/meeting expenses from Aerocrine, Boehringer Ingelheim, Mundipharma, Napp, Novartis, Teva Pharmaceuticals, and AstraZeneca; funding for patient enrolment or completion of research from Chiesi, Teva Pharmaceuticals, Zentiva, and Novartis; stock/stock options from AKL Research and Development Ltd, which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd, UK, and 74% of Observational and Pragmatic Research Institute Pte Ltd, Singapore; and is peer reviewer for grant committees of the Medical Research Council, Efficacy and Mechanism Evaluation programme, and Health Technology Assessment.

Sinthia Bosnic-Anticevich: A member of the Teva Pharmaceuticals Devices International Key Experts Panel; received research support from Research in Real Life; payment for lectures/speaking engagements and for developing educational presentations from Teva and Mundipharma; received Honoria from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, for her contribution to advisory boards/key international expert forum.

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Review

Resource-based theory of competitive advantage – a framework for pharmacy practice innovation research

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Abstract

A growing body of research demonstrates the effectiveness of evidence-based pharmacy practice, but too many practice innovations fail to survive past the initial implementation and study phase. This paper presents the resource-based theory of competitive advantage as a framework for describing, understanding, and predicting the adoption and dissemination pharmacy service innovations into routine practice. The theory argues that the sustainability of any business innovation (e.g., pharmacy service) is based upon (1) the internal resources of the firm offering it, (2) the firm's capabilities in using those resources, (3) the competitive advantage to the firm of its resources and capabilities, (4) the attractiveness of the market in which it competes, and (5) the innovation's contribution to financial performance of the firm. This paper argues that the resource-based theory of competitive advantage provides a foundation for comparing findings from different research frameworks and studies relating to innovations in services, service processes, and service business models. The paper also poses a number of research questions related to the theory that can be used to further the literature about pharmacy practice innovations. Finally, it makes a case that competition is a fundamental aspect of pharmacy practice and the resource-based theory of competitive advantage can serve as a general theory for studying innovations in pharmacy practice and in the social and administrative sciences.

Keywords

Pharmacy; Community Pharmacy Services; Diffusion of Innovation; Health Services Research; Economics; Marketing of Health Services

INTRODUCTION

A growing body of research demonstrates the effectiveness of evidence-based pharmacy practice innovations.[1,2] However, showing the effectiveness is not enough. Innovations in pharmacy practice need to be efficiently and effectively adopted, scaled, and sustained.[3]

Unfortunately, too many pharmacy practice innovations fail to survive past the initial implementation and study phase. Numerous potential reasons for this failure exist: mismatches between pharmacy business priorities and the interventions, insufficient support from stakeholders and customers, a poor match between the customer and the pharmacist's value proposition, inadequate advocacy about the intervention's benefits and value, and an unsustainable profit model. Available models of practice research have yet to show how pharmacists can consistently scale practice innovations in a sustainable way.

Numerous frameworks have been used to describe, understand, and predict the adoption and dissemination of evidence-based innovations into routine practice. This paper proposes a framework from the business literature, the resource-based theory of competitive advantage, which can be used for conducting research about innovations in pharmacy practice.

Originating from the strategic planning literature[4], the resource-based theory of competitive advantage addresses the complexity of innovation adoption, diffusion, and sustained success in competitive practice settings.[5] It is an interdisciplinary theory developed from wide ranging disciplines including marketing, management, ethics, law, supply chain management, and general business.[6] Its deceptively simple premise is that the sustainability of innovations comes from developing superior capabilities and resources.[4]

It offers a theoretical foundation for evaluating innovations that can be used in the context of pharmacy practice.[6] Pharmacy practice happens in competitive environments, so any theory should be consistent with a general theory of competition. As the name implies, the resource-based theory competitive advantage fits this requirement. Another argument for the theory is that it provides a foundation for standard theories of pharmacy practice research including implementation science[7], pharmacoeconomics[8], Donabedian's structure-process-outcome framework[9], operations research[10], amongst others. This provides an opportunity to unite a number of research streams into a single coherent framework. In fact, the resource-based theory of competitive advantage can serve as a general theory for social and administrative sciences in pharmacy and pharmacy practice.

RESOURCE-BASED THEORY OF COMPETITIVE ADVANTAGE

The resource-based theory of competitive advantage argues that the long-term success of any business innovation (e.g., pharmacy service) is based upon the internal resources of the firm offering it, the firm's capabilities in using those resources to develop a competitive advantage over competing options, and the innovation's contribution to financial performance of the firm in a market.[5] It is predictive because it hypothesizes directional relationships between the concepts of competition.

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In this theory, the "firm" is defined as a business organization, such as an independent pharmacy, pharmacy chain, hospital, or other organizational entity that offers goods and services. In this paper, the term "firm" will be used interchangeably with the terms "business" and "organization."

The theory considers innovating to be an evolutionary process founded on the following premises:[6]

1. Demand continually varies in market segments;
2. Consumers and firms lack perfect information;
3. Humans are motivated by self-interest;
4. Firms seek superior financial performance;
5. The firm's heterogeneous resources are physical, human, and organizational capital;
6. Competition is the source of innovation and it comes from a firm's ability to recognize, understand, create, select, implement, and modify strategies to its situation;
7. Financial performance between firms varies depending on their resources and capabilities.

Resource-based theory of competitive advantage argues that innovations achieve sustainable competitive advantage by accumulating and using resources to serve consumer interests in ways that are hard to substitute for or imitate. It states that successful innovations are determined not just by the innovation. Success is also the result of the people involved, the organization(s) behind the innovation, contextual factors surrounding its implementation and dissemination, and the innovation's benefits to stakeholders and the firm. The theory has been studied extensively[4-6,11], and it allows researchers to understand and explain what works, where it works, and why.

A resource-based model of pharmacy innovation is illustrated in Figure 1 and is based upon the work of several authors.[4-6,11] In the framework, the sustainability of an innovation (e.g., a pharmacy service) depends on the

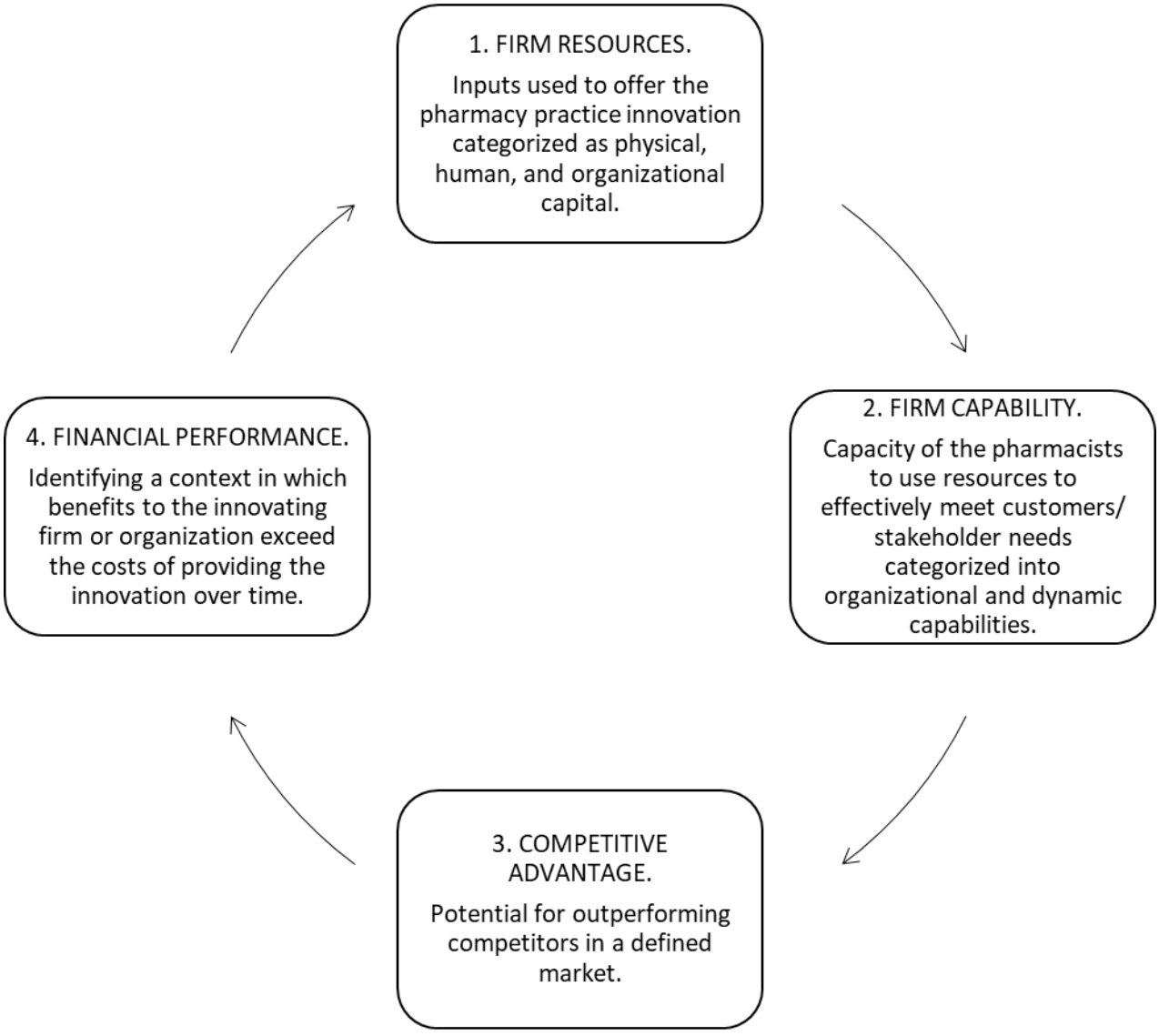

Figure 1. A resource-based model of pharmacy practice innovation.

innovation's potential for adding to the firm's competitive advantage and financial performance in the market environment in which the innovation is introduced. Furthermore, an innovation's competitive advantage and financial performance depends on the dynamics of the marketplace and the firm's ability to adapt the innovation to customer needs and wants better than competing options.

PHARMACY PRACTICE INNOVATIONS

Pharmacy Practice

For the purpose of this paper, pharmacy practice is defined as the provision of services by pharmacists and pharmacy organizations to respond to the medication-related needs of the people. Pharmacy practice has long been associated with the provision of tangible objects (i.e., drugs). However, practice really consists of intangible actions that facilitate the medication use process. They typically accompany a tangible drug, but the value provided by pharmacists lies not in tangible things but through intangible services.[12]

The definition above is broader than but consistent with the prescriptive vision of the Joint Commission for Pharmacy Practitioners, which sees pharmacist services as a way to help "patients achieve optimal health and medication outcomes with pharmacists as essential and accountable providers within patient-centered, team-based healthcare".[13] It is more consistent with Moulin et al. for professional pharmacy services which are defined as "an action or set of actions undertaken in or organised by a pharmacy, delivered by a pharmacist or other health practitioner, who applies their specialised health knowledge personally or via an intermediary, with a patient/client, population or other health professional, to optimise the process of care, with the aim to improve health outcomes and the value of healthcare".[14] All three stress the importance of pharmacies and pharmacy organizations in providing professional expertise to achieve desired outcomes relating to medications.

The definition of pharmacy practice is made purposely broad in order to capture the wide range of activities that pharmacists provide to serve customers and stakeholders (e.g., other professionals, the firm's C-suite). As long as the services involve 1) pharmacists or pharmacy organizations, 2) an attempt to respond to needs associated with medications, and 3) people including patients, the public, payers, stakeholders, and others, they can be classified as pharmacy practice.

Practice Innovations

Innovations in pharmacy practice consist of any changes in the provision of pharmacy services that are perceived as new by consumers, payers, or stakeholders. Practice innovations can be in the services themselves, the service process, or the service business model (Table 1).[15]

Table 1. Categories and examples of pharmacy practice innovations

Category	Examples
New services or service bundles	• Offering something new (e.g., specialty pharmacy services) • Finding new customers (e.g., offering veterinary pharmacy services to customers with pets) • Expanding a product line (e.g., adding immunizations to basic dispensing services) • Growing services (e.g., moving into new regional, national, or international markets) • Changing the service bundle (e.g., unbundling medication therapy management services into components), • Modifying existing service bundles (e.g., offering counseling in a private counseling area) • Repositioning an existing service bundle (e.g., promoting the pharmacist in advertisements instead of merchandise)
Service process innovations	• Improvements in the patient journey from the hospital to home through transitions in care programs • Pharmacy loyalty programs which reward patients for enrolling in medication adherence or medication therapy management programs • Use of practice guidelines and practice models • Retail clinics in pharmacies which permit one-stop health care for minor ailments • Smartphone apps which combine medication reminders, gamified health promotion, telepharmacy, and other services on one device • Use of artificial intelligence to personalize care to patients • Electronic point-of-care technology that offers discounts or some other form of value • Cashier-free stores which track items placed in carts by shoppers and automatically charge customers when they leave the store with those items • Shopping in pharmacies using augmented and virtual reality technology
Business model innovation	• Hospital Inpatient Value-Based Purchasing Program, which changes Medicare compensation to hospitals based on value-based purchasing measures relating to clinical processes, patient outcomes, measures of efficiency, and patient experience. • Federal 340B Drug Pricing Program, which allows eligible healthcare institutions to purchase outpatient drugs at significantly reduced prices from drug manufacturers. Savings can be used to expand service to Medicaid patients, the uninsured, and some other patients. • "Incident to" models in which pharmacists charge Medicare for clinical services provided under a physician's National Provider Identifier (NPI) number. They are called "incident to" because they are provided alongside a physician evaluation or other service covered by Medicare. • Medicare Star Rating Program, which uses a star rating system to assess the performance of Medicare Advantage and prescription drug (Part D) plans. Compensation to plans is based on scores, which range from one to five stars. • Pay-for-performance contracts, which reward providers for meeting established performance measures for quality and efficiency. Alternatively, they may penalize providers who are associated with poor outcomes, medical errors, or increased costs.

Service innovation

Innovations in services occur when services or service bundles are offered which are new to the market, firm, or industry.[15] They can be radical innovations such as novel offerings (e.g., drone delivery) or entry into new markets (e.g., international expansion). Alternatively, service innovations can be incremental such as minor tweaks in the services offered, service improvements, or new promotional practices.

Service process innovation

Service process innovations are changes in service operations and processes that influence the consumer experience and outcomes.[15] Process innovations may change the way information is exchanged between parties, improve back-office processes, or alter the structure in which services are provided. Because processes are so closely aligned with the services offered, they often result in new service or service bundles too. For example, appointment-based pharmacy services, in which enrolled patients have a designated monthly appointment day to pick up all chronic medications, are both a change in service process and a new service bundle.[16] Like service innovations, service process innovations can be radical, consisting of fundamental changes to existing processes (e.g., appointment-based medication synchronization) or incremental, minor changes like altering pharmacy workflow. Whether radical or incremental, process innovations either change the customer experience (e.g., greater convenience), achieve new customer outcomes (e.g., improved medication adherence), or both.

Service business model innovation

Business model innovations are major changes in the way in which services generate revenues and/or earn profits.[15] A service business model describes how service businesses (e.g., pharmacies) or their components (e.g., pharmacy department) generate sufficient revenues to cover the costs of providing services.[17] In pharmacy, a business model innovation might be a move from the traditional practice of generating revenues by selling merchandise or providing services for a fee to new value-based, pay-for-performance, and other forms of business models.[17]

Business model innovations often lead to innovations in both service bundles and processes. Movement from fee-for-service to pay-for-performance pharmacy contracts, for example, has encouraged the bundling of unit dose packaging, smartphone apps, medication synchronization, and patient counseling to improve patients' adherence to their medication regimens.

CONSTRUCTS AND THEIR RELATIONSHIPS

The key constructs and their relationships in resource-based theory of competitive advantage are described in Figure 2. Key constructs in the theory are: (1) firm

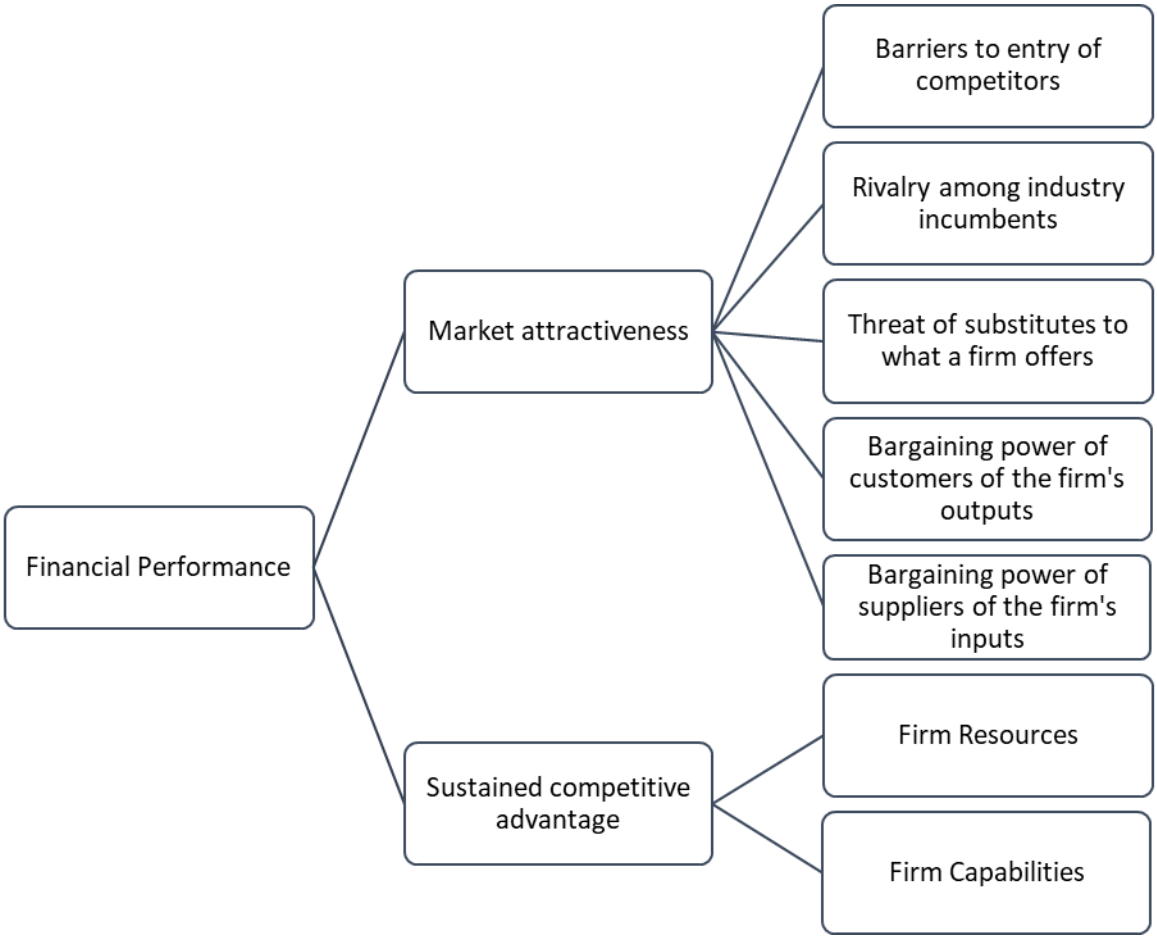

Figure 2. Key constructs and their relationships in resource-based theory

resources and capabilities employed in generating competitive advantage in a potential market, (2) sustainable competitive advantage, (3) market attractiveness (or potential), and (4) financial performance.

Firm Resources

Barney states that resources are "all assets, capabilities, organizational processes, firm attributes, information, knowledge, etc. controlled by a firm that enable the firm to conceive of and implement strategies that improve its efficiency and effectiveness".[4] Resources can be:

- Financial (e.g., cash, access to credit);
- Physical (e.g., building, fixtures, equipment);
- Legal (e.g., patents, trademarks);
- Human (e.g., clinical, managerial, and interpersonal skills);
- Organizational (e.g., culture, institutional knowledge, policies);
- Informational (e.g., proprietary knowledge about operations and market);
- Relational (e.g., relationships with suppliers and customers).

Resources can also be classified as tangible and intangible. Tangible resources are physical things like buildings, fixtures, land, machines, people, and technology. An intangible resource is any nonphysical thing that resides within a firm, including institutional knowledge, proprietary information, brand reputation, management expertise, financial assets, and organizational culture.

Firms that accumulate the right tangible and intangible resources can have a competitive advantage over other firms if those resources help them offer service innovations that are better and difficult to imitate or copy. In general, intangible resources offer more sustainable competitive advantages because they are difficult to copy. Tangible innovations like drive-through services, patient counseling areas, and touch-screen interactive kiosks offer an advantage for only a short time period because competitors can more easily duplicate or purchase them. Intangible factors like a pharmacist's expertise in serving patients at the drive-through and counseling areas or the proprietary software embedded within the kiosk are more difficult to reproduce.

A broad range of resources associated with competitive advantage have been identified from the pharmacy literature (Table 2).[18-23] Although the literature has examined a substantial number of resources supporting innovative pharmacy services, the studies are disconnected from any overall framework and have resulted in only a fragmentary understanding of their roles in competitive advantage.

Firm Capabilities

Capabilities describe the capacity of firms to use its resources to effectively meet customers' / stakeholders' needs. They can be divided into organizational and dynamic capabilities.[24] Organizational capabilities are a firm's ability to perform coordinated series of tasks using organizational resources to achieve a particular outcome. Dynamic capabilities are a firm's capacity to harness physical, human, and organizational resources to adapt to and thrive in rapidly changing environments.

Organizational capabilities describe the ability to manage order, while dynamic capabilities describe a firm's ability to respond to change. Kotter[25] would call the former "management ability" and the latter "leadership ability." Capabilities can be classified into basic managerial and leadership competencies of managerial, marketing, financial, and technical dimensions of business.

Prahalad and Hamel[26] introduced the concept of core competence to describe a firm's distinctive capabilities. They described core competencies as a congruent blend of resources and skills that distinguish a firm in a marketplace. To be competitive, core competencies need to:

1. Allow access to a broad variety of markets;
2. Make a significant contribution to the perceived customer benefits of the end product;
3. Be difficult to imitate by competitors.

Table 2. Resource types, capability category, and examples from the pharmacy literature

Resource type	Examples from pharmacy literature
Financial	A business case for stakeholders, allocation of financial resources
Physical	Physical environment of pharmacy (e.g., adequate space/privacy and workflow), equipment and technology (e.g., computers); location
Legal	Prescriptive authority, collaborative practice agreements, provider status, credentialing
Human	Pharmacist competence, education and training for personnel, communication skills, motivation, leadership skills, professional satisfaction, pharmacist knowledge of and attitude toward cognitive services, pharmacists' self-efficacy, autonomy, attitude of staff, sufficient staff
Organizational	Culture of pharmacy, innovative practice orientation, script volume, management support, reputation with the community
Informational	Access to patient records, access to reference literature, evidence of benefits of services
Relational	Relationships with physicians, pharmacist/patient relationship, support from professional organizations and/or government, external advisors or mentors
Capability Category	**Examples from pharmacy literature**
Managerial	Use of pharmacy technicians, delegation of tasks, organizational flexibility, human resources management
Marketing	Customer service, market segmentation, proactive entrepreneurial behaviors, services management, active relationship management with stakeholders
Financial	Cross-subsidization of expanded services, financial management
Technical	Being patient-centered, use of protocols, interaction with other pharmacists, use of a documentation system, learning from others, working in interprofessional teams

Core pharmacy practice competencies of individuals and firms associated with competitive advantage have been described in the literature (Table 2).[18,19,23,27,28] Firm resources and firm capabilities can be thought of as the strengths and weaknesses portion of a SWOT analysis that describes the things about a firm most likely to be a competitive advantage or weakness within a market.

Sustained Competitive Advantage

Resources and capabilities are the sources of competitive advantage in resource-based theory.[4] Competitive advantage occurs when a firm uses its resources and capacities to offer something new and valued that differentiates itself from competitors.

Competitive advantage only results from determinant attributes — those that determine choice between competitors. An innovation that is perceived as having a clear benefit on determinant attributes offers a competitive advantage. For instance, personalized services offered by an independent pharmacy might give them a competitive advantage for customers who value customized treatment. Therefore, the goal of positioning is to identify determinant attributes about an innovation and highlight their advantages over the competition.

Competitive advantage is a function of a pharmacy practice innovation's positioning relative to competitors. Positioning describes an innovation's image in the mind of customers. Competitive advantage results from an image that is clear, distinct, and valued in the mind of customers. Positioning also refers to the attributes about an innovation (e.g., convenient, personalized) that distinguish it from competing options.

Competitive advantage must be sustained over time for financial benefits to occur. Sustainability means that the innovation offers an advantage that can be defended in a market for a significant period. This occurs when firms utilize resources and capabilities in ways that are difficult to imitate, as discussed above, and fend off competitors' efforts to diminish their competitive advantage.[6] Thus, competition is a constant struggle between firms to position themselves with a clear and unique value proposition. Firms with an advantage must continually innovate by investing in resources and developing competencies, as firms which have a broad range of distinctive competencies across different market segments may be able to outperform firms that have relatively few competencies.[23] Accordingly, Prahalad and Hamel[26] state that a portfolio of core competencies can be used to invent new markets, exploit emerging opportunities, and develop a sustainable competitive advantage. Overall, then, competitive advantage "has no end stage, only a never-ending process of change".[6]

A variety of studies have examined competitive advantage in pharmacy practice. Some have focused on identifying determinant attributes of pharmacy patronage[29,30] and patient preferences for pharmacy services.[31,32] Others have looked at the sustainability of services[33], science of implementation[7,34], and distinctive competencies.[23] Findings of the research indicate that competitive advantage in pharmacy practice is situational and specific to the markets in which practice occurs.

Market attractiveness

Market attractiveness describes the potential of a market to a firm's success. "Market" refers to segments and not the total market because mass market innovations are rare in any industry. Therefore, competitive advantage needs to consider the potential of defined market segments for an innovation to succeed.

The ability to exploit market potential comes from a firm's ability to use its internal and external competencies and resources to rapidly adapt to changing market environments.[11] An innovation may succeed in one market segment but not another. The key is to match competitive advantage to the right segments.

A popular framework for assessing the attractiveness of a market is Porter's five forces.[35] In this framework, the intensity of competition in a market is determined by five industry forces: barriers to entry of competitors, rivalry among industry incumbents, the threat of substitutes to what a firm offers, the bargaining power of buyers of the firm's outputs, and the bargaining power of suppliers of the firm's inputs. An attractive market is one where a competitive advantage can be profitably developed and maintained. An unattractive market is one where competition for customers is fierce and costly.

Porter's framework requires firms to understand the forces most relevant to their market segments. Therefore, the forces affecting the financial performance of a pharmacy innovation in one market can differ from the forces in another. However, there are some major forces affecting competition in most pharmacy markets.

Barriers to entry

Profitable markets attract new firms into the market. New competitors will increase supply and drive down prices, thereby decreasing the profitability of all firms in the industry. Barriers to market entry determine the ease to which these new competitors can enter into a market.

A broad number of barriers exist in pharmacy markets. Pharmacy practice is subject to oversight by an array of local, state, and federal agencies, making it one of the most regulated professions. Any entrant into the market must jump through a large number of regulatory hurdles. Barriers also exist due to economies of scale available to large pharmacy chains which make up a major part of the prescription drug market. Access to those health insurance markets is biased toward larger firms who can provide wide geographic coverage to covered patients. In addition, these larger firms can more easily accept low profit margins on the sales of prescription drugs, thereby making the market less desirable to new entrants. Switching costs are another barrier due to the influence of pharmacy benefit managers (PBMs) which act as intermediaries between pharmacies and healthcare insurers. PBMs push pharmacies to participate in limited networks that give network pharmacies exclusive access to insured patients. Pharmacies outside of the network are blocked from receiving compensation for insured patients, while pharmacies inside of the network must accept stringent terms of service and undergo controversial auditing procedures. Switching costs of leaving those networks are

high because switching shuts pharmacies out of substantial markets of insured individuals.

Nevertheless, pharmacies with unique value propositions can still enter the market. For example, the online pharmacy PillPack, recently purchased by Amazon.com for approximately USD1 billion, carved out a place in the market by offering a consumer-friendly full-service pharmacy that fills prescriptions and ships drugs packaged in pre-sorted doses to make it easier to manage multiple medications.

Industry rivalry

The intensity of competition is high in the US, with 89% of Americans living within 5 miles of a pharmacy.[36] In some locations, two or three community pharmacies may be located at a single road intersection. Prescription drugs can be purchased at independent or chain pharmacies, grocery stores, large discount stores, pharmacy benefit managers and many other outlets. Omnichannel retail strategies make it possible for patients to purchase prescription drugs 24/7, 365 days a week using online, smartphone apps, drive-through, drone delivery, and even face-to-face interactions with a pharmacist.

Although the rivalry for selling drugs is intense, opportunities still exist for pharmacy innovations. There are many geographic locations that are far from a pharmacy or contain populations underserved by pharmacy services.[37] Another opportunity is for pharmacists to move from dispensing responsibilities to roles in primary care[38], as is seen in new business models like the pharmacy hub. In the hub model, the neighborhood pharmacy is a source of "primary care, prescriptions, point-of-care diagnostics, insurance, financing and insight into how to be well and stay well".[38,39]

Threat of substitutes

A substitute for a service bundle is one that is distinctly different but nevertheless meets similar customer needs and wants. Substitutes for pharmacists in dispensing activities are pharmacy technicians and technology such as robots. Substitutes for pharmacist services in primary care include physicians, nurses, nurse practitioners, physicians' assistants, and other health care professionals. Each offers a unique primary care approach that meets similar patient needs.

The threat of primary care substitutes is real and requires pharmacists to leverage their resources and capabilities to compete. One obvious advantage is the accessibility of pharmacists in the community. Each visit to a pharmacy is an opportunity to develop a therapeutic relationship with a patient. Another advantage is a pharmacist's' expertise with medications and drug-related problems. This can be used in innovations in improving medication adherence, vaccinations and health promotion, non-prescription medication use, and more. Pharmacists must market themselves effectively to tap into these opportunities.[40]

Bargaining power of buyers

The buyers' bargaining power describes their sensitivity to price changes in what is being offered. When buyers have bargaining power, they can put pharmacies under pressure to accept lower prices for their output.[41] In the US pharmacy market, buyers of pharmacist services have significant power over sellers. One of the major buyers of pharmacist services is the PBM industry, where approximately 70–75 percent of all prescription claims are handled by the three companies: Express Scripts, CVS Caremark, and OptumRx.[42] Another major buyer with significant power is the US government, which is forcing pharmacies to innovate under pay-for-performance and value-based purchasing plans. Large pharmacy chains have attempted to adapt through consolidation (pharmacies purchasing other pharmacies) and vertical integration[43] (pharmacies merging with healthcare insurers and wholesalers).

One hope for pharmacists is that the Federal Government will recognize pharmacists as providers and set higher expectations for the scope and quality of pharmacy services. Buyers in the private market typically follow Federal practices, so the government can drive pharmacies to engage in more primary care services. Rather than relying on hope, pharmacists are attempting to work within the business models established by various payers.[17]

Bargaining power of suppliers

The bargaining power of suppliers describes the degree to which suppliers can put firms under pressure to pay more for inputs. Suppliers to pharmacy service providers can be drug manufacturers, wholesalers, labor, services, or other inputs. Supplier bargaining power is usually a function of the number of suppliers of inputs or the availability of supplier substitutes. In extreme cases of supplier power, firms have few alternatives to accepting whatever terms suppliers demand.

In pharmacy practice, the major suppliers are pharmaceutical companies and the pharmacist labor pool. Pharmaceutical companies have significant ability to set the price for their single source drugs but less so with multisource medications. The pharmacist labor pool has lost significant bargaining power with employers because of the oversupply of pharmacists in some markets. Anecdotal reports suggest that the lower cost of pharmacist labor resulting from oversupply may lower the cost of labor-intensive pharmacist innovations.

Financial performance

Financial performance is the ability of a firm to earn excess financial benefits from an innovation in a defined market. Financial performance in the resource-based theory typically refers to profits, which generally describes what is left from the revenue generated by a firm after it pays for the expenses for resources and capabilities used in generating that revenue. However, it can also describe other measures of financial performance such as return-on-investment (ROI), cost-benefit, and budget impact. In many cases, these measures of financial performance will be more appropriate for describing the impact of pharmacy practice innovations.

Financial performance is determined by a firm's competitive advantage over rivals and the attractiveness of the market in which it competes.[5] Therefore, profitability of a service innovation lies both in its ability to develop a

competitive advantage and to identify a potential market where the benefits to the innovating firm or organization exceed the costs of providing the innovation over time. An innovation that is not supported by market conditions cannot be financially viable and sustain itself.

The pharmacy literature has attempted to measure the financial performance of pharmacies and innovations in a variety of studies. A study of competition in the German pharmacy market[44] found significant relationships between economic success (measured by net revenue development and sales profitability) and both resources (i.e., staff number) and capabilities (i.e., active customer oriented-management, aggressive attitude to competitors). Market attractiveness was not found to be associated with financial performance because competitive pressures were not considered by respondents to be a major concern in strategic decision making. A study of individual service innovations at a single pharmacy examined financial performance using net profitability.[45] The authors found that most of their 11 services showed an annual positive net gain. Business cases for pharmacist services have emphasized ROI to measure financial performance.[22] Cost benefit and other economic analyses have also been used to assess pharmacy practice innovations.[46,47]

In resource-based theory, firm profitability is the end goal for any business activities. Other measures of financial performance like ROI, cost benefit, and budget impact are intermediaries to profitability. Therefore, the sustainability of pharmacy practice innovations relies heavily on the business case made for its contribution to the firm's financial well-being.

USING RESOURCE-BASED THEORY TO INFORM PHARMACY PRACTICE RESEARCH

A significant body of research about pharmacy practice innovations has been developed over the years using a variety of conceptual frameworks, theories, and models of implementation.[48] Other studies have offered no explicit theoretical rationale for evaluating their practice interventions.

The variety of approaches to innovation research has fragmented the literature and given vague guidance to practitioners and researchers about how to develop successful pharmacy practice innovations. Variations in theories and frameworks have led to different terminology and classifications for innovation concepts. Without a common nomenclature and framework, pieces of the puzzle about the value of pharmacy interventions can be missed or never examined.

Resource-based theory of competitive advantage offers a way of harmonizing innovation research. As a theory, it both explains the relationships between concepts and offers hypotheses on the directional relationships of variables. It is highly applicable to practice because it addresses innovations within the real-life context of competition in the healthcare marketplace. Furthermore, it provides a foundation for comparing research findings from different research frameworks.

Table 3 compares major concepts in resource-based theory with those of other evaluation frameworks with disciplines that are common to pharmacy practice. The most common frameworks and disciplines are Donabedian's structure-process-outcome quality measurement; operations research; implementation science; and pharmacoeconomics. They each propose independent variables, dependent variables, and covariates relating to pharmacy practice. Like resource-based theory, they all see innovations in a context (e.g., attractiveness of market) of inputs (e.g., resources), transformation processes (e.g., competencies), and outcomes, both intermediate (e.g., sustained competitive advantage) and final (e.g., financial performance). Understanding commonalities in frameworks and discplines allows researchers to compare findings across distinct research streams.

The resource-based theory of competitive advantage provides a framework for posing a number of research questions about pharmacy practice innovations. They include the following:

RQ1. How does the pharmacy practice literature explain the competitive advantages of professional services?

RQ2. What pharmacy practice resources are associated with competitive advantage?

RQ3. What competencies of pharmacy practice are associated with competitive advantage?

RQ4: How would pharmacists' competitive advantage change if they had access to new resources (e.g., full patient data)?

RQ5: How would pharmacists' competitive advantage change with different competencies (e.g., entrepreneurial processes)?

RQ6: Under what conditions of the pharmacy market does

Table 3. Comparing frameworks/disciplines for evaluating pharmacy practice innovations

Research Framework	Resource-based Theory[5]	Donabedian[9]	Operations Research[10]	Implementation Science[48]	Pharmacoeconomics[8]
Independent Variables	Resources	Structures	Inputs	Factors	Medications
	Competencies	Processes	Transformation Processes	Factors	Value-added services
Dependent Variables	Sustained Competitive Advantage	Intermediate outcomes	Outputs	Strategies	Intermediaries
	Financial Performance	Health outcomes	Outputs	Evaluations	Economic, clinical, humanistic outcomes
Covariates	Attractiveness of Market	Patient clinical, demographic, & preference factors	System	Context of implementation	Perspective of analysis

competitive advantage lead to financial performance of firms?

RQ 7: What advances in market segmentation can be used to exploit the competitive advantages of pharmacy practice innovations?

RQ8: What competencies of individual pharmacists are needed to maximize their contribution to the competitive advantage of firms?

RQ9: What characteristics of markets (i.e., Porter's five factors) positively influence innovations in pharmacy practice?

RQ10: What constructs and dimensions define innovative pharmacy services and their contributions to competitive advantage?

RQ11: What proportion of published pharmacy practice innovations are sustained 2 years past the initial implementation and study phase?

RQ12: What resources and competencies are associated with financial performance of pharmacies?

CONCLUSIONS

Competition is a fundamental aspect of business and innovation. Innovations in pharmacy practice occur in competitive markets in response to opportunities and threats to pharmacy firms. The types of innovations are determined by the strengths and weaknesses of pharmacies offering them. Pharmacy innovations can only sustain themselves with positive financial performance.

External forces in the healthcare market are causing greater urgency for pharmacists to change their models of practice. Pharmacists and pharmacies have known for a long time that a product focus was not a viable future for the profession. It is only in recent years, however, that product-centered business models have become increasingly unprofitable. The status quo in pharmacy practice is not sustainable, but it is also not clear what practice models can succeed.

Resource-based theory of competitive advantage provides a way of explaining how pharmacy practice innovations can be sustained in various markets. It is relevant and useful to pharmacy practice research because it addresses the issue of competition in healthcare marketplace. It also offers a way of comparing research findings from different research frameworks. A case is made in this paper that the resource-based theory of competitive advantage can serve as a general theory for research in pharmacy practice and in the social and administrative sciences.

This paper shows how the findings of past research in pharmacy practice innovations can be applied to resource-based theory. It also suggests ways to tie those findings together into a more cohesive plan for future research that can guide practitioners and researchers about how to develop successful pharmacy practice innovations.

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CONFLICT OF INTEREST

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Erratum

Erratum to: What drives using antibiotic without prescriptions? A qualitative interview study of university students in United Arab Emirates

Khalid A. AL-KUBAISI, Mark DE STE CROIX, Don VINSON, Suleiman I. SHARIF, Abduelmula R. ABDUELKAREM.

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Book Comment

The Pharmacist Guide to Implementing Pharmaceutical Care

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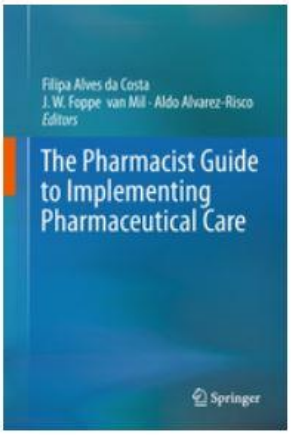

The Pharmacist Guide to Implementing Pharmaceutical Care is published by Springer and focuses on the implementation of pharmaceutical care. This book provides an in-depth analysis of particularities in care recipients and care environment impacting on service provision, complemented with practical examples. This book is aimed at pharmacists and pharmacy students, and edited by three experts in pharmaceutical care.

The book is structured in eight parts, covering 40 chapters:

Part I: What is Pharmaceutical Care, and Part II: Pharmaceutical Care Processes, discuss the pillars of pharmaceutical care, including the philosophy of practice, the central aim of the service focused around the identification and solving of drug related problems, the documentation needed, the indicators to monitor the process and the outcomes for the service beneficiaries and aspects of inter-professional collaboration. Specific services within pharmaceutical care are highlighted, such as contributing to medication adherence, providing medication review, and medication reconciliation.

Part III: Pharmaceutical Care around the World provides an overview of practice and research around five continents, aiming to enable the identification of crucial aspects of implementation that might impact of transferability of concepts.

Part IV: Implementing Pharmaceutical Care in Different Settings starts by focusing on general implementation strategies, followed by specific aspects related to the setting, highlighting aspects relevant to community pharmacy, hospitals and clinics, and finally nursing homes.

Part V: Delivering Pharmaceutical Care in Practice focuses on structural and complementary aspects of pharmaceutical care, and is divided into health promotion and disease prevention, dispensing medicines, pharmaceutical care around OTC medication and around medical devices.

Part VI: Pharmaceutical Care for Specific Patient Groups details the general aspects covered in part I considering the particularities of the medical condition debated, covering non-communicable diseases, such as asthma, diabetes, cardiovascular diseases and oncology, to name a few, but also communicable diseases, such as viral diseases, including Hepatitis and HIV.

Part VII: Remuneration of Pharmaceutical Care provides the readers with basic economy concepts applied to health research, expanding then to remuneration models in general and in pharmacy practice in particular.

Part VIII: Teaching Pharmaceutical Care is a part particularly intended for educators, both working in academia and in pharmacy practice focusing on professional continuous development. This part provides a detailed overview of teaching methods, also providing practical examples of curricular restructuring aimed at alignment with practice.

The book was developed with the contribution of 67 authors from all continents, selected as experts in the different fields of practice. Additionally, 17 reputed researchers contributed by reviewing the chapters in an external peer-review process.

The book is really comprehensive, and very useful for everyone willing to start implementing pharmaceutical care, or improving the success of implementation. It is an exhaustive book which can efficiently guide the implementation of enhanced person-centred care. Like every book, it reflects the current situation, and hopefully the publisher will make sure it is updated regularly.

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