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Original Article

Cognitive Screening within Advanced Pharmaceutical Care in Elderly Patients with Suspected Metabolic Syndrome

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SUMMARY

Background: Cognitive screening by pharmacists may help to identify seniors with metabolic syndrome (MetS)-related cognitive impairment. We aimed to evaluate the implementation of an easy-to-use cognitive screening into the pharmaceutical care of seniors and to test whether cognitive decline is associated with suspected MetS (sMetS).
Methods: Questionnaires were completed by 323 randomly selected elderly patients receiving pharmaceutical care in community pharmacies or in senior care centres in Slovakia. The presence of sMetS was estimated according to criteria of the International Diabetes Federation. Cognitive performance was evaluated by the Montreal Cognitive Assessment (MoCA) test and its short form (s-MoCA). In these tests, the cut-offs for impaired cognitive status were ≤ 24, and ≤ 12, respectively.
Results: 56% of participants scored below the screening cut-off MoCA threshold. Cognitive impairment was significantly more frequent in sMetS+ subjects (71%) vs. sMetS- (52%; $p < 0.05$). MoCA scores were significantly lower in sMetS+ (mean $\pm$ SD = 20.0 $\pm$ 5.9 points) vs. sMetS- (22.2 $\pm$ 5.4 points; $p < 0.05$). sMetS components type 2 diabetes mellitus, hypertension and obesity, but not dyslipidaemia, had an influence on lower cognitive performance.
Conclusions: We unveiled a significant relationship of cognitive dysfunction to sMetS in elderly patients. A quick and simple cognitive assessment could be a helpful extension of pharmaceutical care.

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1. Introduction

A pharmacist in a community pharmacy is the most accessible public healthcare provider which provides clinical screening e.g. for cardiovascular diseases and diabetes mellitus (DM),[1] identification of inappropriate medication use in the elderly,[2] patient pharmacotherapy and food supplement counselling, life-style change management and education on medications.[1] Effectiveness of pharmaceutical counselling, such as reducing the number and improving the appropriateness of medicines was demonstrated.[3] In addition, pharmacists can detect early cognitive impairment in elderly patients during medication reviews and refer risk patients to further medical care.[4,5] Consequently, patients' satisfaction with community pharmacy services had a positive impact on their health,[1] clinical outcomes and therapeutic aims[1,6] Community pharmacist-provided cognition assessment could be an effective and valuable pharmaceutical service and can be easily integrated into pharmacy care for early identification of patients with a cognitive disease risk.[6] Whether a pharmacist might contribute universally to the identification of cognitive impairment remains unclear.

Metabolic syndrome (MetS) is a cardiometabolic disorder cluster, including central obesity, glucose intolerance, hypertension, hypertriglyceridemia, decreased high-density lipoprotein cholesterol, a proinflammatory and prothrombotic state.[7] The prevalence of MetS increases with age and is related to a worsenened overall health status.[8,9] The prevalence of mild cognitive impairment is inversely related to the cognitive test score with an increasing number of MetS components.[10] MetS is associated with impaired alternating attention, processing speed, language, executive functions, working and episodic memory.[11]

Early management of MetS and its components may also help control cognitive decline and identify high-risk individuals for mild cognitive impairment earlier.[10] The components of metabolic syndrome are well determinable in a community pharmacy by routine counselling, although this estimation of MetS may be discrepant from the proper diagnostic procedure at a medical examination. Whether such suspected MetS (sMetS) is related to MetS-related complications remains unclear. Using the universally accepted screening measure, the MoCA and its short variant s-MoCA, we evaluated the implementation of this simple, easy to use cognitive screening into the pharmaceutical care of senior patients (over 60 years of

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age) having suspected MetS (sMetS).

2. Material and methods

2.1. Study participants

Randomly selected age 60+ years old patients receiving pharmaceutical care who were able to complete the questionnaires and provided voluntary consent were included in this randomised pilot study. The data were collected from February 2018 to February 2019 in 16 community pharmacies and 3 senior care centres in Slovakia. 323 participants were enrolled (68% females, 32% males), 222 of whom were from community pharmacies (mean age ± SD: 69 ± 6.34 and 101 from senior care centres (mean age ± SD: 81 ± 7.98). The mean age of all participants was 72.9 ± 8.98 years, and the established inclusion criteria were age 60+, visitor of community pharmacy or resident of care centre for seniors at the time of the study. Exclusion criteria were physical and/or mental disability. Figure 1 describes the selection. 16 pharmacists with the relevant training in the MoCA screening tool presented the questionnaires to participants. We analysed age, gender, presence of central obesity, education level, relation to physical activity, relation to smoking and pharmacotherapy. Table 1 lists the basic characteristics of the cohort.

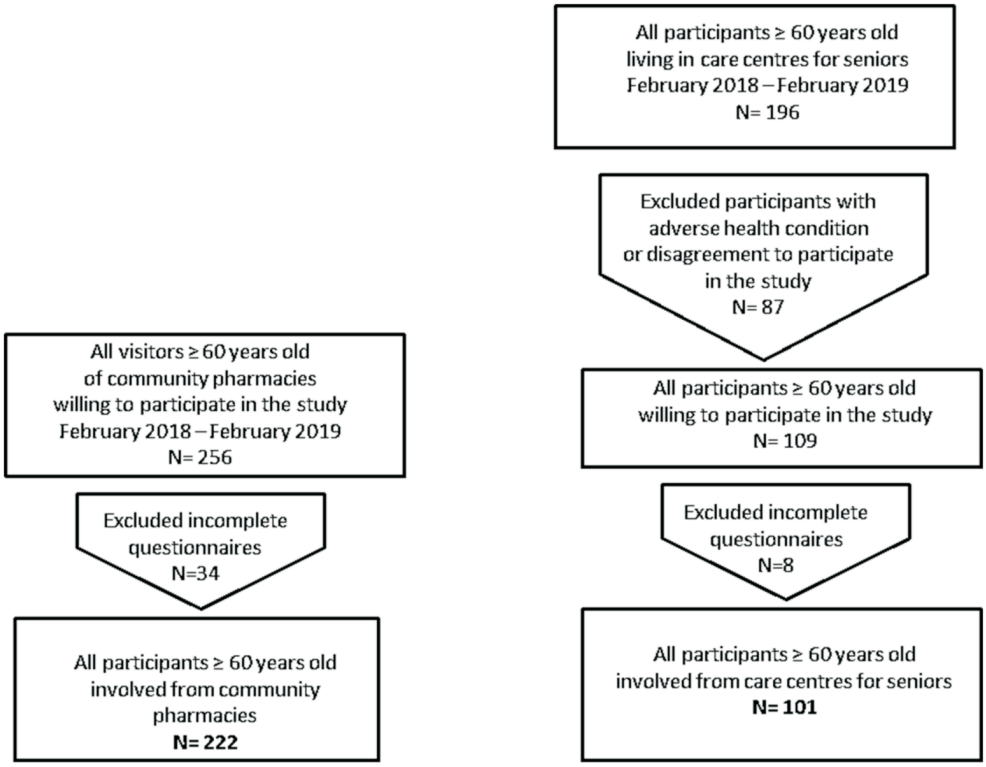

Figure 1. Study flow chart showing the population selection.

Table 1
Basic characteristics of the cohort.

Characteristics	All participants		Community pharmacies		Senior care centres	
	N (%)	Mean ± SD	N (%)	Mean ± SD	N (%)	Mean ± SD
Age groups						
All	323 (100)	72.9 ± 9.0	222 (69)	69.0 ± 6.3	101 (31)	81.0 ± 8.0
60–74	205 (63)	67.1 ± 4.0	183 (82)	66.8 ± 3.9	22 (22)	69.1 ± 4.0
75–84	71 (22)	79.3 ± 3.1	34 (15)	78.2 ± 2.9	37 (36)	80.2 ± 2.9
≥ 85	47 (15)	88.3 ± 2.5	5 (3)	87.2 ± 1.1	42 (42)	88.4 ± 2.7
Gender						
Women	219 (68)		141 (64)		78 (77)	
Men	104 (32)		81 (37)		23 (23)	
Duration of education						
All	323 (100)	12.2 ± 2.2	222 (100)	12.2 ± 2.2	101 (100)	12.2 ± 2.2
≤ 12 years	279 (86)	11.4 ± 1.2	192 (87)	11.4 ± 1.2	87 (86)	11.4 ± 1.2
> 12 years	44 (14)	17.0 ± 0.0	30 (13)	17.0 ± 0.0	14 (14)	17.0 ± 0.0
Smoking						
Current smokers	37 (11)		32 (14)		5 (5)	
Non-smokers	286 (89)		190 (85)		96 (95)	
Regular physical activity						
Yes	164 (51)		132 (59)		32 (32)	
No	159 (49)		83 (37)		69 (68)	

N, number of subjects; SD, standard deviation.

2.2. Ethics approval

The study was approved by the Ethics Committee of Faculty of Pharmacy, Comenius University in Bratislava (EK FaF UK 01/2018). All procedures were performed in accordance with the relevant guidelines and regulations and in accordance with the Declaration of Helsinki.

2.3. Study procedures

2.3.1. Assessment of suspected MetS (sMetS)

The presence of sMetS was estimated according to the International Diabetes Federation Worldwide Definition of MetS, 2005 modified for European population.[7] Accordingly, patients were grouped according to the presence (sMetS+) or absence of suspected MetS (sMetS-).

2.3.2. Cognitive screening

We used the Slovak version of the Montreal Cognitive Assessment (MoCA)[12] with a reduced cut-off of ≤ 24 points for cognitive impairment by Bartoš and Fayette.[13] This is a highly reliable and used tool to identify early cognitive impairment.[12] We also evaluated the short form of the MoCA (s-MoCA), calculated from the full version data, being a validated reduced version of the MoCA.[14] Finally, we compared the full and the short form of the MoCA. According to standard procedure, the MoCA test scale range was 0–30 points, with a time of completion of 15 minutes and the cut-off ≤ 24 points representing cognitive impairment. The short form of the MoCA scale range was 0–16 points; time of completion was reduced to 5 minutes and a cut-off of ≤ 12 representing cognitive impairment.[12–14]

2.4. Statistical analysis

Data were analysed using the SAS Education Analytical Suite for Microsoft Windows, version 9.3 (copyright © 2012 SAS Institute Inc., Cary, NC, USA). Continuous demographic and clinical variables (e.g. age, the MoCA and the s-MoCA score) of the study group were represented by simple arithmetic mean, standard deviation, or the 95% confidence interval. Categorical descriptive variables (e.g. gender, central obesity, dyslipidaemia, hypertension, type 2 DM, the MoCA status) were characterised by absolute frequencies and percentages. When comparing two groups with continuous data, a two-sample t-test was used. The pairwise linear least squares method was used to compare the MoCA and s-MoCA scores, followed by the model significance test with the ANOVA method, and consequently, the significance test of the contrast and slope of the linear model was applied. Pearson's Chi-Squared test and the Fisher exact test of cross-tabulated data were performed to analyse the association between the frequencies of the categorical variables.

The 0.05 significance level was used as a statistical significance threshold, and 0.8 was the minimally acceptable power of tests.

3. Results

3.1. Occurrence of sMetS in the study cohort

sMetS was identified in 22% of subjects (in 70 of 323 subjects), its prevalence was not different with increasing respondent age. Participants in senior care centres had a higher sMetS occurrence (28%) compared to patients tested in pharmacies (19%; $p < 0.05$).

Central obesity prevalence, as a basic component of the sMetS, was 64% (Table 2). The majority of respondents (73%) were hypertensive, 27% of patients had dyslipidemia and 16% had abnormal glycaemia and/or DM. Co-incidence of two MetS components was present in 38% of cases, while 11% of subjects were free of any sMetS component (Table 3).

3.2. Lower MoCA scores in sMetS

Fifty-six percent of subjects achieved lower scores than the normal cognitive performance cut-off in the MoCA cognitive test. Subjects with sMetS achieved lower scores on the MoCA test (mean ± SD: 20.03 ± 5.94 points) as compared to the sMetS- (mean ± SD: 22.18 ± 5.43 points; $p < 0.05$; Figure 2). Moreover, in the MetS+ group we found the same significantly lower score on the s-MoCA test (-1.05 points vs. MetS-; $p < 0.05$). Accordingly, cognitive impairment was identified in 71% of sMetS+ vs. 52% of sMetS- respondents. In both groups, the achieved MoCA score decreased with increasing respondent age (sMetS+: $r^2 = -0.351$; $p < 0.05$; sMetS-: $r^2 = -0.254$; $p < 0.05$). Gender influence analysis showed that women achieved lower MoCA scores (mean ± SD: 21.11 ± 5.98 points) when compared to men (mean ± SD: 22.97 ± 4.51; $p < 0.05$).

To identify the dominant contributing component, we analysed the relationship between individual sMetS components and the MoCA score (Table 2). Treated type 2 DM patients exhibited lower cognitive performance on the MoCA test (-2.22 points in mean) compared to participants without type 2 DM ($p < 0.05$). Similarly, treated hypertensive patients also had a lower MoCA score (also by -2.22 points vs respondents without hypertension; $p < 0.05$). Interestingly,

Table 2
Occurrence of sMetS and its components having influence on MoCA score.

Abnormality	N (%)	Mean MoCA score (SD)	Difference[a]	OR[b]	*p* value[c]
sMetS	70 (22)	20.03 (5.94)	-2.15	2.27	0.0044
Central obesity	208 (64)	21.24 (5.39)	-1.34	1.54	0.0397
Hypertension	236 (73)	21.11 (5.77)	-2.22	2.27	0.0015
Dyslipidaemias	88 (27)	21.32 (5.56)	-0.54	1.61	0.4405
Type 2 DM	51 (16)	19.84 (6.66)	-2.22	1.52	0.0093

[a] The difference between mean MoCA scores of subjects with presence of abnormality vs. those with its absence.
[b] The odds ratio (OR) quantifies the risk of MoCA score decline (being ≤ 24) in presence of sMetS or its particular component as compared to their absence.
[c] The significance of differences between MoCA scores of group with sMetS or its components compared to group of patients free of any sMetS component.
DM, diabetes mellitus; MoCA, Montreal Cognitive Assessment; N, number of subjects; SD, standard deviation; sMetS, suspected Metabolic Syndrome.

Table 3
Number of sMetS components and its impact on the MoCA score of patients.

Number of sMetS components	N (%)	Mean MoCA score	Decreased cognitive performance, N (%)	*p* value[a]
0	37 (11)	24.05	15 (41)	ref.
1	85 (26)	21.95	42 (49)	0.2993
2	122 (38)	22.02	68 (56)	0.2858
3	62 (19)	19.87	45 (73)	0.0027
4	17 (5)	19.88	12 (71)	0.0752

[a] The significance of difference between the MoCA score of group with particular number of sMetS components vs. group of patients free of any sMetS component (0).
MoCA, Montreal Cognitive Assessment; N, number of subjects; ref., reference group; sMetS, suspected Metabolic Syndrome.

while central obesity was associated with a lower MoCA score (-1.34 points vs. respondents without central obesity; $p < 0.05$), we did not find any association between lower MoCA scores and dyslipidemias.

The probability of impaired cognitive functions increased with an increasing number of sMetS components present (Figure 3). While individuals with one or two sMetS components were not significantly affected, the presence of three sMetS components reduced the MoCA score (-4.18 points) compared to sMetS- ($p < 0.05$).

We found marked differences in cognitive performance between participants in community pharmacies and those in senior care centres (-7.24 points in the latter group; $p < 0.05$). While in community pharmacies only 41% of subjects had lower cognitive performance on the MoCA test, up to 90% of patients in senior care centres exhibited subnormal MoCA scores. Participants in senior care centres also exhibited a higher occurrence of sMetS (present in 28% of cases) than participants from community pharmacies (19%).

3.3. Reliability of the short MoCA test

The S-MoCA provided similar findings and we observed a positive correlation between the s-MoCA and full MoCA scores ($r^2 = 0,86$; $p < 0.05$; Figure 4), confirming that the s-MoCA test is a fully comparable and reliable screening tool for cognitive features in the tested cohort.

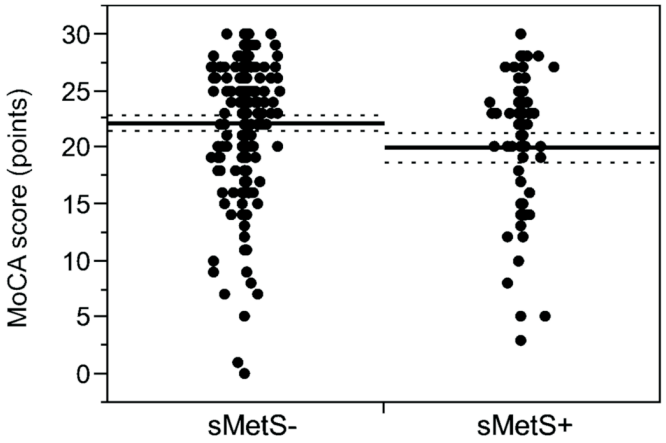

Figure 2. Impact of sMetS presence (MetS+) or absence (MetS-) on achieved MoCA score. Solid lines in the centre of the points show the group means, while dotted lines represent the boundaries of the appropriate confidence intervals.

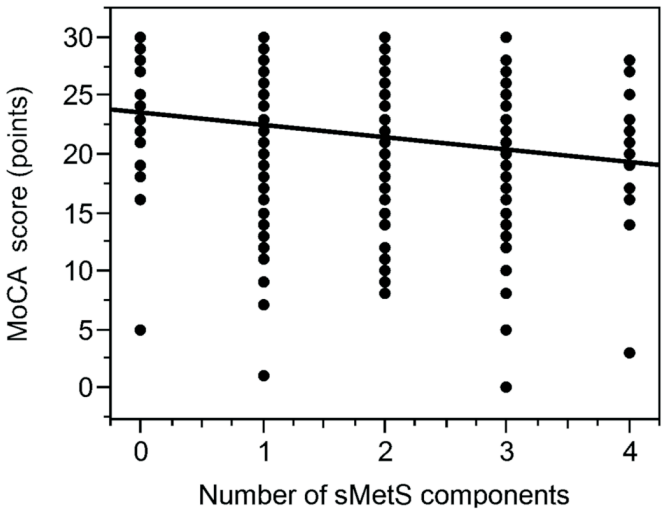

Figure 3. Relationship between the MoCA score and the number of sMetS components. The straight line shows a decreasing trend of the MoCA score with an increasing number of sMetS components.

4. Discussion

We focused on elderly patients, as the risk of MetS and related cognitive impairment becomes more pronounced with aging.[10,11]

Our main findings are that i) 56% of a random population over 60 years of age exhibited lower cognitive performance on the MoCA ii) subnormal MoCA scores were significantly present with increasing age of the respondents, and iii) the presence of MetS moderately but significantly correlated/associated negatively with the MoCA and also with the s-MoCA. Cognitive decline is expected in the elderly;[10,15] however, we observed a markedly higher occurrence of cognitive impairment (56%) in elderly patients than reported elsewhere (16%,[10] 22%,[16] 16%,[17]). An explanation might be that in other studies, cognitive status was evaluated by a physician, neurologist or neuropsychologist in healthcare facilities,[15,16] while pharmacists might be less accurate. On the other hand, pharmacists recognised an early risk for cognitive decline using the anticholinergic cognitive burden scale,[4] and pharmacists' interventions can decrease adverse drug effects on cognition.[3,4] Thus, medication management tools can help indicate a cognitive impairment.[4] Importantly, we studied the general elderly population, while others had robust inclusion and exclusion criteria.[10,15] Different cognitive tests used[15,16] may also explain the discrepancy.

Expectedly,[10] the negative correlation between age and the cognitive test score was also present in our analysed cohort aged 60+. This has already been well explained by changes in the normal aging process in the brain and by a reduction of white and grey matter volume.[18] We hypothesised that metabolic syndrome may further decrease the cognitive performance in the elderly[10] via alterations of brain metabolism and worsening of the blood supply to the brain[19] and/or enhancement of neurodegenerative processes.[11,20] Our observations confirm this hypothesis. Albeit moderate, MetS-related worsening of existing cognitive impairment might further affect late life activities.

We have extended the view on the link of MetS vs. cognitive function by analysing the impact of individual MetS components. Hypertension and type 2 DM strongly predicted cognitive impairment, followed by central obesity. Interestingly, dyslipidaemias were unrelated to the MoCA score.

The association between hypertension and decline of cognitive performance in older subjects is known.[10,21] However, in individuals

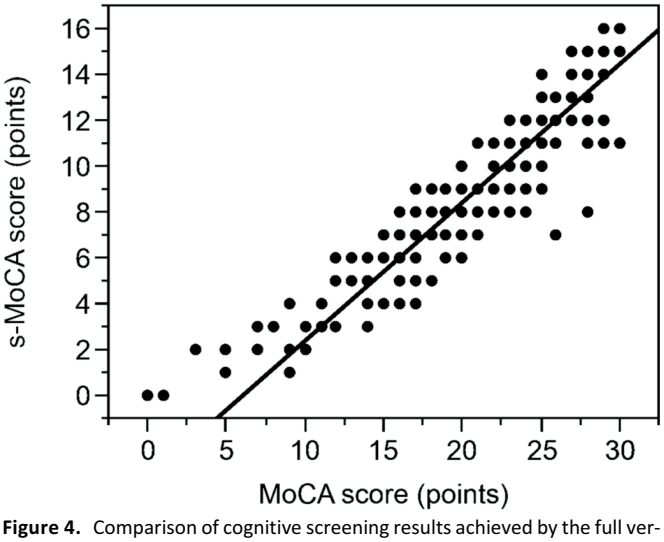

Figure 4. Comparison of cognitive screening results achieved by the full version of the MoCA test and the short form version (s-MoCA). The straight line demonstrates the calculated measure of agreement (86%) between patients' scores, as evaluated by both versions of the MoCA test.

over 80 years of age, the opposite has also been reported.[22] Counterintuitively, low blood pressure was reported to associate with alterations in brain volume, smaller cortical thickness, grey matter atrophy and cognition impairment in the elderly.[21]

The link between type 2 DM and/or hyperglycaemia and higher risk of cognitive decline and even senile dementia, as observed in our study, was previously reported.[10,20,23] Concomitantly, cognitive dysfunction is increasingly recognised as an important comorbidity and complication of DM affecting the quality of life and diabetes self-monitoring and is related to diabetes treatment-related complications.[24] However, the link has not been elucidated. While in healthy seniors higher insulin levels were related to impaired attention and verbal memory, in patients with neurodegenerative disorders, higher insulin rather improved cognitive performance.[23] This may be important when antidiabetic medication is used, leading to oscillations between hyperglycaemia and hypoglycaemia. Whether cognitive dysfunction can also predict these complications[24] remains unclear. Nevertheless, recent guidelines[25] recommend cognitive screening (using the MoCA test) in the routine management of older diabetics.

Interestingly, central obesity but not dyslipidemia were related to reduced cognitive performance. The relationship between obesity and worsened cognitive performance and the outcomes are controversial. One recent study presented that intentional weight loss was associated with cognitive improvement in elderly with mild cognitive impairment.[26] Contrariwise, while being overweight is related to a lower risk of cognitive decline in the elderly population and weight loss later in life can mean an early warning signal for cognitive impairment,[27] central obesity increases its risk.[26] Previous studies suggested that the impact of inflammation and oxidative stress in the brain might link obesity and cognitive decline.[23] Hyperlipidemia or its pharmacotherapy may also influence cognitive function,[11] but reports are inconsistent.[28,29] Links might include blood-brain barrier injury, the influence on small cerebral blood vessels, a decrease of amyloid clearance and a neuroprotective effect.[29]

The feasibility of testing within routine pharmaceutical care is substantial. The MoCA test might be time-consuming, limiting willingness of the pharmacist and the patient. A short form of MoCA test containing selected items but still directly reflecting the full version of MoCA and providing reliable outcomes across diverse neurological disorders might be a solution.[30]

As only the standard MoCA has been validated in Slovakia at the time of performing this study, we used, due to the cultural and social similarities, an adaptation of the Czech version of s-MoCA[14] The shortened version of the MoCA test (completed in 5 minutes), provided the same outcome as the original test (15 minutes), thus confirming its applicability as a reliable equivalent.[14]

5. Conclusion

Our results document the feasibility of cognitive screening within pharmaceutical care and reveal a moderate but significant relationship between cognitive dysfunction and sMetS. In the future, rapid cognitive assessment by trained pharmacists might help to identify the risk groups of patients who would benefit from further cognitive evaluation by a general practitioner or specialist and from individualised patient counselling within pharmaceutical care.

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Competing interests

The authors report no conflict of interest.

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