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Deprescribing and reduction of inappropriate polypharmacy in resource limited settings: Older patients' perception in an Ethiopia University Hospital.

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SCHOLARONE™ Manuscripts Deprescribing and reduction of inappropriate polypharmacy in resource limited settings:

Older patients' perception in an Ethiopia University Hospital

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Abstract

Objectives: We assessed whether socio-demographic and clinical data were associated with older patients' attitude towards deprescribing of inappropriate medications.

Design This was Institutional-based quantitative cross-sectional survey.

Setting Data collection was conducted the outpatient clinics of University of Gondar referral and teaching hospital (UoGRTH) in Ethiopia.

Participants Older patients aged 65 or greater with at least one medication were enrolled in the study from March 1 to June 30, 2017. Exclusion criteria were patients who had severe physical or psychological problems and those who refused to participate. Of 351 eligible participants, 316 elderly patients completed the survey data.

Main outcome measures: Older patients' attitude towards deprescribing was measured using the validated tool of revised Patients' Attitudes towards Deprescribing (rPATD) for older patients. Predictive variables were Sociodemographic and clinical data such as comorbidity and polypharmacy. Older patients' attitude towards deprescribing was an interest of outcome.

Results Of 316 older patients enrolled in this study, most of them (65.2%) have overall poor attitude towards deprescribing. There was a significant difference among polypharmacy and non-polypharmacy in appropriateness factors overall score (10.94 \pm 1.98 Vs. 10.16 \pm 2.09, P= 0.009). Moreover, patients with polypharmacy had more burden factor score than non – polypharmacy patients (12.71 \pm 2.58 Vs. 10.95 \pm 3.23 respectively, P= < 0.0001). Patients who are unable to read and write are more likely to have poor attitude towards deprescribing (AOR [0.219(0.077-0.622), P-value= 0.004]. A one unit increase in patient's number of medications will result in 1.2 increases to good attitude to deprescribing; AOR [1.211(1.026-1.430), P-value= 0.023].

Conclusion: About 65.2% older patients have overall poor attitude toward discontinuing medications (deprescribing). Polypharmacy and educational status were identified as the common risk factors to patients' willingness to deprescribing. Health care providers should be proactive to discuss, evaluate and decision making of potentially in appropriate medications.

Key words: Attitude; medication discontinuation; Deprescribing; Polypharmacy; Elderly; rPATD

Strengths and limitations of this study

- Older patients' attitude towards deprescribing and their willingness to stop medicines has been assessed for the first time in resource limited setting like Ethiopia
- This study utilized a validated multidimensional questionnaire in relatively large number of patients.
- The type of disease they have, the medicine category, type and duration of the medication might affect patients' willingness and perception towards deprescribing.
- Owing to the interviewer based questionnaire structured for quantitative research, it does not permit in-depth investigation of patient attitude.
- Care givers for older patients have not been included as they may affect on the preference and willingness to stop medicines.

Introduction

Polypharmacy often defined as the use of five or more medications, has been linked with pervasive adverse drug events and ultimately leads to increased morbidity, mortality and healthcare costs [1-3]. Polypharmacy-related adverse drug events (ADEs) are very common and estimated to occur in 25% of ambulatory care patients [3].

De-prescribing, one of the approaches to prevent polypharmacy-related ADEs, is a process of detecting and stopping medications when the actual or potential harms exceeds the actual or potential benefits taking into consideration a variety of factors including the individual patient's therapeutic care plans, level of functioning and needs [4]. Deprescribing has a number of benefits to the patient including reducing costs associated with medicines and their ADEs, improving

adherence and overall quality of life [5]. This is especially true in resource limited countries such as Ethiopia, where the main source of drug expenditure is patients' out of pocket money and a significant percentage of the population purchase medicines from private drug retail outlets [6].

While concepts such as adherence and medication reconciliation receive considerable attention, and covered by a wide range of literatures worldwide, little attention has been given to the concept of de-prescribing and reduction of inappropriate polypharmacy [7]. Despite the prescribers' positive attitude on de-prescribing [8], many factors including clinical uncertainty and shared responsibility with other healthcare providers severely impede clinicians' ability to proactivity discontinue medications [9]. Moreover, patient perspectives on deprescribing and their communication with clinicians are equally important in evidence based medication discontinuation process.

Several studies conducted in developed countries regarding older people's attitudes toward deprescribing reported a higher rate of willingness to discontinue their medications ranging from 40.5% to 90% [10-12]. However, no previous study has explored the attitudes of Ethiopian older patients regarding their medications and deprescribing. It is also uncertain how patients would respond to a suggestion from a clinician to intentionally discontinue a medication. Taking the global evidence into consideration and due to lack of data in Ethiopia, we sought to identify Ethiopian older patients' willingness to have their medications deprescribed.

Methods

Study design and setting

Institutional-based quantitative cross-sectional survey was conducted from March 1 to June 30, 2017 at University of Gondar referral and teaching hospital (UoGRTH), Ethiopia. The hospital is located in Gondar town, northwest Ethiopia, 738km away from Addis Ababa and it's the only

referral and teaching center in the area to which majority of patients with chronic diseases including hypertension, diabetes mellitus, cancer and asthma are referred.

Participants

All elderly (≥ 65 years) patients who has been taking at least one medication regardless of their diagnosis and who visited the outpatient clinic of University of Gondar referral and teaching hospital (UoGRTH) for follow-up and medication refill were our study population. Patients who had severe physical or psychological problems which leads to inability to complete the interview and those who refused to participate were excluded from the survey. Of 351 eligible participants obtained during the study period, 316 elderly patients completed the survey data.

Survey instrument

Data was collected by three of the principal investigators through interviewer-administered questionnaire. The investigators were properly trained on the instrument and ways of approaching the patients and securing their permission for interview prior to the data collection process. We used Revised Patients' Attitudes towards Deprescribing (rPATD) questionnaire [13]. It is a validated multidimensional questionnaire which measure patients' attitudes, knowledge and experiences related to medication discontinuation. A 4-point Likert response scale was used (strongly agree, agree, disagree and strongly disagree) in rPATD questionnaire. The rPATD questionnaire has four major factors including Burden factor (4 items); Appropriateness factor (5 items); Concerns about stopping factor (4 items); Involvement factor (4 items) and additional two global questions are also considered. The previously validated tool -Belief in Medicine use Questionnaire (BMQ)-Overuse [14] was utilized for comparison and validation of the rPATD questionnaire. The questionnaire, first prepared in English, was translated to Amharic language and back to English so as to ensure that the translated version

gives the proper meaning. It was further pre-tested on 25 elderly patients, who were not included in the final analysis, and slight modifications were instituted before the commencement of the actual survey. Polypharmacy was defined as the use of ≤ 5 regular medications.

Statistical analysis

All the statistical analyses were done using Statistical Package for Social Sciences (SPSS) software version 21.0 for Windows (SPSS Inc., Chicago, IL). Frequencies and percentages were used to express different variables. Data were screened for normality and homogeneity using the Shapiro–Wilk and Levene tests respectively. Respondents were stratified by polypharmacy status to examine attitudes toward deprescribing in patients with polypharmacy. Binary logistic regression was performed to assess the association between attitude towards deprescribing and predictor variables. The level of statistical significance was defined as p<0.05 and all tests were OLON. two-tailed.

Operational definitions:

Deprescribing: is a process of optimization of medication regimens through termination of potentially in appropriate medications. It is the planned and supervised process of dose reduction or stopping of medication that might be causing harm or might not be longer providing benefit.

Poly pharmacy: Polypharmacy is defined as the practice of prescribing five or more medications to the same person.

Poor attitude: The rPATD questionnaire having 19 items may score ranging from the lowest point of 19 up to the highest 76 and those scored below 50% of the total score taken as a cut of point for poor attitude.

Good attitude: The rPATD score range from the lowest point of 19 up to the highest 76 and the rPATD score above 50% of the total score taken as a cut of point for good attitude.

Ethical Consideration

This study was approved by the Ethical committee of School of Pharmacy, University of Gondar with an approval number of UoG-SoP-131/2017. Written informed consent from the respondents was also obtained before conducting this study. Participants' information obtained was kept confidential.

Results

Out of 351 patients approached, 316 of them completed the questionnaire, giving a response rate of 90 %. Most of the participants were men (173 individuals, 54.92 %) and the mean age was 71.36 ± 6.09 years. The mean number of their daily medications was 3.43 ± 1.50 . From the total number of participants, 62 (19.7%) were on polypharmacy. The most common comorbidities in polypharmacy groups were hypertension, diabetes mellitus and asthma. While in non – polypharmacy study participants, hypertension, heart failure and chronic kidney disease were more prominent. Details of socio characteristics of the study participants is tabulated in Table 1.

Table 1: Sociodemographic and clinical characteristics of study participants, UoGRTH, Ethiopia (n = 316).

Variable	Polypharmacy n (%)		
	Yes (n=62)	No (n=253)	
Gender			
Male	35 (56.45 %)	138 (54.55 %)	
Female	27 (43.55%)	115 (45.45%)	
Age (Mean \pm SD)	69.87 ± 10.11	71.50 ± 6.31	
Educational status			
Unable to read and to write	37 (59.68 %)	165 (65.22 %)	
Primary school	13 (20.97 %)	49 (19.37 %)	
Secondary School	5 (8.06 %)	26 (10.28 %)	
Higher education	7 (11.29 %)	13 (5.14 %)	

Comorbidity		
Hypertension	27 (43.55 %)	67 (26.48 %)
Heart failure	6 (9.68 %)	22 (8.70 %)
Diabetes Mellitus	8 (12.90 %)	13 (5.14 %)
Chronic kidney disease	3 (4.84 %)	20 (7.91 %)
Asthma	5 (8.06 %)	10 (3.95 %)
Rheumatoid Heart Disease	2 (3.23 %)	14 (5.53 %)
Others	11 (17.74 %)	107 (42.29 %)
Charlson Comorbidity index (Mean \pm SD)	2.44 ± 0.90	1.85 ± 0.87
Number of Medication (Mean \pm SD)	5.85 ± 1.32	2.85 ± 0.76

Of 316 older patients, majority of the participants (65.2%) have overall poor attitude towards deprescribing. Figure 1 describes the percentage for Patient perception of deprescribing sub scores. Most of the patients had concerns about stopping factors as it is evidenced by 67.7% polypharmacy and 68.6% non – polypharmacy groups. The least concern was on the general questions on deprescribing (24.35 % of polypharmacy and 24.50 % of non – polypharmacy groups).

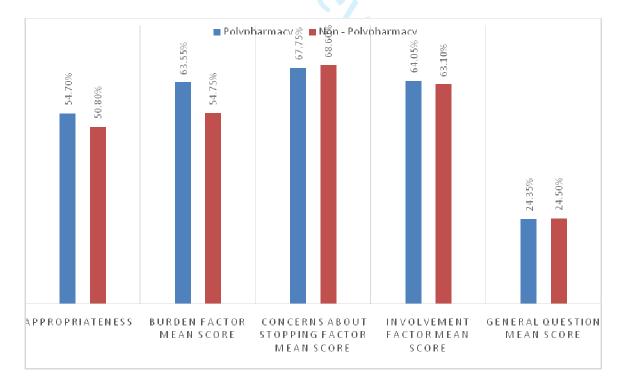


Figure 1: Percentage of the mean scores for rPATD sub scores

There was a significant difference among polypharmacy and non-polypharmacy in appropriateness factors overall score (10.94 ± 1.98 Vs. 10.16 ± 2.09 , P= 0.009). There was also a significant difference among the two groups to the question "I would like my doctor to reduce the dose of one or more of my medicines" (mean score of 2.48 ± 1.13 for polypharmacy groups and 2.01 ± 1.02 for non – polypharmacy groups, P value= 0.001). Moreover, patients with polypharmacy had more burden than non – polypharmacy patients (12.71 ± 2.58 Vs. 10.95 ± 3.23 respectively, P= < 0.0001). (Table 2)

Table 2: Distribution of rPATD sub scores among study participants, UoGRTH, Ethiopia (n = 316).

Variable		Poly Pharma	ey	P- Value
		Yes (n=62)	No (n=253)	
Appropriateness Factor overall score		10.94 ± 1.98	10.16 ± 2.09	0.009*
I feel that I may be taking one or more medicines the	nat I no longer need	2.00 ± 0.87	1.90 ± 0.97	0.417
I would like to try stopping one of my medicine	es to see how I feel	1.31 ± 0.69	1.31 ± 0.73	0.955
without it				
I would like my doctor to reduce the dose of	one or more of my	2.48 ± 1.13	2.01 ± 1.02	0.001*
medicines				
I think one or more of my medicines may not be we	orking	2.90 ± 0.43	2.89 ± 0.40	0.811
I believe one or more of my medicines may be curr	ently giving me side	2.24 ± 1.02	2.06 ± 0.91	0.191
effects				
Burden factor -overall score		12.71 ± 2.58	10.95 ± 3.23	<0.0001*
I spent a lot of money to medicines		2.94 ± 1.23	2.78 ± 1.24	0.372
Taking my medicines every day is very inconvenie	nt	2.37 ± 0.96	2.10 ± 1.54	0.191
I feel that I am taking a large number of medicines		2.84 ± 0.94	2.18 ± 0.93	<0.0001*
I feel that my medicines are a burden to me		2.45 ± 0.86	1.96 ± 0.92	<0.0001*
Sometimes I think I take too many medicines		2.11 ± 0.96	1.92 ± 0.92	0.152
Concerns about stopping Factor score		13.55 ± 2.12	13.72 ± 2.37	0.612
Involvement Factor score		12.81 ± 3.25	12.62 ± 3.13	0.671

General Questions score

 4.87 ± 1.14

 4.90 ± 1.11

0.868

The descriptive analysis of patients' response to each questions of rPATD questionnaire has been described in table 3.

Table 3: Percentage distribution of patients' response to the survey questions, UoGRTH, Ethiopia (n = 316).

Survey questions	Strongly disagree	Disagree	Agree	Strongly agree
Burden Factor				- 6
I Spent a lot of money to medicines	87(27)	15(4.7)	84(26.6)	130(41.1)
Taking my medicines every day is very inconvenient	104(32.9)	92(29.1)	107(33.9)	13(4.1)
I feel that I am taking a large number of medicine	88(27.8)	68(21.5)	135(42.7)	25(7.9)
I feel that my medicines are a burden to me	114(36.1)	80(25.4)	110(34.8)	12(3.8)
Sometimes I think I take too many medicines	134(42.4)	69(21.8)	105(33.2)	8(2.5)
Appropriateness Factor	, , ,		, ,	
I feel that I may be taking one or medicines that I no longer need	95(30.1)	12(3.8)	144(45.6)	65(20.6)
I wants to stop and try one of my medicines to see how I feel without it	257(81.3)	29(9.2)	21(6.6)	9(2.8)
I would like my doctor to reduce the dose of one or more my medicines	104(32.9)	30(9.5)	133(42.1)	49(15.5)
I think one or more of my medicines may not be working	7(2.2)	24(7.6)	281(88.9)	4(1.3)
I believe one or more of my medicines may be currently giving me side effects	121(38.3)	11(3.5)	114(36.1)	70(22.2)
Concerns about stopping factor				
I not agree to stop the medicine which I took for a long period of time	109(34.5)	119(37.7)	65(20.6)	23(7.3)
If I stop one of the medicines which I take I believe that I will not be healthy	9(2.8)	25(7.9)	122(38.6)	160(50.6)
If there is a change in the medicine, I feel not happy	87(27.5)	81(25.6)	132(41.8)	16(5.1)
If my doctor wants to stop my medicines I feel that I am hopeless	146(46.2)	82(25.9)	63(19.9)	25(7.9)
I have a bad experience of medicine discontinuation before	186(58.9)	47(14.9)	45(14.2)	38(12.0)
Involvement Factor I have a good knowledge for each medicine that are prescribed for me	59(18.7)	44(13.9)	168(53.2)	45(14.2)

^{*}statistically significant (p<0.05)

I have a good knowledge about my drug and I	114(36.1)	126(39.9)	65(20.6)	11(3.5)
would document if there is any change on my drug				
I am interested to know about the medicines	71(22.5)	54(17.1)	162(51.3)	29(9.2)
I participate with my doctor when decisions are	32(10.1)	93(29.4)	165(52.2)	26(8.2)
made on my drug				
I always ask my doctor /a pharmacist if there is	19(6.0)	40(12.7)	161(50.9)	96(30.4)
any miss-understanding				
General Questions				
I agree to stop one of the medicines if my doctor	22(7.0)	36(11.4)	74(23.4)	184(58.2)
ordered/asked me to stop				
I am very happy about the medicines which I am	9(2.8)	16(5.1)	120(38.0)	171(54.1)
taking				

Patients who are unable to read and write have 78.1% less to good attitude towards deprescribing as compared with those patients who are attending higher education; AOR [0.219(0.077-0.622), P-value= 0.004]. Increase by one medicine in patient's number of medications will result 1.2 increases to good attitude to deprescribing; AOR [1.211(1.026-1.430), P-value= 0.023].(Table 4)

Table 4: Binary logistic regression test for Attitude of elderly patients towards deprescribing at Gondar University Hospital, 2017 (N=316)

³ V ariable	Attitude t	o deprescribing	Crude OR	p-value	Adjusted OR	p-value
35	Poor	Good				
36 37 Sex 38 Male 38 D						0.938
Male 20	107	66	1.388(0.868-2.219)	0.171	0.979(0.570-1.681)	
39 Female	99	44	1		1	
4gAge				0.175		0.173
4 ₁ 65-69	86	56	1.682(0.797-3.549)	0.172	1.660(0.752-3.667)	0.210
4270-74	65	25	0.994(0.442-2.234)	0.988	1.001(0.425-2.357)	0.997
4375-79	24	17	1.830(0.736-4.551)	0.194	2.101(0.802-5.503)	0.131
44≥ 80	31	12	1		1	
4 £ ducational status				0.000**		0.002**
46Unable to read and write	149	53	0.192(0.073-0.506)	0.001**	0.219(0.077-0.622)	0.004*
47Primary school	34	28	0.443(0.156-1.262)	0.128	0.506(0.168-1.523)	0.225
48Secondary school	16	16	0.538(0.170-1.702)	0.292	0.596(0.177-2.010)	0.404
49Higher education	7	13	1		1	
⁵ Comorbidty				0.251		0.619
51Hypertension	57	37	1.235(0.705-2.163)	0.461	0.960(0.520-1.772)	0.895
⁵² Heart failure	18	10	0.519(0.195-1.381)	0.189	0.512(0.184-1.421)	0.199
⁵³ Diabetes mellitus	17	4	1.729(0.678-4.410)	0.251	1.468(0.551-3.915)	0.443
54Chronic kidney disease	17	6	0.671(0.246-1.834)	0.437	0.614(0.216-1.747)	0.360
55 Asthma	10	5	1.665(0.564-4.914)	0.356	0.997(0.303-3.285)	0.996

Rheumatic heart disease	9	7	0.439(0.118-1.629)	0.218	0.481(0.123-1.886)	0.293
5 Others	78	41	1		1	
6 Number of medications			1.180(1.013-1.375)	0.034*	1.211(1.026-1.430)	0.023*

* P-value < 0.05, ** p-value < 0.01 OR- Odds ratio

Discussion

Elderly patients are prone to multi-morbidity with high medication regimens complexity needing stopping of medications, a growing concept so called deprescribing [11]. Elderly patients receiving many medications with their underlined medical illness are vulnerable to rehospitalization, drug induced complications and morbidity. Moreover, polypharmacy compromises patient adherence and lead to incur additional costs to manage unnecessary adverse outcomes [15-20]. Hence, mutual agreement between patients and clinical practitioners should be sought to optimize the elderly 'patients' medication regimen keeping with few numbers of medications [21]. To our knowledge, this is a first study to have been conducted on this study area in resource limited settings like Ethiopia.

The mean number of daily medications of elderly patients in this study was 3.43 ± 1.50 . Findings from Kalogianis MJ et al. study conducted in Australia shows total number of medications per patient was 14.6 ± 5.3 , which is a lot higher than our result [10]. The Australian study included all potential regular and complementary medicines which may explain the difference in average medications per patient.

Majority (81.6%) of the patients agreed to stop one of the medicines if their doctor ordered/asked them to stop. This is consistent with previous studies conducted by Mona et al [10] and Reeve et al [11] having 80% and 89% of patients' willingness rate to stop their medicines, respectively. This previews the importance of proactive engagement of health care professionals in

deprescribing process for elderly patients and should discuss with their patients on how to optimize and simplify the dosage regimens.

In our study, most of patients with polypharmacy had more concerns on appropriateness and burden of the medications they took as compared with their non polypharmacy counterparts. This shows patients on polypharmacy are more willing to have one of the medications deprescribed owing to patients complain on appropriateness, having a large number of medicines, feeling of medicines burden. In contrast, a study conducted in aged care facility highlighted that the desire to stop medications was not influenced by the number of medicines taken [10]. This disparity may be explained by number of medications being a pushing factor to deprescribing in our study. As stated by various studies [10, 11, 22, 23], the variation might also be attributable to the difference in study settings like aged care facility center and usual care in our study.

Two third of patients believe that they spent a lot of money to medicines; one of the single most indicator to patients medications burden. In this regard medications costs are contributing to the patients to have positive attitude to deprescribing as they are willing to reduce one of the medicines. Other study has reported that patients having to pay less for their medications would influence their willingness to have medications deprescribed and paying more encourage deprescribing [10]. It is always important to consider cost implications in therapeutic decision making and drug selection in elderly patients as those patients are prone to prolonged care, polypharmacy and less productivity to handle their therapeutic expenses [24].

Majority of the respondents feel that they took at least one of the medicines neither needed longer nor working anymore. Despite of this perception, elderly patients are solely dependent on the physician decision and look to hear the likelihood of stopping the medicine from the doctor side [11].

Overall attitude towards deprescribing is significantly related with only two of the predictor variables; educational status and the number of medications taken by the patients. Those who are not able to read and write had poor attitude towards deprescribing as compared with those who attended higher education. On the contrary, every increase in a number of medicines was associated with 21% increase to good attitude towards deprescribing. This is supported by one study; patient willingness to stop medication was correlated with a desire to take few medicines and the feeling of taking a large number of medications and being less comfortable with current medications [11].

Majority of the elderly patients have curiosity to know about their medicines, ask their healthcare provider and involve in the clinical decision making process. This is very important to patient-provider relationships, encircling on the sub-themes of trust, relying on expertise and shared decision making which are imperative to better patient outcomes. In spite of these, majority of elderly patients do not have good knowledge of their medicines and merely dependent on the health care providers to initiate decisions about their medications. Moreover, many patients who have a preference to take fewer medicines do not share their beliefs with providers and waiting for provider initiated medication discontinuation [25]. Thus health professionals should use a patient centered approach to outweigh the risks and benefits of every medicine against the particular goals of the elderly patient, with the aim of minimizing the total number of prescribed medicines [26].

Strengths and Limitations

This is the first study in Ethiopia to assess elderly patients' perception towards deprescribing and their willingness to stop medicines by using validated multidimensional questionnaire in relatively large number of patients. Despite of this, it is interviewer based questionnaire

structured for quantitative research, which does not permit in-depth investigation of patient attitude. The type of disease they have, the medicine category, type and duration of the medication might affect patients' willingness and perception towards deprecibing.

Conclusion

About 65.2% older patients have overall poor attitude toward discontinuing medications (deprescribing). However, they are willing to stop their medications if the doctor said it is possible. Most of the patients who are in polypharmacy doubt the necessity of all the medicines and feel that a lot of burden in terms of medication expenses. Polypharmacy was the common driving factor to patients' willingness to deprescribing. Elderly patients are found to be exclusively dependent on the clinician's decision to deprescribing. Therefore, health care providers should be proactive to discuss, evaluate and decision making of potentially in appropriate medications. Further study with potentially large number of study participants and qualitative study is warranted to fully evaluate the deprescribing attitude in different disease categories and prospective significance to Ethiopian elderly patients' health.

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Contributors HGT has contributed to the conception, study design, prepared the study protocol and drafted the manuscript. YGT and DAE performed literature review, carried out statistical analyses, and interpreted the results. FC and YA acquired and managed the data. KTH, TBA, AAA wrote the manuscript and reviewed the manuscript for critical revisions. All authors approved the final manuscript.

Competing interests None declared.

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	yes
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	yes
Objectives	3	State specific objectives, including any prespecified hypotheses	yes
Methods			
Study design	4	Present key elements of study design early in the paper	yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	yes
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	yes
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Yes
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	Yes
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Yes
		(b) Describe any methods used to examine subgroups and interactions	Yes
		(c) Explain how missing data were addressed	Yes
		(d) If applicable, describe analytical methods taking account of sampling strategy	Yes
		(e) Describe any sensitivity analyses	Yes
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	Yes
·		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
Outcome data	15*	Report numbers of outcome events or summary measures	Yes
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Yes
		(b) Report category boundaries when continuous variables were categorized	Yes
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Yes
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			Yes
Key results	18	Summarise key results with reference to study objectives	Yes
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes
Other information		06.	Yes
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

Abb: NA- Not applicable

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

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Older patients' perception to Deprescribing in resource limited settings: A cross sectional study in an Ethiopia University Hospital.

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SCHOLARONE™ Manuscripts Older patients' perception to Deprescribing in resource limited settings: A cross sectional study in an Ethiopia University Hospital.

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Abstract

Objectives: We assessed whether socio-demographic and clinical data were associated with older patients' attitude towards deprescribing of inappropriate medications.

Design This was Institutional-based quantitative cross-sectional survey.

Setting Data collection was conducted the outpatient clinics of University of Gondar referral and teaching hospital (UoGRTH) in Ethiopia.

Participants Older patients aged 65 or greater with at least one medication were enrolled in the study from March 1 to June 30, 2017. Exclusion criteria were patients who had severe physical or psychological problems and those who refused to participate. Of 351 eligible participants, 316 elderly patients completed the survey data.

Main outcome measures: Older patients' attitude towards deprescribing was measured using the validated tool of revised Patients' Attitudes towards Deprescribing (rPATD) for older patients. Predictive variables were Sociodemographic and clinical data such as comorbidity and polypharmacy. Older patients' willingness to deprescribing was an interest of outcome.

Results Of 316 older patients enrolled in this study, 54.7 % were men; the median number of their daily medications was3 (IQR: 2-4). Most of the participants (81.6%; 95CI: 77%-86%) were willing to stop one or more of their medications if advised by doctor even if a significant number of participants were overall satisfied with medications they were taking (92.1%; 95CI: 89%-95%). This willingness was correlated with seven items of the rPATD including strong correlation with overall satisfaction of patients with their medication taken.

Conclusion: Most of the participants (81.6%) were still willing to reduce one or more of their medications if advised by their doctor. Health care providers should be proactive to discuss, evaluate and decision making of potentially in appropriate medications.

Key words: Attitude; medication discontinuation; Deprescribing; Polypharmacy; Elderly; rPATD

Strengths and limitations of this study

- Older patients' attitude towards deprescribing and their willingness to stop medicines has been assessed for the first time in resource limited setting like Ethiopia
- This study utilized a validated multidimensional questionnaire in relatively large number of patients.
- The validated tool of rPATD however, has not been tested in a culturally different settings like Ethiopia
- Owing to the interviewer based questionnaire structured for quantitative research, it does not permit in-depth investigation of patient attitude.
- Care givers for older patients have not been included in the current study as they may affect on the preference and willingness to stop medicines.

Introduction

Polypharmacy often defined as the practice of prescribing five or more medications to the same person, has been linked with pervasive adverse drug events and ultimately leads to increased morbidity, mortality and healthcare costs [1-3]. Polypharmacy-related adverse drug events (ADEs) are very common and estimated to occur in 25% of ambulatory care patients [3]. Deprescribing, one of the approaches to prevent polypharmacy-related ADEs, is defined as the 'the process of withdrawal of inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes' [4]. Given the holistic and patient-centered nature of deprescribing, it has a number of benefits to the patient. A recent systematic review conducted by Page et al. reported that individualized deprescribing interventions to reduce inappropriate polypharmacy may improve mortality [5]. Deprescribing also has potentially additional benefits to the patient such as increasing patient engagement in

medication therapy management and improving adherence possibly through reducing polypharmacy [6].

The impact of deprescribing is conceivably beneficial for older patients living in resource limited countries such as Ethiopia, where the incidence of chronic non-communicable diseases and multimorbidity is mounting in alarming rate [7]. Moreover, the main source of drug expenditure in Ethiopian patients' out of pocket money and a significant percentage of the population purchase medicines from private drug retail outlets, which are usually not affordable by patients [8].

While concepts such as adherence and medication reconciliation receive considerable attention, and covered by a wide range of literatures worldwide, little attention has been given to the concept of deprescribing and reduction of inappropriate polypharmacy [9]. Despite the prescribers' positive attitude on deprescribing [10], many factors including clinical uncertainty and shared responsibility with other healthcare providers severely impede clinicians' ability to proactivity discontinue medications [11]. Moreover, patient perspectives on deprescribing and their communication with clinicians are equally important in evidence based medication discontinuation process. Several studies conducted in developed countries regarding older people's attitudes toward deprescribing reported a higher rate of willingness to discontinue their medications [12-16]. However, no previous study has explored the attitudes of Ethiopian older patients regarding their medications and deprescribing. It is also uncertain how patients would respond to a suggestion from a clinician to intentionally discontinue a medication. Taking the global evidence into consideration and due to lack of data in Ethiopia, we sought to identify Ethiopian older patients' willingness to have their medications deprescribed.

Methods

Study design and setting

Institutional-based quantitative cross-sectional survey was conducted from March 1 to June 30, 2017 at University of Gondar referral and teaching hospital (UoGRTH), Ethiopia. The hospital is located in Gondar town, northwest Ethiopia, 738km away from Addis Ababa and it's the only referral and teaching center in the area to which majority of patients with chronic diseases including hypertension, diabetes mellitus, cancer and asthma are referred.

Participants

All older patients (≥ 65 years) who has been taking at least one medication regardless of their diagnosis and who visited the outpatient clinic of University of Gondar referral and teaching hospital (UoGRTH) for follow-up and medication refill were our study population. Patients who had severe physical or psychological problems which leads to inability to complete the interview and those who refused to participate were excluded from the survey. Of 351 eligible participants obtained during the study period, 316 elderly patients completed the survey data.

Main outcome measures: Older patients' attitude towards deprescribing was measured using the validated tool of revised Patients' Attitudes towards Deprescribing (rPATD) for older patients. Predictive variables were Sociodemographic and clinical data such as comorbidity and polypharmacy. Older patients' willingness to deprescribing was an interest of outcome.

Survey instrument

Data was collected by three of the principal investigators through interviewer-administered questionnaire. The investigators were properly trained on the instrument and ways of approaching the patients and securing their permission for interview prior to the data collection process. We used Revised Patients' Attitudes towards Deprescribing (rPATD) questionnaire

[17]. It is a validated multidimensional questionnaire which measure patients' attitudes, knowledge and experiences related to medication discontinuation. The original a 5-point Likert scale in rPATD questionnaire, was changed to a 4-point Likert scale (strongly agree, agree, disagree and strongly disagree) in the current study as it may allow the participants to be more discriminating and avoid misinterpretation of mid points. The rPATD questionnaire has four major factors including Burden factor (5 items); Appropriateness factor (5 items); Concerns about stopping factor (5 items); Involvement factor (5 items) and additional two global questions are also considered. The previously validated tool -Belief in Medicine use Questionnaire (BMQ)-Overuse [18] was utilized for comparison and validation of the rPATD questionnaire. The questionnaire, first prepared in English, was translated to Amharic language and back to English so as to ensure that the translated version gives the proper meaning. It was further pre-tested on 25 elderly patients, who were not included in the final analysis, and slight modifications were instituted before the commencement of the actual survey. Polypharmacy was defined as the use of >5 regular medications.

Statistical analysis

All the statistical analyses were done using Statistical Package for Social Sciences (SPSS) software version 21.0 for Windows (SPSS Inc., Chicago, IL) [19]. Frequencies and percentages were used to express different variables. Data were screened for normality using both the Shapiro–Wilk and Kolmogorov-Smirnov. Respondents were stratified by polypharmacy status to examine attitudes toward deprescribing in patients with polypharmacy.

Correlation analysis using Spearman's Rho, was used to assess the associations between all rPATD items and three individual questions like Patients' perception of side effect from their medicines, the patients' willingness to discontinue their medications if advised by doctor, and

Overall satisfaction of patients with their medication taken. Binary logistic regression was performed to assess the association between willingness to stop medication if advised by doctors and predictor variables. In Univariate analysis, variables with P<0.2 were selected for final model. But none of the variables fit these criteria. The level of statistical significance was defined as p<0.05 and all tests were two-tailed.

Operational definitions:

Deprescribing: is 'the process of withdrawal of inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes'. It is the planned and supervised process of dose reduction or stopping of medication that might be causing harm or might not be longer providing benefit.

Poly pharmacy: is defined as the practice of prescribing five or more medications to the same person.

Ethical Consideration

This study was approved by the Ethical committee of School of Pharmacy, University of Gondar with an approval number of UoG-SoP-131/2017. Written informed consent from the respondents was also obtained before conducting this study. Participants' information obtained was kept confidential.

Results

Out of 351 patients approached, 316 of them completed the questionnaire, giving a response rate of 90 %. The median age was 70 years (IQR: 67-75). The mean and median number of their daily medications was 3.43 ± 1.50 and 3 (IQR: 2-4), respectively. From the total number of participants, 62 (19.7%) were on polypharmacy. The most common reason of hospital visit in

polypharmacy groups were diabetes mellitus (DM), hypertension, and Rheumatic heart Disease (RHD). While in non – polypharmacy study participants, hypertension, DM and heart failure were more prominent. A detail of socio characteristics of the study participants is tabulated in Table 1.

Table 1: Sociodemographic and clinical characteristics of study participants, (n = 316).

Variable	Participants, N	Polyphar	macy n (%)
	(%)	Yes (n=62)	No (n=254)
Gender			
Male	173(54.7)	35 (56.45 %)	138 (54.55 %)
Female	143 (45.3)	27 (43.55%)	116 (45.45%)
Age(median; Interquartile range(IQR))	70(67-75)	70(67-73	70(67-75)
Educational status			
Unable to read and to write	202 (64)	37 (59.68 %)	165 (65.2 %)
Primary school	62 (19.6)	13 (20.97 %)	49 (19.37 %)
Secondary School	32 (10.1)	5 (8.06 %)	26 (10.28 %)
Higher education	20 (6.3)	7 (11.29 %)	13 (5.14 %)
Reason of hospital visit (N=315)			
Hypertension	128(40.5)	20 (32.3%)	108 (42.5)
Heart failure	23(7.3)	8 (1.3%)	15 (5.9)
Diabetes Mellitus	105(33.2)	22 (35.5%)	83 (32.7)
Chronic kidney disease	14(4.4)	1 (1.6%)	13 (5.1)
Asthma	8 (2.5)	2 (3.2%)	6 (2.4)
Rheumatoid Heart Disease	10(3.2)	4 (6.5%)	6 (2.4)
Others	27(8.6) ^a	5 (8.1%)	22 (9.1) a
Charlson Comorbidity index ^a	2(1-2)	2(2-3)	2(1-2)
(median;IQR) (N=315)			
Number of Medication (median; IQR)	3(2-4)	5(5-6)	3(2-3)

Note: ^a data was missing for one participant

As reported in table 2, a total of 316 participants have responded to 22 rPATD questions. In a burden factor domain, a total of 214 older patients (67.7%; 95%CI: 63%-73%) taught they spend a lot of money on their medicines. However, a considerable percentage of participants (61.5%) didn't feel their medications are a burden to them. Appropriateness factor domain showed that only 9.4% would like to try stopping one of their medications to see how they feel without it,

even though most of the participants (90.2%) taught one or more of their medicines may not be working. Concerns about stopping factor; most of the respondents (89.2%; 95CI: 86%-93%) would be worried about missing out on future benefits if one of their medications was stopped.. In the involvement factor, majority of the respondents [257 participants; 81.3%;95CI: (77%-86%)] ask their doctor, pharmacist or other health care professional if there is any missunderstanding about their medications. If ordered by the doctor, about 258 individuals (81.6%; 95CI: 77%-86%) were willing to stop one or more of their regular medications although a significant number of participants were overall satisfied with medications they were taking (92.1%; 95CI: 89%-95%) (Table 2).

Patients' perception of side effect from their medicines is positively associated the thirteen items but negatively associated with the three factors. Those patients who thought their medications are a burden to them are more likely to perceive side effects from one or more medications. Patients didn't have overall satisfaction with their medications if they perceive side effect from one or more of the medications (table 3).

The patients' willingness to discontinue their medications if advised by doctor was correlated with seven items of the rPATD. Of the three items positively associated with this question, patients are still willing to stop one or more of their medications if advised by doctor even though they may be worried about missing out on future benefits while stopping one of their medications. In contrary, four of the items were negatively correlated with willingness to discontinue their medications if advised by doctor such as belief that participants were taking too many medicines, were perceiving side effects from one or more of their medicines, were reluctant to stop a medication taken for a long time, and perceived their doctor giving up on them If their doctor

recommended stopping a medicine. Overall satisfaction of patients with their medication taken was correlated with many items of rPATD questionnaire as described in detail in Table 3.

Table 2: Patients' attitudes towards deprescribing based on the rPATD questionnaire (n = 316).

Sui	rvey questions	Strongly disagree	Disagree	Agree	Strongly agree	Strongly agree/ Agree % (95% CI)
Bu	rden Factor		- I		<u>'</u>	,
B1	I spent a lot of money on my medicines	87(27)	15(4.7)	84(26.6)	130(41.1)	67.7% (63-73)
B2	Taking my medicines every day is very inconvenient	104(32.9)	92(29.1)	107(33.9)	13(4.1)	38% (32.6-43.4)
ВЗ	I feel that I am taking a large number of medicine	88(27.8)	68(21.5)	135(42.7)	25(7.9)	50.6% (45-56)
B4	I feel that my medicines are a burden to me	114(36.1)	80(25.4)	110(34.8)	12(3.8)	38.6% (33-44)
В5	Sometimes I think I take too many medicines	134(42.4)	69(21.8)	105(33.2)	8(2.5)	35.7% (30-41)
Ap	propriateness Factor					
A 1	I feel that I may be taking one or medicines that I no longer need	144(45.6)	65(20.6)	95(30.1)	12(3.8)	33.9% (29-39)
A2	I would like to try stopping one of my medicines to see how I feel without it	257(81.3)	29(9.2)	21(6.6)	9(2.8)	9.4% (6-13)
A3	I would like my doctor to reduce the dose of one or more my medicines	133(42.1)	49(15.5)	104(32.9)	30(9.5)	42.4% (37-48)
A4	I think one or more of my medicines may not be working	7(2.2)	24(7.6)	281(88.9)	4(1.3)	90.2% (87-93)
A5	I believe one or more of my medicines may be currently giving me side effects	114(36.1)	70(22.2)	121(38.3)	11(3.5)	41.8% (36-47)
Co	ncerns about stopping factor					
C1	I would be reluctant to stop a medicine that I had been taking for a long time	109(34.5)	119(37.7)	65(20.6)	23(7.3)	27.9% (23-33)
C2	If one of my medicines was stopped I would be worried about missing out on future benefits	9(2.8)	25(7.9)	122(38.6)	160(50.6)	89.2% (86-93)
C3	I get stressed whenever changes are made to my medicines	87(27.5)	81(25.6)	132(41.8)	16(5.1)	46.9% (41-52)
C4	If my doctor recommended stopping a medicine I would feel that he/she was giving up on me	146(46.2)	82(25.9)	63(19.9)	25(7.9)	27.8% (23-33)
C5	I have a bad experience when stopping a medicine before	186(58.9)	47(14.9)	45(14.2)	38(12.0)	26.5% (21-31)
Inv	olvement Factor					

I1	I have a good understanding of the	59(18.7)	44(13.9)	168(53.2)	45(14.2)	67.4% (62-73)
	reasons I was prescribed each of my					
	medicines					
I2	I know exactly what medicines I am	114(36.1)	126(39.9)	65(20.6)	11(3.5)	24.1% (19-29)
	currently taking, and/or I keep an up to					
	date list of my medicines					
I3	I like to know as much as possible about	71(22.5)	54(17.1)	162(51.3)	29(9.2)	60.5% (55-66)
	my medicines					
I4	I like to be involved in making decisions	32(10.1)	93(29.4)	165(52.2)	26(8.2)	60.4% (55-66)
	about my medicines with my doctors					
I5	I always ask my doctor, pharmacist or	19(6.0)	40(12.7)	161(50.9)	96(30.4)	81.3% (77-86)
	other health care professional if there is					
	something I don't understand about my					
	medicines					
Ge	neral Questions					
G1	If my doctor said it was possible I would	22(7.0)	36(11.4)	74(23.4)	184(58.2)	81.6% (77-86)
	be willing to stop one or more of my					
	regular medicines					
G2	Overall, I am satisfied with my current	9(2.8)	16(5.1)	120(38.0)	171(54.1)	92.1% (89-95)
	medicines					

Adopted from Revised Patients' Attitudes Towards Deprescribing (rPATD) Questionnaire (17)

Binary logistic regression was performed after dichotomizing the two outcome variables (willingness to deprescribe one or more of their regular medications if advised by doctor and overall satisfaction with their prescribed medications), but none of the variables fits the final model (P>0.2). And all variables didn't have statistically significant association with both outcome variables.

Table 3. Spearman Correlation of responses within the rPATD questionnaire

rPATD questions	10.I believe one or more of my	21. If my doctor said it	22.Overall, I	am
Spearman Correlation	medicines may be currently	was possible I would be	satisfied with	my
(p-value)	giving me side effects	willing to stop one or	current medicines	
		more of my regular		
		medicines		
Burden Factor				
1. I spend a lot of money on my medicines	0.03,0.63	0.14, 0.06	0.16, 0.00	
2. Taking my medicines every day is very inconvenient	0.24,0.00	-0.07, 0.19	-0.28,0.00	
3.I feel that I am taking a large number of medicine	0.15,0.01	-0.096,0.09	-0.35, 0.00	
4.I feel that my medicines are a burden to me	0.31,0.00	-0.08, 0.17	-0.35,0.00	
5. Sometimes I think I take too many medicines	0.25,0.00	-0.22, 0.00	-0.53,0.00	
Appropriateness Factor				
6.I feel that I may be taking one or medicines that I no	0.25,0.00	-0.09, 0.13	-0.38,0.00	
longer need				
7. I would like to try stopping one of my	0.06,0.32	-0.04, 0.48	-0.1,0.42	
medicines to see how I feel without it	10.			
8.I would like my doctor to reduce the dose of one or	0.14,0.02	0.04,0.4	-0.25,0.001	
more my medicines				
9.I think one or more of my medicines may not be	-0.11,0.04	0.01,0.8	0.14,0.009	
working				
10.I believe one or more of my medicines may be	1	-0.14,0.08	-0.31,0.00	
currently giving me side effects				
Concerns about stopping factor				
11.I would be reluctant to stop a medicine that I	0.19,0.001	-0.3,0.00	-0.26,0.001	
had been taking for a long time				
12.If one of my medicines was stopped I would	-0.20,0.00	0.26,0.00	0.55,0.00	
be worried about missing out on future benefits				
13.I get stressed whenever changes are made to	0.27,0.00	-0.07,0.19	-0.17,0.002	
my medicines				
14.If my doctor recommended stopping a	0.12,0.03	-0.37, 0.00	-0.34,0.00	
medicine I would feel that he/she was giving up				
on me				
15.I have a bad experience when stopping a	0.19,0.001	-0.07,0.22	-0.18,0.027	

Involvement Factor 16.I have a good understanding of the reasons I was prescribed each of my medicines 17.I know exactly what medicines I am currently taking, and/or I keep an up to date list of my medicines 18.I like to know as much as possible about my medicines 19.I like to be involved in making decisions about my medicines with my doctors 20.I always ask my doctor, pharmacist or other health care professional if there is something I don't understand about my medicines 21.If my doctor said it was possible I would be willing to stop one or more of my regular	good understanding of the reasons I bed each of my medicines exactly what medicines I am currently for I keep an up to date list of my know as much as possible about my be involved in making decisions about es with my doctors ask my doctor, pharmacist or other professional if there is something I stand about my medicines existions cotor said it was possible I would be stop one or more of my regular 1. I am satisfied with my current 1. 0.14,0.01 1. 0.04,0.53 1. 0.02,0.71 1. 0.001,0.98 1. 0.02,0.71 1. 0.001,0.98 1. 0.001,0.98 1. 0.005,0.45 1. 0.005,0.45 1. 0.34,0.00 1. 0.34,0.00 1. 0.34,0.00 1. 0.34,0.00 1. 0.34,0.00	edicine before			
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medicines		edicines			
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medicines					

Discussion

Elderly patients are prone to multi-morbidity with high medication regimens complexity needing stopping of medications, a growing concept so called deprescribing [13]. Elderly patients receiving many medications with their underlined medical illness are vulnerable to rehospitalization, drug induced complications and morbidity. Moreover, polypharmacy compromises patient adherence and lead to incur additional costs to manage unnecessary adverse outcomes [20-25]. Hence, mutual agreement between patients and clinical practitioners should be sought to optimize the elderly 'patients' medication regimen keeping with few numbers of medications [26]. To our knowledge, this is a first study to have been conducted on this study area in resource limited settings like Ethiopia.

In the current study, the mean and median number of their daily medications was 3.43 and 3 respectively which is very low as compared to other studies such as the mean of Kalogianis et al. study [12] was 14.6, while the median was 6 and 11 in Sirois et al study [16] and Reeve et al [13], respectively. In spite of having low median number of medications in the current study, majority (81.6%) of the patients still agreed to stop one of the medicines if their doctor advised them to stop. This is also consistent with previous studies conducted by Mona et al [12], Reeve et al [13] and Alessandro et al [27] having 80%, 68%, and 89% of patients' willingness rate to stop their medicines, respectively. This previews the importance of proactive engagement of health care professionals in deprescribing process for elderly patients and should discuss with their patients on how to optimize and simplify the dosage regimens.

Two third of patients believe that they spent a lot of money to medicines. In this regard medications costs are contributing to the patients to have positive attitude to deprescribing as they are willing to reduce one of the medicines. Other study has reported that patients having to

pay less for their medications would influence their willingness to have medications deprescribed and paying more encourage deprescribing [12]. It is always important to consider cost implications in therapeutic decision making and drug selection in elderly patients as those patients are prone to prolonged care, polypharmacy and less productivity to handle their therapeutic expenses [28].

This study has showed the association between each item and the selected three questions of the survey items like perceiving of side effects from one or more of medicines taken, willingness to stop one or more of medicines if advised by doctor, and overall satisfaction with their current medications. In the current study, patient were willing to stop one or more of medications if advised by doctor even if they were taking few medications, didn't perceive side effects from one or more of their medications, were not reluctant to stop a medicine taken for a long time and had overall satisfaction with their medications. Other studies also reported that patient willingness to stop medication was correlated with a desire to take few medicines and the feeling of taking a large number of medications and being less comfortable with current medications [13, 15, 16].

Majority of the elderly patients have curiosity to know about their medicines, ask their healthcare provider and involve in the clinical decision making process. This is very important to patient—provider relationships, encircling on the sub-themes of trust, relying on expertise and shared decision making which are imperative to better patient outcomes. In spite of these, majority of elderly patients do not have good knowledge of their medicines and merely dependent on the health care providers to initiate decisions about their medications. Moreover, many patients who have a preference to take fewer medicines do not share their beliefs with providers and waiting for provider initiated medication discontinuation [29]. Thus health professionals should use a

patient centered approach to outweigh the risks and benefits of every medicine against the particular goals of the elderly patient, with the aim of minimizing the total number of prescribed medicines [30-32].

Strengths and Limitations

This is the first study in Ethiopia to assess elderly patients' perception towards deprescribing and their willingness to stop medicines by using validated multidimensional questionnaire in relatively large number of patients. Yet, the results of the current study should be interpreted with caution due to some limitations. It is interviewer based questionnaire structured for quantitative research, which does not permit in-depth investigation of patient attitude. The rPATD questionnaire has not been yet validated in culturally different settings like Ethiopia. This study may suffer from generalizability as the study was done in a single-center university hospital.

Conclusion

Most of older patients (92.1%) were overall satisfied with medications they were taking. However, majority of the participants (81.6%) were still willing to reduce one or more of their medications if advised by their doctor. Therefore, health care providers should be proactive to discuss, evaluate and decision making of potentially in appropriate medications. Further study with potentially large number of study participants and qualitative study is warranted to fully evaluate the deprescribing attitude in different disease categories and prospective significance to Ethiopian elderly patients' health.

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Contributors HGT has contributed to the conception, study design, prepared the study protocol and drafted the manuscript. YGT and DAE performed literature review, carried out statistical analyses, and interpreted the results. FC and YA acquired and managed the data. KTH, TBA, AAA wrote the manuscript and reviewed the manuscript for critical revisions. All authors approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

Ethics approval Ethical committee of School of Pharmacy, University of Gondar

Provenance and peer review not commissioned; externally peer reviewed.

Data sharing statement No additional data are available

Funding Statement Not funded

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	P1,L2 and P2, L4
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2, L1-23
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3,L13-24 and P4,L1- 20
Objectives	3	State specific objectives, including any prespecified hypotheses	P4, L18-20
Methods			
Study design	4	Present key elements of study design early in the paper	P5,L1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5,P2-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	P5, L7-12
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P5,L13-16
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	P5,L18-23 and P6,1-
measurement		comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	P6,L11-14
Study size	10	Explain how the study size was arrived at	P5, L14 and L15
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	P7,L4-6
		(b) Describe any methods used to examine subgroups and interactions	P6,22-23
		(c) Explain how missing data were addressed	NA
		(d) If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P7,L20-22
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P8,L1-5
		(b) Indicate number of participants with missing data for each variable of interest	P8,L7
Outcome data	15*	Report numbers of outcome events or summary measures	P9,L1-10
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 10, Table 2
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P14-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P16, L7-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P16, L7-8
Generalisability	21	Discuss the generalisability (external validity) of the study results	P16, L10-11
Other information		1)/.	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

Abb: NA- Not applicable

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.



BMJ Open

Older patients' perception to deprescribing in resource limited settings: A cross sectional study in an Ethiopia University Hospital.

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Secondary Subject Heading:	Medical management, Patient-centred medicine, Communication, General practice / Family practice
Keywords:	Attitude, medication discontinuation, Deprescribing, Polypharmacy, elderly, rPATD

SCHOLARONE™ Manuscripts Older patients' perception to deprescribing in resource limited settings: A cross sectional study in an Ethiopia University Hospital.

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Abstract

Objectives: To assess older patients' attitude towards deprescribing of inappropriate medications.

Design: This was an institutional-based quantitative cross-sectional survey.

Setting: Outpatient clinics of the University of Gondar referral and teaching hospital (UoGRTH) in Ethiopia.

Participants: Patients aged 65 or older with at least one medication were enrolled in the study from March 1 to June 30, 2017. Excluded patients were those who had severe physical or psychological problems and refused to participate.

Main outcome measures: Older patients' attitude towards deprescribing was measured using a validated instrument, 'the revised Patients' Attitudes towards Deprescribing' (rPATD) tool for older patients. Data were collected on sociodemographic characteristics and clinical data such as co-morbidity and polypharmacy, and the main outcome was older patients' willingness to deprescribing of inappropriate medications.

Results: Of the 351 eligible participants, 316 patients completed the survey. Of the 316 patients, 54.7 % were men and were taking a median of 3 (IQR: 2–4) medications daily. Overall, most of the participants (92.1%; 95% CI: 89%–95%) were satisfied with the medications they were taking; however, still a significant number of participants (81.6%; 95%CI: 77%–86%) were willing to stop one or more of their medications if possible and agreed by their doctor. This willingness was correlated with seven items of the rPATD, including strong correlation with the overall satisfaction of patients with their medication taken.

Conclusion: Many older patients have shown their willingness for a reduction in one or more of their medications if their doctor said it was possible. Health care providers should be proactive to discuss and evaluate potentially inappropriate medications for better clinical decision making.

Key words: Attitude; medication discontinuation; deprescribing; polypharmacy; elderly

Strengths and limitations of this study

- Older patients' attitude towards deprescribing and their willingness to stop medications
 has been assessed for the first time in resource limited setting.
- This study utilized a validated multidimensional questionnaire in a relatively large number of patients.
- The validated tool of rPATD, however, has not been tested in a culturally diverse settings, such as Ethiopia
- Owing to the interviewer based questionnaire structured for quantitative research, it does not permit in-depth investigation of patient attitude.
- Care givers for older patients have not been included in the current study as they may affect on the preference and willingness to stop medications.

Introduction

Polypharmacy often defined as the practice of prescribing five or more medications to the same person, has been linked with pervasive adverse drug events and ultimately leads to increased morbidity, mortality and healthcare costs [1-3]. Polypharmacy-related adverse drug events (ADEs) are very common and estimated to occur in 25% of ambulatory care patients [3]. Deprescribing, one of the approaches to prevent polypharmacy-related ADEs, is defined as the 'the process of withdrawal of inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes' [4]. Given the holistic and patient-centered nature of deprescribing, it has a number of benefits to the patient. A recent systematic review conducted by Page et al. reported that individualized deprescribing interventions to reduce inappropriate polypharmacy may improve mortality [5]. Deprescribingalso has potentially additional benefits to the patient such as increasing patient

engagement in medication therapy management and improving adherence possibly through reducing polypharmacy [6].

The impact of deprescribing is conceivably beneficial for older patients living in resource limited countries such as Ethiopia, where the incidence of chronic non-communicable diseases and multimorbidity is mounting in alarming rate [7]. The burden of chronic diseases alongside with Ethiopian patients' out of pocket expenses and affordability for drug purchases particularly from private drug retail outlets is challenging for most patients. [8]

While concepts such as adherence and medication reconciliation received considerable attention, and covered by a wide range of literatures worldwide, little attention has been given to the concept of deprescribing and reduction of inappropriate polypharmacy [9]. Despite the prescribers' positive attitude on deprescribing [10], many factors including clinical uncertainty and shared responsibility with other healthcare providers severely impede clinicians' ability to proactively discontinue medications [11]. Moreover, patient perspectives on deprescribing and their communication with clinicians are equally important in evidence based medication discontinuation process. Several studies conducted in developed countries regarding older peoples' attitudes toward deprescribing reported a higher rate of willingness to discontinue their medications [12-16]. However, no previous study has explored the attitudes of Ethiopian older patients regarding their medications and deprescribing. It is also uncertain how patients would respond to a suggestion from a clinician to intentionally discontinue a medication. Taking the global evidence into consideration and due to lack of data in Ethiopia, we sought to identify Ethiopian older patients' willingness to have their medications deprescribed.

Methods

Study design and setting

Institutional-based quantitative cross-sectional survey was conducted from March 1 to June 30, 2017 at the University of Gondar referral and teaching hospital (UoGRTH), Ethiopia. The hospital is located in Gondar town, northwest Ethiopia, 738km away from Addis Ababa and it's the only referral and teaching center in the area where majority of patients with chronic diseases including hypertension, diabetes mellitus, cancer and asthma are referred.

Participants

All older patients (≥ 65 years) who had been taking at least one medication regardless of their diagnosis and who visited the outpatient clinic of the University of Gondar referral and teaching hospital (UoGRTH) for follow-up as well as medication refill were included. Patients who had severe physical or psychological problems and those who refused to participate were excluded from the survey. Of 351 eligible participants obtained during the study period, 316 older adult patients completed the survey data.

Main outcome measures: Older patients' attitude towards deprescribing was measured using the validated tool of revised the Patients' Attitudes towards Deprescribing (rPATD) for older patients. Predictive variables were Sociodemographic and clinical data such as comorbidity and polypharmacy. The main outcome of interest was older patients' willingness to deprescribing of their medications.

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Survey instrument

We used the revised patients' attitudes towards deprescribing (rPATD) questionnaire [17]. It is a validated multidimensional questionnaire which measure patients' attitudes, knowledge and experiences related to medication discontinuation. The original a 5-point Likert scale in rPATD questionnaire, was changed to a 4-point Likert scale (strongly agree, agree, disagree and strongly disagree) in the current study as it may allow the participants to be more discriminating and avoid misinterpretation of mid points. The rPATD questionnaire has four major factors including Burden factor (5 items); Appropriateness factor (5 items); Concerns about stopping factor (5 items); Involvement factor (5 items) and additional two global questions are also considered. The previously validated tool -Belief in Medicine use Questionnaire (BMQ)-Overuse [18] was utilized for comparison and validation of the rPATD questionnaire. The questionnaire, first prepared in English, was translated into Amharic language and back to English so as to ensure that the translated version gave the proper meaning. It was further pre-tested on 25 elderly patients, who were not included in the final analysis, and slight modifications were instituted before the commencement of the final survey. Polypharmacy was defined as the use of >5 regular medications.

Data were collected by three of the principal investigators through interviewer-administered questionnaire. Due to low literacy level of the participants in our study setting, we were forced to interview most of the patients rather than self administration to clarify the questions. The investigators were properly trained on the instrument and ways of approaching the patients and securing their permission for interview prior to the data collection process. This training was conducted in the actual place of study setting to see if the investigators could manage data

collection efficiently with adequate background knowledge about the study; working independently; and good communication skills.

Patient and Public Involvement statement

Research questions have been identified during medication review and provision of counseling to older patients while in efforts to get older patients involved in decision making process. Moreover, the local advocacy group so called Young professionals chronic disease network (YP-CDN) Ethiopia chapter has worked with older patients living with chronic diseases and identified their priorities for advocacy and used as an input for this research project.

Patients were involved in the design of this study by identifying the research question; and identifying the need for preliminary study. However, they were not involved in the recruitment and conduct of the study.

The study results will be disseminated both to the study participants and to the wider public using easy and accessible formats with understandable language by the public during health care provision and health education program. The Authors will communicate the findings through national and international conferences. It will also be posted in an international advocacy websites such as YP-CDN website.

Statistical analysis

All the statistical analyses were done using Statistical Package for Social Sciences (SPSS) software version 21.0 for Windows (SPSS Inc., Chicago, IL) [19]. Data were summarized as frequencies and percentages.. Data were screened for normality using both the Shapiro–Wilk and Kolmogorov-Smirnov tests. Respondents were stratified by polypharmacy status to examine patients' attitude towards deprescribing..

Correlation analysis using Spearman's Rho was used to assess the associations between all rPATD items and three individual questions: patients' perception of side effect from their medications, patients' willingness to discontinue their medications if the doctor said possible, and overall satisfaction of patients with their medication taken. Binary logistic regression was performed after dichotomizing the two item questions (willingness to deprescribe one or more of their regular medications if the doctor said it was possible and overall satisfaction with their prescribed medications) by grouping the 4 Likert responses to "strongly agree and agree" versus "strongly disagree and disagree" as shown in supplementary table.

Ethical Consideration

This study was approved by the Ethical committee of School of Pharmacy, University of Gondar with an approval number of UoG-SoP-131/2017. Written informed consent from the respondents was also obtained before conducting this study. Participants' information obtained was kept confidential.

Results

A total of 351 patients were approached; of whom, 316 completed the questionnaire (response rate, 90%). The median age of the participants was 70 years (IQR: 67-75). The median number of their daily medications was 3 (IQR: 2-4). From the total number of participants, 62 (19.7%) were on polypharmacy. The commonest reason for hospital visits both in the polypharmacy and non-polypharmacy groups were hypertension and diabetes mellitus (DM). A detail of sociodemographic characteristics of the study participants is tabulated in Table 1.

Table 1: Sociodemographic and clinical characteristics of study participants, (n = 316).

Variable	Participants, N	Polypharmacy N (%)		
	(%)	Yes (N=62)	No (N=254)	
Gender			·	
Male	173(54.7)	35 (56.45)	138 (54.55)	
Female	143 (45.3)	27 (43.55)	116 (45.45)	
Age(median; Interquartile range(IQR))	70(67-75)	70(67-73)	70(67-75)	
Educational status				
Unable to read and to write	202 (64)	37 (59.68)	165 (65.2)	
Primary school	62 (19.6)	13 (20.97)	49 (19.37)	
Secondary School	32 (10.1)	5 (8.06)	26 (10.28)	
Higher education	20 (6.3)	7 (11.29)	13 (5.14)	
Reason of hospital visit(N=315)				
Hypertension	128(40.5)	20(32.3)	108 (42.5)	
Heart failure	23(7.3)	8(1.3)	15 (5.9)	
Diabetes Mellitus	105(33.2)	22(35.5)	83 (32.7)	
Chronic kidney disease	14(4.4)	1(1.6)	13 (5.1)	
Asthma	8 (2.5)	2(3.2)	6 (2.4)	
Rheumatoid Heart Disease	10(3.2)	4(6.5)	6 (2.4)	
Others	27(8.6) ^a	5(8.1)	22 (9.1) a	
Charlson Comorbidity index	2(1-2)	2(2-3)	2(1-2)	
a(median;IQR) (N=315)				
Number of Medication (median;IQR)	3(2-4)	5(5-6)	3(2-3)	

Note: adata was missing for one participant

As reported in table 2, a total of 316 participants responded to 22 rPATD questions. In a burden factor domain, a total of 214 older patients (67.7%; 95%CI: 63%–73%) taught that they spent a lot of money for purchasing their medications, yet, there had been a considerable percentage of participants (61.5%) that did not feel their medications were a burden to them. Appropriateness factor domain showed that close to 90% of the participants thought that one or more of their medications may not be working if stopped taking, and this was further confirmed from their intention to stop their medications; only 9.4% had tried stopping medications in order to see how they felt without taking medications. ..Concerns about stopping factor; most of the respondents (89.2%; 95% CI: 86%-93%) were worried about missing out the future benefits if one of their medications had been stopped. In the involvement factor, majority of the respondents [257]

participants; 81.3%;95% CI: (77%-86%)] asked their doctor, pharmacist or other health care professional if there was any miss-understanding about their medications. If the doctor said it was possible, about 258 individuals (81.6%; 95%CI: 77%-86%) were willing to stop one or more of their regular medications although a significant number of participants were overall satisfied with medications they were taking (92.1%; 95% CI: 89%-95%) (Table 2).

Patients' perception of side effect from their medications was positively associated with the thirteen items but negatively with the three items. Those patients who thought their medications are a burden to them were more likely perceived side effects from one or more medications. There had been a lack of an overall satisfaction with the medications patients were taking if they perceived side effects from one or more of their medications (Table 3).

The patients' willingness to discontinue their medications if their doctor said it was possible was correlated with seven items of the rPATD. Of the three items positively associated with this question, patients are willing to stop one or more of their medications if they were told to do by their doctor even though they may be worried about missing out the future benefits while stopping one of their medications. In the contrary, four of the items were negatively correlated with willingness to discontinue their medications if the doctor said it was possible such as belief that participants were taking too many medications, were perceiving side effects from one or more of their medications, were reluctant to stop a medication taken for a long time, and perceived their doctor giving up on them if their doctor recommended stopping a medicine. The overall satisfaction of patients with their medication taken was correlated with many items of the rPATD questionnaire as described in detail in Table 3.

Table 2:Patients' attitudes towards deprescribing based on the rPATD questionnaire (n = 316).

Sui	rvey questions	Strongly disagree	Disagree	Agree	Strongly agree	Strongly agree/ Agree % (95% CI)
Ru	rden Factor					(CI)
B1	I spent a lot of money on my medicines	87(27)	15(4.7)	84(26.6)	130(41.1)	67.7% (63-73)
B2	Taking my medicines every day is very inconvenient	104(32.9)	92(29.1)	107(33.9)	13(4.1)	38% (32.6-43.4)
В3	I feel that I am taking a large number of	88(27.8)	68(21.5)	135(42.7)	25(7.9)	50.6% (45-56)
D 4	medicine	111(2(1)	00(05.4)	110(210)	12(2.0)	20.60/.(22.44)
B4	I feel that my medicines are a burden to me	114(36.1)	80(25.4)	110(34.8)	12(3.8)	38.6% (33-44)
В5	Sometimes I think I take too many medicines	134(42.4)	69(21.8)	105(33.2)	8(2.5)	35.7% (30-41)
Ap	propriateness Factor	1	.	•	•	1
A1	I feel that I may be taking one or medicines that I no longer need	144(45.6)	65(20.6)	95(30.1)	12(3.8)	33.9% (29-39)
A2	I would like to try stoppingone of my medicines to see how I feel without it	257(81.3)	29(9.2)	21(6.6)	9(2.8)	9.4% (6-13)
A3	I would like my doctor to reduce the dose of one or more my medicines	133(42.1)	49(15.5)	104(32.9)	30(9.5)	42.4% (37-48)
A4	I think one or more of my medicines may not be working	7(2.2)	24(7.6)	281(88.9)	4(1.3)	90.2% (87-93)
A5	I believe one or more of my medicines may be currently giving me side effects	114(36.1)	70(22.2)	121(38.3)	11(3.5)	41.8% (36-47)
Co	ncerns about stopping factor		4)	ı	<u> </u>	l
C1	I would be reluctant to stop a medicine that I had been taking for a long time	109(34.5)	119(37.7)	65(20.6)	23(7.3)	27.9% (23-33)
C2	If one of my medicines was stopped I would be worried about missing out on future benefits	9(2.8)	25(7.9)	122(38.6)	160(50.6)	89.2% (86-93)
C3	I get stressed whenever changes are made to my medicines	87(27.5)	81(25.6)	132(41.8)	16(5.1)	46.9% (41-52)
C4	If my doctor recommended stopping a medicine I would feel that he/she was giving up on me	146(46.2)	82(25.9)	63(19.9)	25(7.9)	27.8% (23-33)
C5	I have a bad experience when stopping a medicine before	186(58.9)	47(14.9)	45(14.2)	38(12.0)	26.5% (21-31)
Inv	olvement Factor				1	ı
I1	I have a good understanding of the reasons I was prescribed each of my medicines	59(18.7)	44(13.9)	168(53.2)	45(14.2)	67.4% (62-73)
I2	I know exactly what medicines I am currently taking, and/or I keep an up to date list of my medicines	114(36.1)	126(39.9)	65(20.6)	11(3.5)	24.1% (19-29)

I3	I like to know as much as possible about	71(22.5)	54(17.1)	162(51.3)	29(9.2)	60.5% (55-66)
	my medicines					
I4	I like to be involved in making decisions	32(10.1)	93(29.4)	165(52.2)	26(8.2)	60.4% (55-66)
	about my medicines with my doctors		,	, ,	, ,	, ,
I5	I always ask my doctor, pharmacist or	19(6.0)	40(12.7)	161(50.9)	96(30.4)	81.3% (77-86)
	other health care professional if there is					
	something I don't understand about my					
	medicines					
Ge	neral Questions					
G1	If my doctor said it was possible I would	22(7.0)	36(11.4)	74(23.4)	184(58.2)	81.6% (77-86)
	be willing to stop one or more of my					·
	regular medicines					
G2	Overall, I am satisfied with my current	9(2.8)	16(5.1)	120(38.0)	171(54.1)	92.1% (89-95)
	medicines	, ,	, ,	,	, ,	` ,

Adopted from the revised Patients' Attitudes Towards Deprescribing (rPATD) Questionnaire (17)

Table 3. Spearman Correlation of responses within the rPATD questionnaire

rPATD questions	10.I believe one or more of my	21. If my doctor said it	22.Overall. I	am
Spearman Correlation	medicines may be currently	was possible I would be	-	my
(p-value)	giving me side effects	willing to stop one or		1113
		more of my regular		
		medicines		
Burden Factor		medicines		
1. I spend a lot of money on my medicines	0.03,0.63	0.14, 0.06	0.16, 0.00	
2. Taking my medicines every day is very inconvenient	0.24,0.00	-0.07, 0.19	-0.28,0.00	
3.I feel that I am taking a large number of medicine	0.15,0.01	-0.096,0.09	-0.35, 0.00	
4.I feel that my medicines are a burden to me	0.31,0.00	-0.08, 0.17	-0.35,0.00	
5. Sometimes I think I take too many medicines	0.25,0.00	-0.22, 0.00	-0.53,0.00	
Appropriateness Factor				
6.I feel that I may be taking one or medicines that I no	0.25,0.00	-0.09, 0.13	-0.38,0.00	
longer need				
7. I would like to try stoppingone of my	0.06,0.32	-0.04, 0.48	-0.1,0.42	
medicines to see how I feel without it	10,			
8.I would like my doctor to reduce the dose of one or	0.14,0.02	0.04,0.4	-0.25,0.001	
more my medicines				
9.I think one or more of my medicines may not be	-0.11,0.04	0.01,0.8	0.14,0.009	
working	1	0.140.00	0.21.0.00	
10.I believe one or more of my medicines may be	1	-0.14,0.08	-0.31,0.00	
currently giving me side effects		<u> </u>		
Concerns about stopping factor 11.I would be reluctant to stop a medicine that I	0.19,0.001	-0.3,0.00	-0.26,0.001	
had been taking for a long time	0.19,0.001	-0.3,0.00	-0.20,0.001	
	-0.20,0.00	0.26.0.00	0.55,0.00	
12.If one of my medicines was stopped I would	-0.20,0.00	0.26,0.00	0.55,0.00	
be worried about missing out on future benefits	0.27.0.00	0.07.0.10	0.17.0.003	
13.I get stressed whenever changes are made to	0.27,0.00	-0.07,0.19	-0.17,0.002	
my medicines	0.42.0.02	0.27.000	0.24.0.00	
14.If my doctor recommended stopping a	0.12,0.03	-0.37, 0.00	-0.34,0.00	
medicine I would feel that he/she was giving up				
on me				
15.I have a bad experience when stopping a	0.19,0.001	-0.07,0.22	-0.18,0.027	

nedicine before			
nvolvement Factor			
6.I have a good understanding of the reasons I	0.14,0.01	0.04,0.53	0.02,0.74
was prescribed each of my medicines		,	, , , , , , , , , , , , , , , , , , , ,
7.I know exactly what medicines I am currently	0.12,0.03	-0.02,0.71	-0.001,0.98
aking, and/or I keep an up to date list of my	,	,	,
medicines			
8.I like to know as much as possible about my	0.18, 0.001	-0.08,0.14	-0.11,0.175
medicines	,	,	,
9.I like to be involved in making decisions about	-0.01,0.79	-0.01,0.81	0.065,0.45
my medicines with my doctors	•		·
20.I always ask my doctor, pharmacist or other	0.05,0.36	0.13, 0.02	0.18,0.032
nealth care professional if there is something I			
lon't understand about my medicines			
General Questions			
21.If my doctor said it was possible I would be	-0.14,0.08	1	0.34,0.00
willing to stop one or more of my regular	' (2)		
nedicines			
22. Overall, I am satisfied with my current	-0.31,0.00	0.34, 0.00	1
nedicines			

Discussion

Older adult patients are prone to multi-morbidity with high medication regimens complexity needing stopping of medications, a growing concept so called deprescribing [13]. Elderly patients receiving many medications with their underlined medical illness are vulnerable to rehospitalization, drug induced complications and morbidity. Moreover, polypharmacy compromises patient adherence and lead to incur additional costs to manage unnecessary adverse outcomes [20-25]. Hence, mutual agreement between patients and clinical practitioners should be sought to optimize the elderly 'patients' medication regimen keeping with few numbers of medications [26]. To our knowledge, this is a first study to have been conducted on this study area in resource limited settings like Ethiopia.

In the current study, the median number of their daily medications (3) was very low as compared to other studies such as the mean of Kalogianis et al. study [12] was 14.6, while the median was 6 and 11 in Sirois et al [16] and Reeve et al study [13], respectively. In spite of having low median number of medications in the current study, majority (81.6%) of the patients agreed to stop one of the medicines if their doctor said it was possible. This is also consistent with previous studies conducted by Mona et al [12], Alessandro et al [27] and Reeve et al having 80%, 89% and 92% of patients' willingness rate to stop their medicines if informed to do by their doctor, respectively. This previews the importance of proactive engagement of health care professionals in deprescribing process for older adult patients and should discuss with their patients on how to optimize and simplify the dosage regimens. A small percentage (9.4%) of older patients would like to try stopping one of their medications to see how they feel without it and most of the respondents (89.2%) would be worried about missing out on future benefits if one of their medications was stopped. In this regard, older patients' hesitation to stop one of their

medications might be reasonable, but it might also a potential barrier to discontinuation of inappropriate medication. The suitability of deprescribing process of a particular medicine in variety of populations should be decided by the integrated approach of patients, caregivers, other health care providers based on the benefits and potential harms [28, 29].

Two third of patients believe that they spent a lot of money to medicines. Even though in current study this variable was not correlated with the patients' willingness to stop one or more of the medicines if the doctor said it was possible, medications costs might contribute to the patients' positive attitude to deprescribing in resource limited setting. Other study has reported that patients having to pay less for their medications would influence their willingness to have medications deprescribed and paying more encourage deprescribing [12]. It is always important to consider cost implications in therapeutic decision making and drug selection in elderly patients as those patients are prone to prolonged care, polypharmacy and less productivity to handle their therapeutic expenses [30].

This study has showed the association between each item and the selected three questions of the survey items like perceiving of side effects from one or more of medicines taken, willingness to stop one or more of medicines if the doctor said it was possible, and overall satisfaction with their current medications. Patients didn't have overall satisfaction with their medications if they perceive side effect from one or more of the medications. In the current study, "Patients' willingness to stop one or more of medications if advised by doctor" were negatively correlated with others item questions such as "Sometimes I think I take too many medicines", "perceiving of side effects from one or more of their medications" and "being reluctant to stop a medicine taken for a long time. However, it was positively associated with "overall satisfaction with their medications" which in other words, patients were willing to stop one or more of medications if

the doctor said, it was possible, even if they had overall satisfaction with their medications. Other studies also reported that patient willingness to stop medication was correlated with a desire to take few medicines and the feeling of taking a large number of medications and being less comfortable with current medications [13, 15, 16].

Majority of the respondents ask their doctor, pharmacist or other health care professional if there is any miss-understanding about their medications. This imply older adults curiosity to know about their medicines, ask their healthcare provider and involve in the clinical decision making process. This is very important to patient—provider relationships, encircling on the sub-themes of trust, relying on expertise and shared decision making which are imperative to better patient outcomes. In spite of these, majority of older adult participants do not have good knowledge of their medicines and merely dependent on the health care providers to initiate decisions about their medications. Moreover, many patients who have a preference to take fewer medicines do not share their beliefs with providers and waiting for provider initiated medication discontinuation [31]. Thus health professionals should use a patient centered approach to outweigh the risks and benefits of every medicine against the particular goals of the elderly patient, with the aim of minimizing the total number of prescribed medicines [32-34].

Strengths and Limitations

This is the first study in Ethiopia to assess older adults' perception towards deprescribing and their willingness to stop medicines by using validated multidimensional questionnaire in relatively large number of patients. Yet, the results of the current study should be interpreted with caution due to some limitations. It is interviewer based questionnaire structured for quantitative research, which does not permit in-depth investigation of patient attitude. The rPATD questionnaire has not been yet validated in culturally different settings like

Ethiopia. This study may suffer from generalizability as the study was done in a single-center university hospital.

Conclusion

Most of older patients (92.1%) were overall satisfied with medications they were taking. However, majority of the participants (81.6%) were willing to reduce one or more of their medications if their doctor said it was possible. Therefore, health care providers should be proactive to discuss, evaluate and decision making of potentially in appropriate medications. Further study with potentially large number of study participants and qualitative study is warranted to fully evaluate the deprescribing attitude in different disease categories and prospective significance to Ethiopian older adults' health.

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Contributors HGT has contributed to the conception, study design, prepared the study protocol and drafted the manuscript. YGT and DAE performed literature review, carried out statistical analyses, and interpreted the results. FC and YA acquired and managed the data. KTH, TBA, AAA wrote the manuscript and reviewed the manuscript for critical revisions. All authors approved the final manuscript.

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Supplementary material

Binary logistic regression was performed after dichotomizing the two item questions (willingness to deprescribe one or more of their regular medications if the doctor said it was possible and overall satisfaction with their prescribed medications) by grouping the 4 Likert responses to "strongly agree and agree" versus "strongly disagree and disagree".

However, in Univariate analysis, Sociodemographic and clinical variables like Age, sex, Education, charlson comorbidity index (CCI) and reason of hospital visit (chief complaint) didn't fit final model according to the Hosmer-Lemeshow assumption owing to having p >0.2. The level of statistical significance was defined as p<0.05 and all tests were two-tailed as shown in the table below.

<u>Supplementary Table:</u> Univariate analysis of Sociodemographic and clinical variables with the two item questions

Variables	21.Willingness	to stop one or	22. Overall satisfa	ction with the
	more of regular	medicines if the	current medication	ns (agreed/strongly
	doctor said it wa	as possible	agreed)	
	(agreed/strongly	agreed)	7_	
	COR (95%	P-Value	COR (95% CI)	P-Value
	CI)			
Age	1.02(0.98-1.06)	0.37	0.89(0.93-1.04)	0.60
Sex (male)	0.94(0.53-1.66)	0.83	1.26(0.55-2.9)	0.58
Education	-	0.59	-	0.35
Unable to read and write	1.39(0.48-4.06)	0.54	1.76(0.36-8.5)	0.48
Primary school	2.25(0.64-7.89)	0.20	0.75(0.15-3.86)	0.73
Secondary school	1.44(0.37-5.5)	0.59	1.07(0.16-7.06)	0.94
Higher education	1	-	1	-
Reason of admission	-	0.96	-	0.92
CCI	0.85(0.63-1.15)	0.37	0.82(0.54-1.25)	0.35

Abbreviation: CCI: Charlson Comorbidity Index, CI: Confidence Interval, COR: Crude Odds Ratio

Note: None of the variables fits the final model (P>0.2)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	P1,L2 and P2, L4
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2, L1-23
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	P3,L13-24 and P4,L1- 20
Objectives	3	State specific objectives, including any prespecified hypotheses	P4, L18-20
Methods			
Study design	4	Present key elements of study design early in the paper	P5,L1
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	P5,P2-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	P5, L7-12
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	P5,L13-16
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	P5,L18-23 and P6,1-
measurement		comparability of assessment methods if there is more than one group	11
Bias	9	Describe any efforts to address potential sources of bias	P6,L11-14
Study size	10	Explain how the study size was arrived at	P5, L14 and L15
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	NA
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	P7,L4-6
		(b) Describe any methods used to examine subgroups and interactions	P6,22-23
		(c) Explain how missing data were addressed	NA
		(d) If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	P7,L20-22
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P8,L1-5
		(b) Indicate number of participants with missing data for each variable of interest	P8,L7
Outcome data	15*	Report numbers of outcome events or summary measures	P9,L1-10
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 10, Table 2
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	P14-16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	P16, L7-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	P16, L7-8
Generalisability	21	Discuss the generalisability (external validity) of the study results	P16, L10-11
Other information		1)/.	
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	NA

Abb: NA- Not applicable

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

