sciendo 10.2478/sjph-2022-0007 Zdr Varst. 2022;61(1):40-47

Petek D, Assenova R, Foreva G, Gašparović Babić S, Petek Šter M, Prebil N, Puia A, Smyrnakis E, Harris M. Primary care system factors and clinical decision-making in patients that could have lung cancer: a vignette study in five Balkan region countries. Zdr Varst. 2022;61(1):40-47. doi: 10.2478/sjph-2022-0007.

PRIMARY CARE SYSTEM FACTORS AND CLINICAL DECISION-MAKING IN PATIENTS THAT COULD HAVE LUNG CANCER: A VIGNETTE STUDY IN FIVE BALKAN REGION COUNTRIES

DEJAVNIKI PRIMARNEGA ZDRAVSTVA IN KLINIČNO ODLOČANJE PRI BOLNIKIH, KI BI LAHKO IMELI PLJUČNEGA RAKA: RAZISKAVA S POMOČJO VINJETE V PETIH DRŽAVAH BALKANSKE REGIJE

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Received: Dec 21, 2020
Accepted: Nov 19, 2021

Original scientific article

ABSTRACT

Introduction: Lung cancer is the leading cause of cancer death, with wide variations in national survival rates. This study compares primary care system factors and primary care practitioners' (PCPs') clinical decision-making for a vignette of a patient that could have lung cancer in five Balkan region countries (Slovenia, Croatia, Bulgaria, Greece, Romania).

Methods: PCPs participated in an online questionnaire that asked for demographic data, practice characteristics, and information on health system factors. Participants were also asked to make clinical decisions in a vignette of a patient with possible lung cancer.

Results: The survey was completed by 475 PCPs. There were significant national differences in PCPs' direct access to investigations, particularly to advanced imaging. PCPs from Bulgaria, Greece, and Romania were more likely to organise relevant investigations. The highest specialist referral rates were in Bulgaria and Romania. PCPs in Bulgaria were less likely to have access to clinical guidelines, and PCPs from Slovenia and Croatia were more likely to have access to a cancer fast-track specialist appointment system. The PCPs' country had a significant effect on their likelihood of investigating or referring the patient.

Conclusions: There are large differences between Balkan region countries in PCPs' levels of direct access to investigations. When faced with a vignette of a patient with the possibility of having lung cancer, their investigation and referral rates vary considerably. To reduce diagnostic delay in lung cancer, direct PCP access to advanced imaging, availability of relevant clinical guidelines, and fast-track referral systems are needed.

Keywords:
lung cancer, primary care, gatekeeping, early diagnosis

IZVLEČEK

Uvod: *Pljučni rak je vodilni vzrok smrti zaradi raka, pri čemer se nacionalne stopnje preživetja zelo razlikujejo. Ta študija primerja dejavnike sistema primarnega zdravstvenega varstva (PZV) in klinično odločanje izvajalcev PZV v petih državah balkanske regije na primeru vinjete bolnika, ki bi lahko imel pljučnega raka.*

Metode: *Zdravniki PZV iz petih evropskih držav jugovzhodne regije (Slovenije, Hrvaške, Bolgarije, Grčije in Romunije) so izpolnili spletni vprašalnik, ki je zajemal njihove demografske značilnosti, značilnosti ambulante in zdravstvenega sistema. Udeleženci so bili pozvani, naj sprejmejo klinične odločitve za v obliki vinjete predstavljenega hipotetičnega bolnika, ki bi lahko imel pljučnega raka.*

Rezultati: *Anketo je izpolnilo 475 oseb. Statistično značilne razlike med državami so bile ugotovljene v neposrednem dostopu zdravnikov PZV do preiskav, zlasti zahtevnejših slikovnih preiskav. Zdravniki iz Bolgarije, Grčije in Romunije so se v primeru iz vinjete pogosteje odločili za ustrezne preiskave kot zdravniki iz Slovenije in Hrvaške. Najvišji stopnji napotitve k specialistu sta bili ugotovljeni v Bolgariji in Romuniji. Najslabša dostopnost kliničnih smernic je bila ugotovljena v Bolgariji. Najdostopnejši sistem hitre/prednostne diagnostične obravnave oz. napotitve pri sumu na raka je bil ugotovljen v Sloveniji in Hrvaški. Država je bila edini napovedni dejavnik za verjetnost napotitve bolnika na preiskave ali specialistično obravnavo v primeru klinične vinjete.*

Zaključek: *Med sodelujočimi državami balkanske regije obstajajo velike razlike v neposrednem dostopu zdravnikov PZV do preiskav. V primeru klinične vinjete bolnika z možnostjo pljučnega raka se stopnje odločanja za preiskave in napotitve pomembno razlikujejo po državah. Za zmanjšanje diagnostične zamude pri pljučnem raku je treba izboljšati neposredni dostop zdravnikov PZV do naprednih slikovnih preiskav, razpoložljivost ustreznih kliničnih smernic in uveljaviti hitre napotitvene sisteme.*

Ključne besede:
rak pljuč, primarno zdravstvo, sistem vratarja, zgodnja diagnostika

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1 INTRODUCTION

Cancer survival rates across Europe differ considerably, and data from the European Cancer Registry-based Study on Survival and Care of Cancer Patients (EUROCARE-5) show that the national 1-year relative survival rates for all cancer sites vary from 58.2% to 81.1% (1). While 1-year relative survival can be affected by differences in registration as well as lead-time and overdiagnosis biases (2, 3), it is thought to be an indicator of more advanced disease at diagnosis (4, 5). This is associated with diagnostic delay, which leads to poorer patient outcomes and survival rates (4, 6–8). The more advanced a cancer is, the more difficult it is to treat it successfully (9). For patients with lung cancer, disease stage at diagnosis is associated with survival (10).

Lung cancer is the most commonly diagnosed cancer worldwide (11.6% of all cancers) and the leading cause of cancer death (18.4% of all cancer deaths). This is a particular problem in countries in the Balkan region (1). Out of 23 world regions, Eastern Europe has the second-highest incidence of age-standardised and region-specific incidence for lung cancer in men, southern Europe has the fifth-highest (11), while age-standardised mortality rates for lung cancer in men in both regions are above the global average (171 and 132 respectively, compared with the world average of 123). The 5-year age-standardised net survival rate for lung cancer in 2010-2014 in the Balkan region countries included in this study is low, at 14.8% for Slovenia, 10.0% for Croatia, 7.7% for Bulgaria, and 11.1% for Romania (Cluj) (12). However, apparent differences in national cancer relative survival may reflect differences in calculation methodology (13). There are no data for lung cancer survival rates in Greece.

There are national variations in public awareness of cancer symptoms, as well as in the funding and organisation of health-care systems, which might affect the timeliness of cancer diagnosis in primary care (14). Screening is also increasingly important, with evidence that volume CT screening of those at high risk significantly lowers lung cancer mortality (15, 16).

The aims of this study were, in five Balkan region countries, to explore whether PCPs have direct access to relevant investigations, their clinical decision-making in a patient that could have lung cancer, to find out how PCP demographics and system factors affect these decisions, and to identify how these compare between countries.

2 METHODS

2.1 Design and study setting

The Örenäs Research Group (ÖRG), a European group of primary care cancer researchers, performed a twenty-country European on-line cross-sectional survey of PCPs to identify the factors associated with national variations in cancer survival. The survey methodology is described in detail elsewhere (17). This analysis uses data from the Balkan region countries that agreed to participate in the study: Bulgaria, Croatia, Greece, Romania, and Slovenia.

2.2 The questionnaire

The questionnaire consisted of four sections:

- PCPs' demographic data and practice characteristics: sex, number of years since graduation, location of practice, and number of doctors in practice
- availability of direct PCP access to relevant investigations: plain X-ray, contrast X-ray, computerised tomography (CT), positron emission tomography CT (PET CT) and magnetic resonance imaging (MRI)
- PCPs' stated clinical actions for a vignette of a patient with symptoms that could be due to lung cancer
- PCPs' levels of agreement with statements on health system factor items that could influence the timeliness of cancer diagnoses. In this section, PCPs were asked to rate how much they agreed with each item in relation to their referral decision-making using a 5-point Likert scale.

The vignette described a 62-year-old male smoker with a respiratory tract infection, increased sputum production, left shoulder pain, a history of chronic obstructive pulmonary disease, but no significant findings on physical examination. The vignette was designed to have a low but significant possibility of lung cancer, with a positive predictive value of 3.6% (18) .

The health system factor statements were designed to indicate the availability of clinical guidelines giving advice on which patients to refer, the availability of a fast-track specialist appointment system for patients who may have cancer, and the ability of patients to self-refer to specialists (an indication of the degree of PCP gatekeeping).

2.3 Participants and recruitment

In each country a lead ÖRG member was asked to recruit at least 50 PCPs (physicians working mainly in primary care in the community) to the study, by emailing survey invitations to PCPs in their areas. In Romania and Slovenia the survey was conducted nationwide, and the survey invitation was sent through the Association of Family Physicians database. In other countries it was conducted in a local healthcare district. Consent was implied by agreeing to take part in the survey. All data were collected anonymously.

2.4 Statistical analysis

Likert scale responses were converted to numerical scores ('strongly disagree'=1, 'strongly agree'=5). Descriptive statistics were used to report demographic data, practice

characteristics, availability of relevant investigations, PCPs' actions, and mean Likert scores for the health system factor statements. To compare the Likert scores, we fitted an analysis of variance (ANOVA) model to investigate whether the differences between countries were statistically significant. The chi-square test was used to test between-country differences in PCPs' access to investigations, as well as their likelihood of testing and referring the patient in the clinical vignette.

We used a binary logistic regression to test associations between whether or not the PCP would (a) investigate the patient and (b) refer to a specialist and: PCP sex, years since graduation, type of practice, number of PCPs in their practice, availability of clinical guidelines, availability of a fast-track specialist appointment system, ability of patients to self-refer to specialists, availability of direct PCP access to relevant investigations, and country. In the regression, 'access to investigations' is a compound variable, with possible access scores ranging from 0 (none of the investigations listed above directly available to PCPs) to 5 (all five of the listed investigations directly available), with 0 as the reference variable. Urban practice had the most participants in its group, and so was chosen as the reference variables for 'Type of practice'. For the three Likert scale sets of answers and for 'Country', we chose the first possible option in each answer as the reference variable ('Strongly disagree' and Bulgaria respectively). Tests were 2-tailed, with statistical significance defined as $P \leq 0.05$. Data were analysed using IBM SPSS v25.

3 RESULTS

A total of 475 Balkan region PCPs completed the questionnaire. The response rates and demographics are given in Tables 1 and 2 respectively.

Table 1. Number of participants and response rates in each of the five participating countries.

	Bulgaria	Croatia	Greece	Romania	Slovenia
Number of respondents	59	67	68	177	104
Number invited	90	292	318	Unknown	352
Response rate (%)	65.6	22.9	21.4	Unknown	29.5

Table 2. Participants' demographic and practice information for each of the five participating countries.

		Bulgaria n (%)	Croatia n (%)	Greece n (%)	Romania n (%)	Slovenia n (%)
Sex	Male	13 (22.0)	12 (17.9)	34 (50.0)	21 (11.9)	25 (24.0)
	Female	44 (74.6)	54 (80.6)	34 (50.0)	154 (87.0)	78 (75.0)
	Not given	2 (3.4)	1 (1.5)	0 (0.0)	2 (1.2)	1 (1.0)
Years since graduation	Less than 10	8 (13.6)	11 (16.4)	0 (0.0)	8 (4.5)	17 (16.3)
	10 to 19	11 (18.6)	10 (14.9)	38 (55.9)	42 (23.7)	34 (32.7)
	20 to 29	23 (39.0)	22 (32.8)	25 (36.8)	75 (42.4)	32 (30.8)
	30 to 39	11 (18.6)	21 (31.3)	5 (7.4)	50 (28.2)	16 (15.4)
	40 or more	5 (8.5)	1 (1.5)	0 (0.0)	0 (0.0)	5 (4.8)
	Not given	1 (1.7)	2 (3.0)	0 (0.0)	2 (1.1)	0 (0.0)
Type of practice	Urban	44 (74.6)	31 (46.3)	20 (29.4)	108 (61.0)	44 (42.3)
	Rural	5 (8.5)	23 (34.3)	34 (50.0)	60 (33.9)	31 (29.8)
	Mixed	9 (15.3)	13 (19.4)	14 (20.6)	7 (4.0)	29 (27.9)
	Not given	1 (1.7)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
Number of PCPs in the practice	1	32 (54.2)	33 (49.3)	24 (35.3)	64 (36.2)	7 (6.7)
	2	8 (13.6)	9 (19.4)	8 (11.8)	33 (18.6)	10 (9.6)
	3	8 (13.6)	6 (9.0)	3 (4.4)	17 (9.6)	14 (13.5)
	4-5	1 (1.7)	6 (9.0)	11 (16.2)	20 (11.3)	10 (9.6)
	6-7	1 (1.7)	6 (9.0)	6 (8.8)	9 (5.1)	12 (11.5)
	8-9	1 (1.7)	5 (7.5)	1 (1.5)	5 (2.8)	15 (14.4)
	10 or more	7 (11.9)	2 (3.0)	13 (19.1)	22 (12.4)	36 (34.6)
	Not given	1 (1.7)	0 (0.0)	2 (2.9)	7 (4.0)	0 (0.0)

3.1 Availability of direct access to investigations

Over 80% of PCPs had direct access to plain X-rays in each of the countries, though there was significant between-country variation. A larger difference, also significant, was seen in direct access to advanced imaging, with less than a quarter of PCPs in Bulgaria, Croatia and Romania having this access (Table 3).

3.2 PCPs' actions for the clinical vignette

With the exception of PCPs in Greece, over half of PCPs would have written a prescription for the patient at the index consultation (Figure 1). At least three-quarters of PCPs from each country would have scheduled a follow-up appointment for the patient. There was a significant difference in the proportion of doctors who would arrange a chest X-ray, tumour marker, or another special investigation or imaging: in Bulgaria, Greece, and Romania over 80% of PCPs would do this, compared with less than 60% in Slovenia and Croatia (X^2=49.39, df=4, P<0.001). The largest between-country variation in PCPs' stated actions was for referral to a specialist, ranging from Greece (8.1% would refer), through Slovenia (14.9%), Croatia (18.6%), and Bulgaria (36.5%) to Romania (65.8%). This difference was statistically significant (X^2=106.9, df=4, P<0.001).

3.3 PCPs' views on health system factors that influence their clinical decision-making

Local or national referral guidelines were least likely to be available to Bulgarian PCPs (Table 4). Fast track appointment systems for patients who may have cancer were more likely to be available in Slovenia and Croatia. Slovenian PCPs were least likely to consider that their patients could self-refer to a specialist. For each of these factors, there were statistically significant differences between the national means.

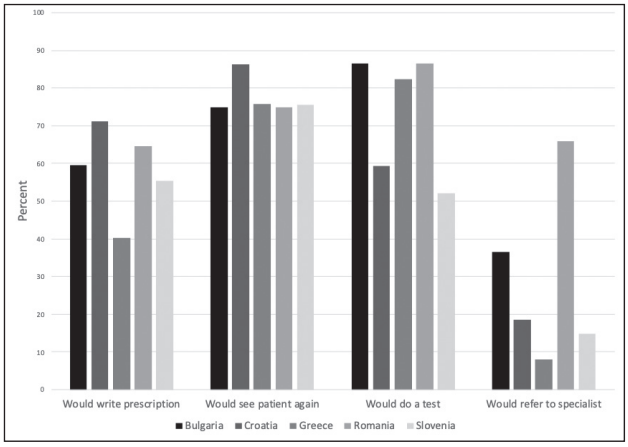

Figure 1. National comparisons of PCPs stated clinical actions for vignette of a patient with symptoms that could be due to lung cancer.

Table 3. Number of PCPs who have direct access to relevant imaging for lung cancer.

	Bulgaria n (%)	Croatia n (%)	Greece n (%)	Romania n (%)	Slovenia n (%)	Significance (P value)
Plain X-ray	54 (91.5)	64 (95.5)	66 (97.1)	149 (84.2)	90 (86.5)	<0.006
CT and/or PET CT and/or MRI	7 (11.9)	16 (23.9)	53 (77.9)	23 (13.0)	71 (68.3)	<0.001

Table 4. PCPs' levels of agreement with statements on health system factors that could influence the timeliness of cancer diagnosis.

Statement	Mean Likert scores (SD)[1]					Significance (P value)
	Bulgaria	Croatia	Greece	Romania	Slovenia	
'Common presentations and advice to which to refer are covered by local or national guidelines'	2.76 (1.01)	3.22 (0.98)	3.59 (1.01)	3.37 (1.00)	3.73 (0.84)	<0.001
'We have access to a fast-track specialist appointment system if cancer is suspected'	2.71 (1.19)	3.22 (1.17)	2.45 (1.11)	2.58 (1.08)	3.22 (1.22)	<0.001
'Patients can self-refer to specialists, so GPs don't need to act as gatekeepers.'	2.39 (1.04)	2.04 (1.02)	2.58 (1.30)	2.38 (1.15)	1.55 (0.85)	<0.001

[1]Mean and standard deviation (SD) for the answers on Likert scale: 1=strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, 5=strongly agree.

3.4 Effects of different factors on PCPs' likelihood of investigating or referring in the clinical vignette

Table 5 shows the regression analysis for the association between likelihood of investigation and referral to a specialist and the independent predictors. Country was a significant variable for both of these: Croatian and Slovenian PCPs were less likely to schedule an investigation or refer patients to a specialist than their Bulgarian, Greek, and Romanian colleagues. PCPs in Croatia, Greece, and Slovenia had a significantly lower likelihood of referral than their Bulgarian counterparts, while Romanian PCPs had a significantly increased likelihood. None of the other variables had a significant effect.

4 DISCUSSION

4.1 Main findings

This study examined key factors that could contribute to a primary care delay in the diagnostic process of patients with possible lung cancer. We found significant national differences between the five Balkan region countries in PCPs' direct access to investigations, particularly for advanced imaging. Analysis of the vignette responses showed large differences in specialist referral rates, with the highest rates in Bulgaria and Romania. PCPs from Bulgaria, Greece, and Romania were more likely to schedule relevant investigations.

Table 5. Effects of PCP and practice demographics, system factors, availability of relevant investigations and country on (a) PCPs' likelihood of scheduling an investigation and (b) likelihood of referral patients to a specialist, for a patient with symptoms that could be due to lung cancer.

Statement	a) Effects on PCPs' likelihood of organising an investigation			b) Effects on PCPs' likelihood of referral to a specialist		
	Exp(B)	95% CI	P value	Exp(B)	95% CI	P value
Sex (Male)	0.912	0.478-1.742	0.781	0.806	0.406-1.599	0.536
Type of practice (Urban)			0.899			0.515
Rural	0.823	0.424-1.596	0.564	1.555	0.802-3.015	0.191
Island	1.312	0.264-6.521	0.740	2.198	0.422-11.459	0.350
Mixed	1.028	0.486-2.174	0.943	1.101	0.470-2.580	0.824
Years since graduation (Less than 10)			0.474			0.975
10 to 19	0.948	0.354-2.541	0.916	1.259	0.438-3.616	0.669
20 to 29	0.697	0.267-1.818	0.461	1.105	0.398-3.063	0.848
30 to 39	1.465	0.505-4.249	0.482	1.212	0.405-3.629	0.732
40 or more	1.117	0.201-6.216	0.900	0.784	0.129-4.776	0.792
'Common presentations are covered by local or national guidelines' (Strongly disagree)			0.731			0.662
Disagree	2.017	0.490-8.296	0.331	1.000	0.254-3.940	1.000
Neither agree nor disagree	1.572	0.416-5.936	0.504	1.159	0.316-4.246	0.824
Agree	2.162	0.573-8.162	0.255	1.527	0.423-5.517	0.518
Strongly agree	1.548	0.317-7.547	0.589	0.789	0.152-4.105	0.778
'We have access to a fast-track specialist appointment system' (Strongly disagree)			0.324			0.318
Disagree	0.904	0.371-2.202	0.825	0.647	0.266-1.577	0.338
Neither agree nor disagree	1.960	0.655-5.862	0.229	1.015	0.366-2.809	0.978
Agree	0.840	0.329-2.145	0.716	0.833	0.320-2.169	0.708
Strongly agree	1.885	0.465-7.640	0.375	2.130	0.572-7.931	0.259
'Patients can self-refer to specialists' (Strongly disagree)			0.263			0.910
Disagree	1.407	0.755-2.621	0.283	1.150	0.588-2.247	0.683
Neither agree nor disagree	0.941	0.377-2.348	0.896	1.190	0.470-3.013	0.713
Agree	3.676	0.979-13.807	0.054	0.868	0.341-2.212	0.768
Strongly agree	2.059	0.474-8.952	0.335	1.696	0.414-6.955	0.463
Number of relevant investigations available (None)			0.376			0.257
One	0.250	0.024-2.622	0.248	0.160	0.028-0.907	0.038
Two	0.365	0.043-3.104	0.356	0.358	0.091-1.404	0.141
Three	0.763	0.049-11.952	0.847	0.552	0.065-4.654	0.585
Four	0.552	0.060-5.069	0.599	0.198	0.042-0.929	0.040
Five	0.257	0.027-2.400	0.233	0.251	0.049-1.285	0.097

Statement	a) Effects on PCPs' likelihood of organising an investigation			b) Effects on PCPs' likelihood of referral to a specialist		
	Exp(B)	95% CI	P value	Exp(B)	95% CI	P value
Country (Bulgaria)			<.001			<0.001
Croatia	0.188	0.062-0.572	0.003	0.286	0.098-0.840	0.023
Greece	0.657	0.179-2.414	0.527	0.160	0.042-0.611	0.007
Romania	1.600	0.544-4.705	0.393	3.473	1.544-7.813	0.003
Slovenia	0.210	0.063-0.694	0.011	0.345	0.115-1.033	0.057
Constant	7.205		0.145	1.349		0.781

Hosmer–Lemeshow test for effects on PCPs' likelihood of organising an investigation: X^2=3.95, df=8, P=0.863; for effects on PCPs' likelihood of referral to a specialist: X^2=9.77, df=8, P=0.281

PCPs in Bulgaria were less likely to report having access to clinical guidelines than those in the other countries, but PCPs from Slovenia and Croatia were more likely to agree that a fast-track specialist appointment system for patients who may have cancer was available to them. The ability of patients to self-refer was lowest in Slovenia, suggesting that PCPs have a stronger gate-keeping role there. Of the factors that we investigated, a PCPs' country was the only one that had a significant effect on their likelihood of investigating or referring in the clinical vignette.

4.2 Comparison with existing literature

While GP gate-keeping is associated with better overall health outcomes (19), it has been suggested that it may be linked with poorer survival of patients with cancer (20), and delays in cancer diagnosis have been found in some countries with strong gate-keeping systems (UK, Denmark) (4, 21, 22). However, a European study found no link between a higher probability of initial consultation with a GP and poorer cancer survival rates (23) and, of the countries in our study, Slovenia has both the strongest reported GP gate-keeping role and the best lung cancer 5-year survival rate (12).

Several health systems have, like Slovenia and Croatia in our study, developed fast track systems (24–26). While it is still unclear whether reducing cancer diagnostic or treatment wait times results in improved survival, there is evidence that it can result in earlier cancer stage at time of treatment for non-small cell lung cancer (27), and an increase in the number of therapeutic options (28).

Over 80% of PCPs in each of the countries in our study reported direct access plain X-ray imaging, similar levels to those reported in England (29) and the other International Cancer Benchmarking Partnership (ICBP) countries (18). The levels of direct access to advanced imaging varied considerably in our study. This wide range reflects that seen in the ICPC countries, where direct access to MRI machines, for example, ranged from 11.0% to 91.6% (18). Availability of national guidelines in our study seemed inconsistent, with most respondents stating that they 'neither agree nor disagree' that common presentations and advice to refer are covered by these. This indecision may be because of barriers to their use: 75% of GPs in a Canadian study indicated active use of cancer guidelines, but they reported barriers that included not being aware of them, being too busy, and user unfriendliness of the website (30).

We found that the two countries (Bulgaria and Romania) with the lowest levels of direct access to advanced imaging and low levels of access to fast-track specialist appointment systems had also the highest levels of referral to a specialist in the clinical vignette. Our data do not provide an explanation for this result. It may be that higher levels of referral indicate that this option is relatively quick and easy in these countries, so there is less need for PCPs to have direct access to advanced imaging or fast-track systems. We also believe that GPs are aware of the importance of early diagnosis in the event of suspected cancer and that they adapt their action to the characteristics of the system. However, the availability of a fast-track system can be important in early cancer detection, with evidence that it accelerates the diagnostic work-up process and clinical pathway (31). A higher referral rate to secondary care in the two weeks after first consultation, using a fast-track system was associated with earlier detection of lung cancer (32).

While we found no association between PCP demographics or practice characteristics with the decision to investigate or refer, in another study female doctors were associated with a longer system delay, and GPs that provided more services tended to have shorter system delays (33).

4.3 Strengths and limitations of the study

This is the first study that compares the factors underlying PCPs' referral decision-making in patients that might have lung cancer in Balkan region countries. The data come from a survey that was carefully developed and piloted by PCPs, based on their clinical experience, and it includes the views of PCPs who are not usually involved in research (17). The sample was diverse, with participants varying in

terms of years of clinical practice, sex, and site and size of practice.

While low survey response rates are common in primary care and are known to vary between countries, the response rates in our study were comparable to those of a recent ICBP survey, in which response rates varied from 5.5% to 45.6%. We have no data on non-responders, as the survey was anonymous. However, the respondent anonymity might have reduced the risk of social desirability bias.

Participants in this study were recruited by an on-line questionnaire, and they may not be representative of their populations. Although we asked participants about access to relevant investigations, we did not ask them for data on waiting times for these: longer waiting times for tests have been reported be associated with delays in diagnosis (34).

Vignette design is frequently used to study how individual's thoughts, decisions and behaviour are affected by factors that are difficult to study in real situations (35). While vignettes may not be typical of patients seen by participant PCPs in their everyday practice, and there have been concerns about the validity of such research (35), as clinical decision-making is a complex cognitive process. Despite this potential limitation, well-designed vignette studies can be highly generalisable to 'real-life' behaviour (36).

4.4 Implications for practice

Prompt testing and rapid referral to a specialist are important for the early detection of cancer. Although it has low sensitivity, a chest X-ray is still the most important first-line investigation (37,38) and its use has been found to result in earlier cancer detection (39). More recently, direct access to low dose CT (LDCT) by GPs has also been proposed as a way of improving early lung cancer diagnosis rates (40), and this suggests that levels of direct access to advanced imaging need to be improved in the study's participating countries.

While clinical guidelines do not ensure good clinical practice (41), guidelines may speed up the diagnostic process (42), and well-designed cancer referral guidelines need to be easily accessible in the participating countries.

5 CONCLUSIONS

The five Balkan region countries that participated in this study show large differences between their PCPs' levels of direct access to investigations. When their PCPs are faced with a vignette of a patient with a small but significant possibility of having lung cancer, their investigation and referral rates vary considerably. Research is needed to find out whether these findings are reflected in real-life clinical decision-making. To reduce diagnostic delay in lung cancer, levels of direct PCP access to advanced imaging, availability of relevant clinical guidelines, and fast-track referral systems must be improved.

ACKNOWLEDGEMENTS

The authors are grateful to all the PCPs who piloted the questionnaire and completed the survey. They also thank Professor Gordon Taylor, Professor of Medical Statistics of the University of Exeter, United Kingdom, for his expert help with the data analysis.

CONFLICTS OF INTEREST

None declared.

FUNDING

The study was partly supported by the European General Practice Research Network (EGPRN).

ETHICAL APPROVAL

113/08/14 was received from the National Medical Ethics Committee Republic of Slovenia on December 8th, 2014. Other countries' study leads either achieved local ethical approval or gave statements that formal ethical approval was not needed in their jurisdictions.

REFERENCES

1. Gatta G, Mallone S, van der Zwan JM, Trama A, Siesling S, Capocaccia R, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE-5 - a population-based study. Lancet Oncol. 2014;15:23–34. doi: 10.1016/S1470-2045(13)70546-1.
2. Carter JL, Coletti RJ, Harris RP. Quantifying and monitoring overdiagnosis in cancer screening: a systematic review of methods. BMJ. 2015;350. doi: 10.1136/bmj.g7773.
3. Zahl PH, Jørgensen KJ, Gøtzsche PC. Overestimated lead times in cancer screening has led to substantial underestimation of overdiagnosis. Br J Cancer. 2013;109:2014–9. doi: 10.1038/bjc.2013.427.
4. Richards MA. The size of the prize for earlier diagnosis of cancer in England. Br J Cancer. 2009;101:S125–9. doi: 10.1038/sj.bjc.6605402.
5. Woods LM, Coleman MP, Lawrence G, Rashbass J, Berrino F, Rachet B. Evidence against the proposition that "UK cancer survival statistics are misleading": simulation study with National Cancer Registry data. BMJ. 2011;342. doi: 10.1136/bmj.d3399.
6. Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ. 2020;371:m4087. doi: 10.1136/bmj.m4087.
7. Tørring ML, Frydenberg M, Hansen RP, Olesen F, Vedsted P. Evidence of increasing mortality with longer diagnostic intervals for five common cancers: a cohort study in primary care. Eur J Cancer. 2013;49:2187–98. doi: 10.1016/j.ejca.2013.01.025.

8. Neal RD, Tharmanathan P, France B, Din NU, Cotton S, Fallon-Ferguson J, et al. Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. Br J Cancer. 2015;112:S92–107. doi: 10.1038/bjc.2015.48.
9. Butler J, Foot C, Bomb M, Hiom S, Coleman M, Bryant H, et al. The International Cancer Benchmarking Partnership: an international collaboration to inform cancer policy in Australia, Canada, Denmark, Norway, Sweden and the United Kingdom. Health Policy (New York). 2013;112(1-2):148–55. doi: 10.1016/j.healthpol.2013.03.021.
10. Jacobsen MM, Silverstein SC, Quinn M, Waterston LB, Thomas CA, Benneyan JC, et al. Timeliness of access to lung cancer diagnosis and treatment: a scoping literature review. Lung Cancer. 2017;112:156–64. doi: 10.1016/j.lungcan.2017.08.011.
11. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68:394–424. doi: 10.3322/caac.21492.
12. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018;391:1023–75. doi: 10.1016/S0140-6736(17)33326-3.
13. Zadnik V, Žagar T, Primic Žakelj M. Cancer patients' survival: standard calculation methods and some considerations regarding their interpretation. Zdr Varst. 2016;55:144–51. doi: 10.1515/sjph-2016-0012.
14. Rubin G, Berendsen A, Crawford SM, Dommett R, Earle C, Emery J, et al. The expanding role of primary care in cancer control. Lancet Oncol. 2015;16:1231–72. doi: 10.1016/S1470-2045(15)00205-3.
15. de Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. N Engl J Med. 2020;382(6):503–13. doi: 10.1056/nejmoa1911793.
16. Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395–409. doi: 10.1056/nejmoa1102873.
17. Harris M, Taylor G. How health system factors affect primary care practitioners' decisions to refer patients for further investigation: protocol for a pan-European ecological study. BMC Health Serv Res. 2018;18:338. doi: 10.1186/s12913-018-3170-2.
18. Rose PW, Rubin G, Perera-Salazar R, Almberg SS, Barisic A, Dawes M, et al. Explaining variation in cancer survival between 11 jurisdictions in the International Cancer Benchmarking Partnership: a primary care vignette survey. BMJ Open. 2015;5:e007212. doi: 10.1136/bmjopen-2014-007212.
19. Starfield B, Shi L, Macinko J. Contribution of primary care to health systems and health. Milbank Q. 2005;83:457–502. doi: 10.1111/j.1468-0009.2005.00409.x.
20. Vedsted P, Olesen F. Are the serious problems in cancer survival partly rooted in gatekeeper principles? An ecologic study. Br J Gen Pract. 2011;61:e508-12. doi: 10.3399/bjgp11X588484.
21. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. Br J Cancer. 2009;101:S5–8. doi: 10.1038/sj.bjc.6605383.
22. Coleman MP, Forman D, Bryant H, Butler J, Rachet B, Maringe C, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the international cancer benchmarking partnership): an analysis of population-based cancer registry data. Lancet. 2011;377:127–38. doi: 10.1016/S0140-6736(10)62231-3.
23. Harris M, Frey P, Esteva M, Gašparović Babić S, Marzo-Castillejo M, Petek D, et al. How the probability of presentation to a primary care clinician correlates with cancer survival rates: an European survey using vignettes. Scand J Prim Health Care. 2017;35:27–34. doi: 10.1080/02813432.2017.1288692.
24. Prades J, Espinás JA, Font R, Argimon JM, Borrs JM. Implementing a Cancer Fast-track Programme between primary and specialised care in Catalonia (Spain): a mixed methods study. Br J Cancer. 2011;105:753–9. doi: 10.1038/bjc.2011.308.
25. Probst HB, Hussain ZB, Andersen O. Cancer patient pathways in Denmark as a joint effort between bureaucrats, health professionals and politicians - a national Danish project. Health Policy (New York). 2012;105:65–70. doi: 10.1016/j.healthpol.2011.11.001.
26. Department of Health. The NHS Cancer Plan. Dep Heal. 2000:1–98. Accessed 3rd November, 2020 at: http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4014513.pdf.
27. Christensen ED, Harvald T, Jendresen M, Aggestrup S, Petterson G. The impact of delayed diagnosis of lung cancer on the stage at the time of operation. Eur J Cardio-thoracic Surg. 1997;12:880–4. doi: 10.1016/S1010-7940(97)00275-3.
28. Lo DS, Zeldin RA, Skrastins R, Fraser IM, Newman H, Monavvari A, et al. Time to treat: a system redesign focusing on decreasing the time from suspicion of lung cancer to diagnosis. J Thorac Oncol. 2007;2:1001–6. doi: 10.1097/JTO.0b013e318158d4b6.
29. Nicholson BD, Oke JL, Rose PW, Mant D. Variation in direct access to tests to investigate cancer: a survey of english general practitioners. PLoS One. 2016;11: e0159725. doi: 10.1371/journal.pone.0159725.
30. Sahota IS, Kostaras X, Hagen NA. Improving access to cancer guidelines: feedback from health care professionals. Curr Oncol. 2015;22:392–8. doi: 10.3747/co.22.2704.
31. Hansen RP, Vedsted P, Sokolowski I, Søndergaard J, Olesen F. Time intervals from first symptom to treatment of cancer: a cohort study of 2,212 newly diagnosed cancer patients. BMC Health Serv Res. 2011;11:284. doi: 10.1186/1472-6963-11-284.
32. Maclean R, Jeffreys M, Ives A, Jones T, Verne J, Ben-Shlomo Y. Primary care characteristics and stage of cancer at diagnosis using data from the national cancer registration service, quality outcomes framework and general practice information. BMC Cancer. 2015;15:500. doi: 10.1186/s12885-015-1497-1.
33. Hansen RP, Vedsted P, Sokolowski I, Søndergaard J, Olesen F. General practitioner characteristics and delay in cancer diagnosis: a population-based cohort study. BMC Fam Pract. 2011;12:100. doi: 10.1186/1471-2296-12-100.
34. Aldridge S, The Strategy Unit. Early diagnosis of cancer: evidence review. 2020. Accessed 23rd August, 2021 at: https://www.strategyunitwm.nhs.uk/sites/default/files/2021-04/20210407Early diagnosis of cancer_FINAL_0.pdf.
35. Evans SC, Roberts MC, Keeley JW, Blossom JB, Amaro CM, Garcia AM, et al. Vignette methodologies for studying clinicians' decision-making: validity, utility, and application in ICD-11 field studies. Int J Clin Heal Psychol. 2015;15:160–70. doi: 10.1016/j.ijchp.2014.12.001.
36. Hrisos S, Eccles MP, Francis JJ, Dickinson HO, Kaner EF, Beyer F, et al. Are there valid proxy measures of clinical behaviour? A systematic review. Implement Sci. 2009;4. doi: 10.1186/1748-5908-4-37.
37. Bradley SH, Grice A, Neal RD, Abraham S, Rodriguez Lopez R, Shinkins B, et al. Sensitivity of chest X-ray for detecting lung cancer in people presenting with symptoms: a systematic review. Br J Gen Pract. 2019;69:E827–35. doi: 10.3399/bjgp19X706853.
38. Stapley S, Sharp D, Hamilton W. Negative chest X-rays in primary care patients with lung cancer. Br J Gen Pract. 2006;56:570–3.
39. Kennedy MPT, Cheyne L, Darby M, Plant P, Milton R, Robson JM, et al. Lung cancer stage-shift following a symptom awareness campaign. Thorax. 2018;73:1128–36. doi: 10.1136/thoraxjnl-2018-211842.
40. Bradley SH, Kennedy MPT, Neal RD. Recognising lung cancer in primary care. Adv Ther. 2019;36:19–30. doi: 10.1007/s12325-018-0843-5.
41. Rubin GP, Saunders CL, Abel GA, Mcphail S, Lyratzopoulos G, Neal RD. Impact of investigations in general practice on timeliness of referral for patients subsequently diagnosed with cancer: analysis of national primary care audit data. Br J Cancer. 2015;112:676–87. doi: 10.1038/bjc.2014.634.
42. Neal RD, Din NU, Hamilton W, Ukoumunne OC, Carter B, Stapley S, et al. Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: analysis of data from the UK General Practice Research Database. Br J Cancer. 2014;110:584–92. doi: 10.1038/bjc.2013.791.