To cite: Sipos V, Pálinkás A,

cessation support for regular

primary care: a nationwide

sectional study. BMJ Open

bmjopen-2017-018932

2018;8:e018932. doi:10.1136/

Prepublication history for

this paper is available online.

org/10.1136/bmjopen-2017-

Received 31 July 2017

Revised 29 December 2017

Accepted 8 January 2018

018932).

To view these files, please visit the journal online (http://dx.doi.

Kovács N, et al. Smoking

smokers in Hungarian

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BMJ Open Smoking cessation support for regular smokers in Hungarian primary care: a nationwide representative crosssectional study

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ABSTRACT

Objectives Our study aimed to evaluate the effectiveness of general practitioners' (GPs') smoking cessation support (SCS).

Study design We carried out a cross-sectional study between February and April 2016.

Setting and participant A sample of 2904 regular smokers aged 18 years or older was selected randomly from 18 general medical practices involved in a national representative, general medical practice-based morbidity monitoring system. The GPs surveyed the selected adults and identified 708 regular smokers.

Main outcome measures Multivariate logistic regression models have been applied to evaluate the determinants (age, gender, education, smoking-related comorbidity, smoking intensity, intention to quit smoking and nicotine dependence) of provision of GP-mediated SCS such as brief intervention, pharmacological and nonpharmacological programmatic support.

Results According to the survey, 24.4% of the adults were regular smokers, 30% of them showed high nicotine dependence and 38.2% willing to guit smoking. Most of the smokers were not participated in SCS by GPs: brief intervention, programmatic nonpharmacological support and pharmacotherapy were provided for 25%, 7% and 2% of smokers, respectively. Low-nicotine-dependence individuals were less (OR 0.30, 95% CI 0.12 to 0.75), patients with intention to quit were more (OR 1.49, 95% Cl 1.00 to 2.22) likely to receive a brief intervention. Vocational (OR 1.71, 95% CI 1.13 to 2.59) and high school education (OR 2.08, 95% CI 1.31 to 3.31), chronic obstructive pulmonary disease and cardiovascular diseases (OR 3.34, 95% CI 1.04 to 10.68; OR 3.91, 95% CI 2.33 to 6.54) increased the probability to receive support by GP.

Conclusions Although there are differences among smokers' subgroups, the SCS in Hungarian primary care is generally insufficient, compared with guidelines. Practically, the pharmacological support is not included in Hungarian GPs' practice. GPs should increase substantially the working time devoted to SCS, and the organisation of primary healthcare should support GPs in improving SCS services.

Strengths and limitations of this study

- This paper is the first Hungarian publication on the distribution of nicotine dependence and primary care smoking cessation support for adult smokers.
- The studied sample represents the adult smoker population of the country.
- Since our study was carried out with general practitioners (GPs) who volunteered to participate, the quality of care provided by them may be better than the average GP in Hungary; thus, our results overestimate the actual quality.

INTRODUCTION

One of the defined elements of preventive health services provided in primary healthcare (PHC) is the identification of subjects exposed to risk factors of major chronic diseases. One of the most important risk factors to be controlled is smoking. Although in Hungary, the legal framework covering these activities has been established, smoking behaviour is still being assessed at a low prevalence by general practitioners (GPs).¹²

Nowadays, smoking poses the greatest risk for healthy life years: 15.03% of healthy life years are lost in Hungary as a consequence of smoking, and hence, after Greenland (17.74%), Montenegro (16.02%) and North Korea (15.68%), Hungary has the fourthworst rate worldwide.³ Therefore, reducing smoking-related health loss constitutes a great public health challenge for this country. This unfavourable status draws attention to the fact that evidence-based interventions to control smoking have not been transposed effectively into everyday practice.

To facilitate smoking cessation support (SCS), the Ministry of Human Capacities released the guideline entitled, Guideline on Supporting Smoking Cessation—A Guide for

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Health Professionals, which was prepared on the basis of international recommendations.^{4–6} This guideline specifies that it is the responsibility of all healthcare professionals (GPs among them) to provide SCS for tobacco users according to their position in the healthcare system.

Considering smoking cessation interventions, PHC professionals are in a key position, the help provided to smoking patients in general medical practice (GMP) is the best preventive action in terms of cost-effectiveness, resulting in significant health and economic benefits at the level of the whole society.⁷ Brief interventions (assessment of smoking behaviour, smoking cessation advising, confirmation of intent to quit smoking and motivation thereof) and programmatic forms of support (non-pharmacological and pharmacotherapy) can be incorporated into day-to-day PHC.

Each of these SCS services is among the most efficient smoking intervention strategies. Those smokers receiving such support are more likely to quit smoking.⁸⁹ However, the effectiveness and applicability of support tools depends to a large extent on the smokers' motivation for quitting smoking as well as on the level of nicotine dependence. While brief intervention is a form of intervention applicable for all smokers, the above-mentioned two factors have a significant effect on the use of programmatic support. The motivation to quit smoking is essential for choosing the appropriate method of non-pharmacological programmatic support (namely, individual counselling, group counselling and proactive telephone counselling). Furthermore, counselling is effective for treating both low and high forms of addiction, so their use should not be limited to only severe addiction cases. By contrast, pharmacotherapy (namely, nicotine replacement therapy and varenicline) is only recommended for sufficiently motivated patients suffering from moderate to high nicotine dependence, according to the Hungarian guidelines.⁴

In Hungary, studies to specifically examine the distribution of nicotine dependence as well as to monitor the implementation of activities provided for smokers and specified by guidelines have not yet been carried out. Therefore, our study aimed to establish a SCS-related data collection system and to answer the following questions: (1) What is the distribution of nicotine dependence among adult smokers in Hungary? (2) What types of SCS services do smokers receive within the framework of PHC? (3) What characteristics have an influence on the extent of nicotine dependence and on the usage of GP-based SCS? and (4) Another goal was to investigate the level of burden imposed on PHC workers by SCS services.

METHODS

The University of Debrecen, School of Public Health has been operating the General Practitioners' Morbidity Sentinel Stations Programme (GPMSSP) since 1998, which includes 124 GP providing incidence and prevalence data on the most important non-communicable diseases in terms of public health.¹⁰ The collected data are demographically representative of the Hungarian adult population, providing a useful basis for carrying out different epidemiological studies. Based on the GPMSSP, we carried out a cross-sectional study in 2016 in the period between February and April.

Sampling

The selection of adult smokers was performed by two-step sampling. The first step was to randomly select GMPs from the GPMSSP to participate in the investigation. In this way, 18 practices were selected. After that, patients aged over 18 were selected from the practice list of participating GMPs by simple randomisation.

Taking into consideration that our aim was to investigate 40 patients per practice, and the smoking frequency among adults is 22.5% in Hungary on the basis of the European Health Interview Survey, 2009 (EHIS), the number of selected subjects was 178 per practice. After checking the sampling frame, which consisted of 3204 patients, the GPs compiled the list of patients who received actual care in their practice. Thus, a total of 2904 patients were included in the study.

The GPs surveyed the selected adults in order to identify regular smokers. Pregnant women were excluded from the study. The data collection was carried out among of patients who signed the informed consent.

Data collection

The data collection performed by GPs and practice nurses focused on demographical data (sex and age groups 18-34, 35-64 and over 65 years), level of education (categorised as primary or less, vocational, high school, tertiary), intensity of smoking (number of cigarettes per day, time of smoking the first cigarette after waking up in the morning), intention to quit smoking (answer to 'Do you want to quit smoking?' question categorised as Yes or No), as well as exposure to SCS (distinguishing brief intervention, pharmacological support and programmatic non-pharmacological support according to the Hungarian guidelines for SCS). Accompanying smoking-related diseases with highest prevalence, for example, chronic obstructive pulmonary disease (COPD) and cardiovascular diseases (arterial hypertension, stroke, ischaemic heart disease and acute myocardial infarction) were also covered by data collection.

Because Heaviness of Smoking Index (HSI) has similar effectiveness in assessing nicotine dependence as Fagerström Test for Nicotine Dependence has, but HSI takes less resource in survey,¹¹ ¹² nicotine dependence was calculated on the basis of the HSI from the number of daily cigarettes (≤ 10 : 0 points, 11–20: 1 point, 21–30: 2 points, ≥ 31 : 3 points) and the time of the first cigarette after waking up in the morning (≤ 5 min: 3 points). Accordingly, the severity of smoking was categorised as low (sum of points is 0), moderate (1–3 points) or high (4–6 points).

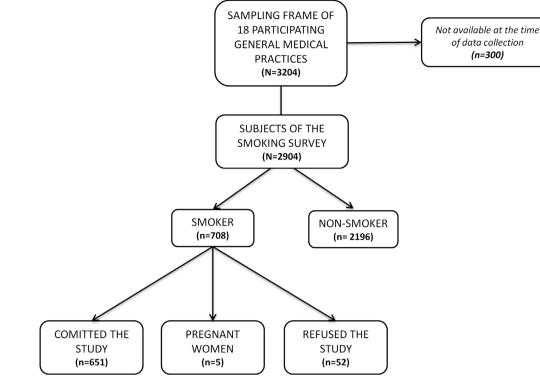


Figure 1 Sampling procedure.

Statistical methods

Multivariate logistic regression models were applied to evaluate the influence of smokers' characteristics on the level of nicotine dependence and on the provision of SCS by GPs. Different SCS services were examined in separate models. The associations were described by the OR and the corresponding 95% CI. The explanatory variables in the regression models for nicotine dependence were age, gender, education and accompanying diseases. In addition to these factors, the extent of nicotine dependence and the intention to quit smoking were also taken into account. Predictive Analytics Software Statistics for Windows, V.18 (SPSS) was used for data processing and statistical analyses.

RESULTS

Descriptive statistics

According to the GP survey, 24.4% of the adults in the sample smoked cigarettes regularly (95% CI 22.8% to 25.9%). The frequency of smoking among men was 30.6% (95% CI 28.1% to 33.1%), while it was 19.3% (95% CI 17.3% to 21.2%) among women. Since 651 of 708 smokers signed the informed consent form, the response rate was 91.9% (figure 1).

The male to female ratio in the sample was 1.411 (N_{male} =381; N_{female} =270).Twenty-seven per cent of the participants were between 18 and 34 years of age, 64% were between 35 and 64 years of age and 9% were over 65 years. Thirty-eight per cent of the respondents had a primary education, 33% of them had vocational qualification, 22% had high school qualifications and 6% had

tertiary education. Fifteen per cent of smokers had some smoking-related diseases, and the diseases with highest frequency were cardiovascular disease (14%) and COPD (2%).

Nicotine dependence was observed to be low in 8% of smokers, while 62% had moderate levels and 30% had high levels of nicotine dependence. 38.2% of the participants stated that they want to quit smoking, and 10%, 67% and 23% of them had low, moderate and high dependence, respectively. In the years prior to the study, 25% of adults had participated in a brief intervention, while this rate was 28% among those who wanted to quit smoking-6%, 76% and 18% for low, moderate and high dependence, respectively. Seven per cent of smokers received programmatic non-pharmacological SCS, while this figure was only 2% regarding those who were involved in pharmacotherapy. Due to these low frequencies, the programmatic pharmacotherapy and non-pharmacological programmatic support were aggregated into a programmatic support category when carrying out the regression analyses. In total, 32% of the respondents received a form of SCS. Eight per cent of smokers interested in quitting tobacco received pharmacotherapy or non-pharmacological programmatic support, while non-pharmacological support among smokers with high dependence was not achieved at all. However, 25% of the high dependence smokers received pharmacological support (table 1).

High-risk groups underserviced

Nicotine dependence was significantly influenced by gender and education level. A low dependence was less likely to occur among men (OR 0.39, 95% CI 0.21 to

 Table 1
 Distribution of nicotine dependence by gender, age, education and smoking cessation support in the years prior to the study according to interest in quitting

	Whole sample	No interest in quitting HSI			Interest in quitting				
					HSI				
Characteristics	n (%)	Low n (%)	Moderate n (%)	High n (%)	P value*	Low n (%)	Moderate n (%)	High n (%)	P value*
Gender									
Female	270 (41)	19 (12)	92 (61)	41 (27)	<0.001	15 (13)	84 (71)	19 (16)	0.026
Male	381 (59)	8 (3)	144 (58)	98 (39)		10 (8)	82 (62)	39 (30)	
Age group									
18–34	179 (27)	9 (9)	63 (60)	33 (31)	0.524	9 (12)	50 (68)	15 (20)	0.777
35–64	414 (64)	17 (7)	151 (59)	88 (34)		15 (10)	103 (65)	40 (25)	
65+	58 (9)	1 (2)	22 (54)	18 (44)		1 (6)	13 (76)	3 (18)	
Education level									
Primary or less	249 (38)	4 (2)	91 (55)	72 (43)	<0.001	7 (8)	45 (55)	30 (37)	0.003
Vocational	216 (33)	5 (4)	83 (63)	44 (33)		5 (6)	62 (74%)	17 (20)	
High school	146 (22)	12 (15)	51 (64)	17 (21)		9 (13)	46 (70)	11 (17)	
Tertiary	40 (6)	6 (26)	11 (48)	6 (26)		4 (24)	13 (76)	0 (0)	
Smoking cessation support									
Brief intervention	163 (25)	2 (2)	56 (61)	34 (37)	0.138	4 (6)	54 (76)	13 (18)	0.117
Non-pharmacological support	45 (7)	2 (6)	21 (68)	8 (26)	0.544	4 (29)	10 (71)	0 (0)	0.014
Pharmacotherapy	11 (2)	0 (0)	3 (100)	0 (0)	0.345	1 (12)	5 (63)	2 (25)	0.960
Programmatic support†	54 (8)	2 (6)	23 (70)	8 (24)	0.392	5 (24)	14 (67)	2 (9)	0.045
Any cessation support	208 (32)	4 (3%)	77 (63)	42 (34)	0.162	8 (9)	63 (74)	14 (17)	0.157
Total	651	27 (7%)	236 (59)	139 (34)		25 (10)	166 (67)	58 (23)	0.002

*χ² test.

†Non-pharmacological programmatic support and pharmacological programmatic support have been summarised as programmatic support.

HSI, Heaviness of Smoking Index.

0.73), while the occurrence of a low dependence among participants with high school qualifications or tertiary education proved to be significantly higher (OR_{high school} 3.37, 95% CI 1.55 to 7.32; OR_{tertiary} 6.95, 95% CI 2.65 to 18.27). A moderate dependence was significantly higher among smokers with a high school education level (OR_{vocational} 1.74, 95% CI 1.19 to 2.54; OR_{high school} 1.62, 95% CI 1.05 to 2.48). A high dependence was more likely to occur among men (OR 1.89, 95% CI 1.31 to 2.72), and it was less likely to arise among smokers with a high school and tertiary education level (OR_{vocational} 0.54, 95% CI 0.36 to 0.80; OR_{high school} 0.36, 95% CI 0.22 to 0.58; OR_{tertiary} 0.27, 95% CI 0.11 to 0.68) (table 2).

Factors affecting the provision of smoking cessation care are shown in table 3. A brief intervention was less likely to be provided to dependent patients over 35 years of age (OR₃₅₋₆₄ 0.46, 95% CI 0.30 to 0.70; OR₆₅₊ 0.41, 95% CI 0.19 to 0.88) or to low dependence smokers (OR 0.30, 95% CI 0.12 to 0.75). By contrast, dependent patients with a high school education level (OR 1.74, 95% CI 1.05 to 2.90), dependents suffering from cardiovascular diseases (OR 6.58, 95% CI 3.80 to 11.37), dependent smokers having COPD (OR 4.58, 95% CI 1.36 to 15.46) and those who

wanted to quit smoking (OR 1.49, 95% CI 1.00 to 2.22) were more likely to receive brief intervention. Men were less likely to receive programmatic support (OR 0.50, 95% CI 0.28 to 0.91). Smokers belonging to the age group 35-64 years of age (OR 2.12, 95% CI 1.01 to 4.46) and dependent patients with a high school education (OR_{vo} _{cational} 2.23, 95% CI 1.03 to 4.84; OR_{high school} 3.42, 95% CI 1.54 to 7.60) were more likely to receive programmatic support. Patients with a high school education (OR_{vo} cational 1.71, 95% CI 1.13 to 2.59; OR_{high school} 2.08, 95% CI 1.31 to 3.31) as well as those suffering from cardiovascular diseases (OR 3.91, 95% CI 2.33 to 6.54) or COPD (OR 3.34, 95% CI 1.04 to 10.68) had a higher chance of receiving a form of SCS. People with a low nicotine dependence were almost significantly less likely to receive any kind of support (OR 0.50, 95% CI 0.24 to 1.01) (table 3).

GP's workload for SCS

Based on the estimated frequency of smoking, and considering that the average number of adults cared for in an average GMP is 1613, there are 394 patients who smoke regularly in a typical medical practice. If the SCS of GPs was only focused on smokers who wanted to quit smoking

Table 2	Factors associated with nicotine dependence among regular smokers according to the multivariate logistic
regressi	on analysis (ORs with corresponding 95% CI)

Variables	Low dependence	Moderate dependence	High dependence		
Gender (reference: female)					
Male	0.39 (0.21 to 0.73)	0.77 (0.55 to 1.07)	1.89 (1.31 to 2.72)		
Age group (reference: 18–34)					
35–64	0.65 (0.33 to 1.26)	0.93 (0.64 to 1.36)	1.25 (0.83 to 1.89)		
65+	0.24 (0.05 to 1.22)	0.92 (0.48 to 1.75)	1.57 (0.79 to 3.12)		
Education level (reference: primary or less)					
Vocational	1.11 (0.46 to 2.68)	1.74 (1.19 to 2.54)	0.54 (0.36 to 0.80)		
High school	3.37 (1.55 to 7.32)	1.62 (1.05 to 2.48)	0.36 (0.22 to 0.58)		
Tertiary	6.95 (2.65 to 18.27)	1.20 (0.60 to 2.38)	0.27 (0.11 to 0.68)		
Tobacco-related diseases (reference: no disease)					
Cardiovascular	1.26 (0.50 to 3.19)	0.97 (0.59 to 1.60)	0.97 (0.56 to 1.66)		
COPD	0.86 (0.10 to 7.69)	1.40 (0.46 to 4.28)	0.72 (0.21 to 2.42)		

COPD, Chronic obstructive pulmonary disease.

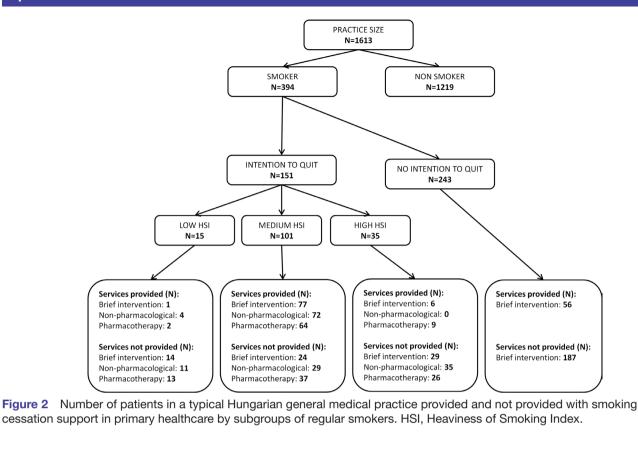
(38.2% of the smokers according to our finding), support would be provided for 151 patients per practice. Considering the distribution of nicotine dependence, this figure would represent 15 patients with a low, 101 patients with a moderate and 35 patients with a high dependence.

Based on the observed care frequency, there is a lack of brief intervention in the case of 14 patients with a low dependence, 24 patients with a moderate dependence and 29 patients with a high dependence. Programmatic non-pharmacological support failed to be provided for 11 patients with a low dependence, 29 patients with a moderate dependence and 35 patients with a high dependence, while in the case of pharmacotherapy, these figures appear to be 13, 37 and 26, respectively.

For the individuals who were unwilling to quit smoking, 187 of the smokers did not receive a brief intervention (figure 2).

Variables	Brief intervention	Programmatic support	Any cessation support
Gender (reference: female)			
Male	0.99 (0.66 to 1.47)	0.50 (0.28 to 0.91)	0.81 (0.56 to 1.15)
Age group (reference: 18–34)			
35–64	0.46 (0.29 to 0.70)	2.12 (1.01 to 4.46)	0.71 (0.48 to 1.06)
65+	0.41 (0.19 to 0.88)	1.46 (0.37 to 5.84)	0.54 (0.26 to 1.11)
Education level (reference: primary or less)			
Vocational	1.46 (0.93 to 2.31)	2.23 (1.03 to 4.84)	1.71 (1.13 to 2.59)
High school	1.74 (1.05 to 2.89)	3.42 (1.54 to 7.60)	2.08 (1.31 to 3.31)
Tertiary	0.50 (0.17 to 1.48)	2.47 (0.77 to 7.88)	1.00 (0.44 to 2.29)
Tobacco-related diseases (reference: no disease)			
Cardiovascular	6.58 (3.80 to 11.37)	0.30 (0.09 to 1.03)	3.91 (2.33 to 6.54)
COPD	4.58 (1.36 to 15.46)	1.22 (0.14 to 10.42)	3.34 (1.04 to 10.68)
HSI (reference: moderate to high)			
Low	0.30 (0.12 to 0.75)	1.30 (0.53 to 3.23)	0.50 (0.24 to 1.01)
Intention to quit (reference: no)			
Yes	1.49 (1.00 to 2.22)	0.87 (0.48 to 1.56)	1.17 (0.82 to 1.67)

COPD, Chronic obstructive pulmonary disease; HSI, Heaviness of Smoking Index.



DISCUSSION

The knowledge of nicotine dependence and its determinants is of key importance for the development of efficient tobacco control strategies and proper application of SCS methods.¹¹ Since in Hungary, no data have yet been published concerning the distribution of nicotine dependence as well as care for adult smokers, our results can fill these gaps.

Main findings in an international context

In Hungary, 30% of tobacco users showed high nicotine dependence. A similar proportion of highly dependent smokers can be observed in Russia (30%) and Poland (28%), while Ukraine (26%) and Romania (25%) show a somewhat lower frequency.¹³ According to our study, a high dependence is more likely to occur among men but less likely among people with a high school and tertiary education level. Our observations were in agreement with findings from Central-Eastern European countries with socioeconomic structures similar to Hungarian ones, and from surveys which applied similar sampling and assessment methods as we did our investigation. The proportion of high dependence among men compared with women was a bit higher than reported in Poland (OR=1.5), Romania (OR=1.5) and less than in Russia (OR=2.7), but neither of them was significant; in Romania, there was a greater likelihood of high dependence among people with low levels of education (OR=2.3) compared with those with a tertiary education level.¹³

SCS activities of Hungarian GPs (25% of tobacco users received brief intervention, 7% and 2% were given

programmatic non-pharmacological and pharmacological support) deviates profoundly from data published in international reports. The corresponding indicators for other countries are remarkably higher. According to a survey conducted in the USA, 50% of tobacco users were provided by counselling in PHC.¹⁵ In Ontario, the rate of smoking cessation counselling is 74%.¹⁶ While the brief intervention frequency exceeds 50% in the UK, this figure in the Netherlands is approximately 10%, and it is 22% in Australia and 27% in Italy.^{17–21} The proportion of programmatic non-pharmacological support is 14.1% in Australia and 27.8% in the UK.¹⁵ In Ontario, 25% of tobacco users received pharmacotherapy.¹⁶ According to a survey conducted in the UK, this proportion was 7%, but other surveys refer to a frequency over 40%.^{15 22}

Altogether, considering the wide variability in published findings, the Hungarian PHC performance in SCS is weak, both in comparison with the evidence-based recommendation and in comparison with the performance reported from other countries. The intensity of brief interventions belongs to the weaker performances. The intensity of programmatic interventions is out of the published range. Pharmacological support for smoking cessation is practically missing from the practice of Hungarian GPs.

Based on our findings, during brief interventions, GPs place greater emphasis on patients suffering from chronic diseases, highly dependent patients and those who want to quit smoking. Bringing the focus on caring for tobacco users who are willing to quit as well as taking greater care of smokers suffering from chronic diseases are good aspects of the Hungarian PHC practice. In this respect, the Hungarian PHC follows international practices.^{22 23}

However, for successful cessation, GPs should focus more on the care of patients with low and moderate dependence. Although highly dependent patients are more likely to seek for SCS, they are less successful in maintaining abstinence compared with low-dependence patients.^{14 24}

Required extra workload to meet recommendations

The regular assessment of smoking behaviour of clients, which covers the assessment of nicotine dependence and willingness to give up smoking, which is completed with brief intervention for the regular smokers, takes substantial working time of the team members of PHC. Initiation of programmatic smoking cessation increases further the needed working time. This amount of work seems to be not expectable from a traditional PHC team of one GP and one nurse providing care for approximately 1600 adult clients, as it is typical in Hungary.

On the other hand, the most activities of SCS do not require medical expertise. Trained health professionals (eg, nurses, public health experts) can provide those. Organised collaboration of traditional PHC team with non-medical health professionals could ensure the base for the required development. The SCS with many other missing preventive services of the PHC belongs to the package of interventions with evidence base, which could improve significantly the health status of provided adults, if the necessary structural development could be implemented somehow.^{25–27}

Strengths and limitations

According to the EHIS data from 2014, 26.4% of the adult population smokes on a regular basis (95% CI 25.3% to 27.6%). The frequency of smoking among men was 32.0% (95% CI 30.2% to 33.8%), while the frequency among women was 21.7% (95% CI 20.2% to 23.1%). As this frequency does not differ significantly from our experience, this survey provides reliable and demographically representative data on the care of smokers.

However, our study was carried out with GPs who undertook voluntary participation in the GPMSSP. It can be supposed that GPs less conscientious in SCS are over-represented in the study. Due to this selection bias, the quality of care provided by GPMSSP members may be better than the average in Hungary. Therefore, our results overestimate the actual quality. The care for adult smokers in Hungary is lagging behind our study results. Consequently, the quality of care by Hungarian GPs for regular smokers is somewhat worse than we could determine, and the gap among reference countries and Hungary is wider than we actually observed.

Our study did not investigate in detail the GMP and patient-related factors which influence the effectiveness of SCS. In addition, having no data on the typical working time for SCS interventions, the number of missing services could not be transformed into number of missing working hours. Therefore, further investigations are needed to explore the determinants of SCS effectiveness, and to estimate the necessary extra working time to make up for missing services.

CONCLUSIONS

The proportion of highly dependent smokers in Hungary shows a pattern similar to Eastern European observations. Based on the process indicators for care, it seems that within the framework of PHC, tobacco users fail to receive the proper support necessary to quit smoking as specified in the guidelines. Healthcare services provided by GPs are mainly influenced by the age, gender, education, existing chronic diseases and the level of nicotine dependence of smokers. According to our estimations, the provision of guideline-adherent SCS could increase the workload of GPs considerably. Therefore, supportive capacities are needed to enable the PHC for providing SCS as it is recommended by evidence-based guidelines.

Contributors VS, MP, RÁ and JS initially planned the study. FV, AP, JGS, KOC, NK, TJ and VS participated in study coordination and the database preparation. VS and JS carried out the statistical analyses. VS, MP and JS interpreted the results. VS and JS prepared the manuscript. RÁ approved the final version to be submitted. All authors read and approved the final manuscript.

Funding The reported study was carried out in the framework of the 'Public Health Focused Model Programme for Organising Primary Care Services Backed by a Virtual Care Service Centre' (SH/8/1). The Model Programme is funded by the Swiss Government via the Swiss Contribution Programme (SH/8/1) in agreement with the Government of Hungary. Additional source of funding was from the grant of Hungarian Academy of Sciences (MTA 11003, 2006TKI227), from IGEN-HUNGARIAN (TÁMOP-4.2.2.AA-11/1/KONV-2012-0031) project which was co-financed by the European Union and the European Social Fund, and from GINOP-2.3.2-15-2016-00005 project which was co-financed by the European Union and the European Regional Development Fund.

Competing interests None declared.

Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

Ethics approval The study protocol was approved by the Ethical Committee of the Hungarian National Scientific Council on Health (ETT TUKEB 48495-2/2014/EKU 475/2014).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The dataset is still subject to further analyses, but will be held and management by the Department of Preventive Medicine, Faculty of Public Health, University of Debrecen, Debrecen, Hungary.

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