OVERDIAGNOSIS: AN UNRECOGNISED AND GROWING WORLDWIDE PROBLEM IN HEALTHCARE

PREDIAGNOSTICIRANJE: NEPREPOZNANA IN RAZŠIRJENA SVETOVNA TEŽAVA V ZDRAVSTVU

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ABSTRACT

Keywords:
overdiagnosis, overdetection, disease mongering

Overdiagnosis is the diagnosis of deviations, abnormalities, risk factors, and pathologies that in themselves would never cause symptoms (this applies only to risk factors and pathology), would never lead to morbidity, and would never be the cause of death. Therefore, treating an overdiagnosed condition (deviation, abnormality, risk factor, pathology) cannot, by definition, improve the patient's prognosis, and can therefore only be harmful.

Overdiagnosis is an extremely harmful and big problem all over the world, and the problem is increasing. This is especially the case in high-income countries, where more sensitive tests, more testing, more screening and earlier diagnosis is in focus, and more of the same will be implemented in the future. Moreover, disease definitions have been and are still being widened, plus thresholds for treating, e.g. risk factors, have been and are still being lowered. Finally, disease mongering is growing, because it is cheaper and faster to invent new "diseases" than new pharmaceutical drugs.

From the definition of overdiagnosis it can be reasoned that a patient who has been correctly diagnosed and a person who has been overdiagnosed can have the same kind of pathologies. Therefore, at the level of the individual person or patient it can never be verified whether he or she has in fact been correctly diagnosed or overdiagnosed. Therefore, the complexity, dilemmas and pitfalls in understanding what overdiagnosis really is so succinctly captured by this quote from the Danish philosopher Søren Kirkegaard (1813-55): 'Life can only be understood backwards; but it must be lived forwards'.

IZVLEČEK

Ključne besede:
prediagnosticiranje, pretirano odkrivanje, napihovanje bolezni

Postavljanje nepotrebne diagnoze je diagnosticiranje odstopanj, nepravilnosti, dejavnikov tveganja in patologij, ki same po sebi nikoli ne povzročajo simptomov (to se nanaša le na dejavnike tveganja in patologije), nikoli ne prehajajo v bolezen ter niso nikoli vzrok za smrt osebe. S tega vidika zdravljenje zmotno prepoznanega stanja (odstopanje, nepravilnost, dejavnik tveganja, patologija) po sami definiciji ne more izboljšati napovedi pacientovega zdravja ter mu lahko le škoduje.

Prediagnosticiranje je izjemno škodljiva in razširjena težava v svetu, sam pojav pa se hitro širi. Predvsem je prisotno v državah z visokimi prihodki, kjer izvajajo presejalne programe, več vrst testiranj in imajo občutljivejše teste, v ospredju pa je predvsem zgodnje odkrivanje bolezni in postavljanje diagnoze. V prihodnosti bo tega vse več. Definicije bolezni se vse bolj razširjajo, meje začetka zdravljenja, na primer dejavnikov tveganja, se pa še vedno nižajo. Napihovanje bolezni je vse pogostejše, saj je ceneje in hitreje ustvariti nove »bolezni« kot izdelati nova farmacevtska zdravila.

Iz same definicije je prediagnosticiranje lahko upravičeno le tako, da imata pacient s pravilno diagnozo in oseba, ki so ji postavili napačno diagnozo, enako vrsto patologij. Tako lahko na stopnji posameznih pacientov ugotovimo in preverimo, če so prejeli pravilno ali pretirano diagnozo. Zapletene dileme in pasti pri razumevanje postavljanja zmotne diagnoze je zelo jedrnato povzeto v citatu danskega filozofa Sørna Kirkegaarda (1813-1855): »Življenje lahko razumemo samo za nazaj, živeti pa ga je treba naprej«.

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Overdiagnosis is the diagnosis of deviations, abnormalities, risk factors, and pathologies that in themselves would never cause symptoms (this applies only to risk factors and pathology), would never lead to morbidity, and would never be the cause of death (1). Therefore, treating an overdiagnosed condition (deviation, abnormality, risk factor, pathology) cannot, by definition, improve the patient's prognosis, and can therefore only be harmful (2). Overdiagnosis is often mistaken from overtreatment and overuse; however, these are three separate concepts with some overlap: Treatment of overdiagnosed conditions is one category of overtreatment. Another type of overtreatment is when the best available scientific evidence shows that the treatment has no beneficial effect(s) on the diagnosed condition and may even be harmful (3). Overuse, better described as overutilisation, is the 'establishment of standard practice in health services or systems that do not provide net benefit to patients or citizens' (3). Overutilisation does not necessarily lead to overdiagnosis or overtreatment, but the risk increases proportionally with the degree of overutilisation. When discussing the three concepts (overdiagnosis, overtreatment and overuse), it should be recognised that they can have different causes and drivers as to why they appear, and especially the consequences of overdiagnosis, overtreatment and overuse can be very different.

Overdiagnosis is an extremely harmful and big problem all over the world, and the problem is increasing. This is especially the case in high-income countries, where more sensitive tests, more testing, more screening and earlier diagnosis are in focus, and more of the same will be implemented in the future. Moreover, disease definitions have been, and are still being, widened, plus thresholds for treating, for example, risk factors have been, and are still being, lowered. Finally, disease mongering is growing, because it is cheaper and faster to invent new "diseases" than new pharmaceutical drugs.

From the definition of overdiagnosis it can be reasoned that a patient who has been correctly diagnosed and a person who has been overdiagnosed can have the same kind of deviations, abnormalities, risk factors or pathologies. Therefore, at the level of the individual person or patient, it can never be verified whether he or she has in fact been correctly diagnosed or overdiagnosed. Only at the end of the patient's life we can, for biomedical conditions, confirm whether the diagnosis was correct or iatrogenic. With respect to psychosocial conditions, illnesses and mental disorders, we can never, at the individual level, answer the question conclusively: Correctly diagnosed or overdiagnosed? Therefore, the complexity, dilemmas and pitfalls in understanding what overdiagnosis really is so succinctly captured by this quote from the Danish philosopher Søren Kirkegaard (1813-55): 'Life can only be understood backwards; but it must be lived forwards'.

Overdiagnosis can be investigated both in phenomenological perspectives and in epidemiological designs.

Using a phenomenological perspective, informants who are most likely overdiagnosed or informants that have had the experience of being overdiagnosed (false positives) for a short period of time can be interviewed: Hansson et al. interviewed 15 men who, via screening, were (over) diagnosed with an abdominal aortic aneurism (AAA) with a median aorta-diameter of 32 mm (4). The AAA was by some of the men described as "a ticking bomb inside your stomach" (4). Another example from a qualitative study was focus group interviews with lung cancer CT screening participants who had had an abnormal screening result later confirmed to be false positive (5). In the critical period (the time period of three months or more from when the abnormal screening result was acknowledged to the point in time the screening participant was cleared of suspicion of lung cancer), these screening participants reported substantial negative psychosocial consequences from living with the uncertainty of possibly having lung cancer (5). The final example is a mixed-methods study, using a phenomenologically-based patient reported outcome measure, quantifying the psychosocial consequences of a false-positive screening mammography, in which more than 1,300 women were included (6). This study revealed that the women still reported substantial negative psychosocial consequences three years after the false-positive screening result (6).

A simple and very robust way to estimate the degree of overdiagnosis in a screening RCT (randomised controlled trial) would be to estimate the cumulative incidence of the condition screened for in the intervention group and in the control group (7). However, two types of biases are of importance: lead-time bias and contamination of the control group. A very didactical example of this is the European Randomized Study of Screening for Prostate Cancer (ERSPC): after 9 years of follow-up, the ratio between one prevented death of prostate cancer and men overdiagnosed with prostate cancer was 1:47, while this ratio decrease to 1:37 at the 11-year follow-up, and to 1:27 after 13 years of follow-up (8-10). Here it is obvious that lead-time is of importance; however, more than 20% of the men in control also had a PSA test in the ERSPC. These two biases, respectively, underestimate and overestimate the degree of overdiagnosis. Therefore, the "true" degree of overdiagnosis is hard to assess; however, it is substantial in PSA screening.

Harris and colleagues have suggested a taxonomy describing seven different categories of harms of screening that could be explored, namely: finan¬cial strain, hassles/

inconveniences, medical costs, op¬por¬tu¬nity costs, physical harms, psy¬cholo¬gi-cal harms, and societal costs (11). In addition, we have identified empirical evidence for an additional category: work-related costs (12). These eight different categories of harms could also be applied to research about harms of overdiagnosis.

In many aspects of overdiagnosis, there is a substantial absence of scientific evidence, e.g. cancer screening (13). Internationally, there is, however, a growing awareness and interest in research about overdiagnosis, especially how to prevent it (14). But before we can answer this questions of how to decrease and prevent overdiagnosis, much more research is needed, e.g. about: the causes and drivers of overdiagnosis; the harms of overdiagnosis; the consequences of overdiagnosis; and how to communicate overdiagnosis to physicians, other healthcare professionals, politicians, healthcare providers and stakeholders, and most importantly, the general population.

CONFLICTS OF INTEREST

The author reports no conflicts of interest.

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ETHICAL APPROVAL

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E-HEALTHCARE FOR DIABETES MELLITUS TYPE 2 PATIENTS – A RANDOMISED CONTROLLED TRIAL IN SLOVENIA

E-ZDRAVSTVENA OSKRBA BOLNIKOV S SLADKORNO BOLEZNIJO TIPA II – RANDOMIZIRANA KONTROLIRANA RAZISKAVA V SLOVENIJI

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ABSTRACT

Keywords:
diabetes mellitus,
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status, HbA1c,
family practice

Background. Telemonitoring and web-based interventions are increasingly used in primary-care practices in many countries for more effective management of patients with diabetes mellitus (DM). A new approach in treating patients with diabetes mellitus in family practices, based on ICT use and nurse practitioners, has been introduced and evaluated in this study.

Method. Fifteen Slovene family practices enrolled 120 DM patients treated only with a diet regime and/or tablets into the study. 58 of them were included into the interventional group, and the other 62 DM patients into the control group, within one-year-long interventional, randomised controlled trial. Patients in the control group had conventional care for DM according to Slovenian professional guidelines, while the patients in the interventional group were using also the eDiabetes application. Patients were randomised through a balanced randomisation process.

Results. Significant reductions of glycated haemoglobin (HbA1c) values were found after 6 and 12 months among patients using this eDiabetes application (p<0.05). Among these patients, a significant correlation was also found between self-monitored blood pressure and the final HbA1c values. Diabetic patients' involvement in web-based intervention had only transient impact on their functional health status.

Conclusion. This eDiabetes application was confirmed to be an innovative approach for better self-management of DM type 2 patients not using insulin. Both a significant reduction of HbA1c values and a significant correlation between the average self-measured blood pressure and the final HbA1c values in the interventional group were found. Nurse practitioners – as diabetes care coordinators – could contribute to better adherence in diabetes e-care.

IZVLEČEK

Ključne besede:
sladkorna bolezen,
telemedicina,
funkcionalni
zdravstveni status,
HbA1c, družinska
medicina

Uvod. Zdravstvena oskrba na daljavo in z uporabo interneta se za učinkovitejšo obravnavo bolnikov s sladkorno boleznijo (SB) pospešeno uporablja v osnovnem zdravstvu številnih držav. Namen raziskave je bil preizkusiti in ovrednotiti pristop k zdravljenju bolnikov s sladkorno boleznijo, ki temelji na uporabi sodobne informacijsko-komunikacijske tehnologije (IKT) in na ustrezno izobraženi medicinski sestri, kot koordinatorju tovrstne zdravstvene oskrbe v ambulanti družinske medicine.

Metode. Petnajst slovenskih ambulant družinske medicine je vključilo 120 bolnikov s SB, ki niso bili zdravljeni z inzulinom. Oseminpetdeset bolnikov je bilo vključenih v intervencijsko skupino in 62 bolnikov v kontrolno skupino; randomizirana kontrolirana raziskava je trajala eno leto. Bolniki v kontrolni skupini so bili deležni običajne oskrbe, po slovenskih strokovnih smernicah, medtem ko so bolniki v intervencijski skupini lahko uporabljali še spletno aplikacijo eDiabetes. Randomizacija je opravljena po metodi uravnoteženega razvrščanja v skupine.

Rezultati. Pomembno zmanjšanje vrednosti HbA1c je bilo ugotovljeno po 6 in 12 mesecih v skupini bolnikov, ki so uporabljali aplikacijo eDiabetes (p<0,05). V isti skupini je ugotovljena pomembna korelacija med vrednostmi samoizmerjenega sistoličnega tlaka in končnimi vrednostmi HbA1c. Uporaba aplikacije eDiabetes je imela le prehoden vpliv na funkcionalni status bolnikov, izmerjen z WONCA-COOP.

Zaključki. Uporaba internetne aplikacije za vodenje in nadzor sladkorne bolezni lahko pomembno vpliva na zmanjšanje vrednosti HbA1c in na povezavo HbA1c s samoizmerjenimi vrednostmi krvnega tlaka pri sladkornih bolnikih, ki niso zdravljeni z inzulinom. Diplomirane medicinske sestre v vlogi koordinatorja e-oskrbe lahko prispevajo k boljšemu sodelovanju bolnikov s SB.

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1 INTRODUCTION

Diabetes mellitus (DM), defined as a "group of common metabolic disorders that share the phenotype of hyperglycaemia", is a very relevant and growing public health problem in all developed countries. Among the most important treatment goals for adults with diabetes are: good glycaemic control (HbA1c<7.0% and fewer hyperglycaemia symptoms), regulation of blood pressure and serum lipids, prevention of complications, and patient education about DM, nutrition and exercise. The measurement of glycated haemoglobin and self-monitoring of blood glucose are standard methods for assessing long-term glycaemic control (1, 2).

Changes in the functional health status of patients with chronic diseases could have a strong impact on the outcome measures of treatment. Studies suggest that the COOP-WONCA charts are a valuable and reliable tool for measuring functional health status in primary care (3, 4). Results from many clinical studies demonstrate the enormous potential of information and communication technology (ICT) to improve health-care outcomes for chronic diseases, including DM. For many researchers, diabetes mellitus is recognised as the chronic condition most suited for self-monitoring, telemonitoring, and the use of electronic Personal Health Records (ePHRs) (5-15). ePHR is defined as an "application through which individuals can access, manage and share their health information in a private, secure, and confidential environment." (16). PHRs could have an important impact on the cost and quality of chronic disease management (10, 11, 16, 17).

The use of ICT in the prevention, diagnosis, treatment, and monitoring of different medical conditions, including DM, is particularly important for primary health-care (PHC) providers (5, 7, 8, 18). In recent research, computer-supported decision-making, accessibility of personal e-health data, and e-prescription were identified by patients, as well as physicians and nurses, as the most important areas for further e-Health development in Slovenia (17).

Web-based interventions are increasingly being used in PHC practices in all developed countries, allowing more effective DM management (17-20). However, it remains a challenge over time to maintain patient interest in blood glucose (BG) control, even with the assistance of ICT (14, 21, 22).

Since 2011, so-called nurse practitioners who are educated and competent especially for disease prevention, health education and the management of the most common chronic diseases according to the prescribed protocols, have been introduced in many Slovenian family practices. The addition of nurse practitioners as diabetes care coordinators has brought better adherence to diabetes treatment and allowed the achievement of higher standards in primary healthcare for patients with DM (5, 17, 23-25).

Numerous studies, systematic reviews, and meta-analyses find a significant potential for contemporary ICT, including the use of electronic personal health records and mobile phone reminders, to improve the glycaemic control of DM type 2 patients not using insulin (5-7, 10- 14, 20, 22). Very few studies have examined the simultaneous effects of remote e-treatment and coordination by nurse practitioners integrated into local family practice teams on glycaemic control, blood pressure, serum lipids, body mass index, and the functional health status of diabetic patients (10, 17, 25).

1.1 Purpose and Objectives

The purpose of the study was to introduce and evaluate a new approach in treating patients with diabetes mellitus type 2, based on ICT use and nurse practitioners as the diabetes care coordinator.

The main hypotheses of the research were:

- web-based supported healthcare for DM type 2 patients not using insulin can significantly improve treatment outcomes compared to usual healthcare, and

- web-based supported healthcare has an effect on the functional health status of patients with DM type 2.

2 METHODOLOGY AND STUDY DESIGN

2.1 Participants and Sampling

This was an interventional, randomised controlled study of patients with DM type 2, treated only with a diet regime and/or tablets. Slovene diabetics treated with insulin are usually treated by diabetes care units, and were therefore not included in this study.

Patients were selected from 22 solicited family practices from 6 different regions in Slovenia (Posavje, Zasavje, Štajerska, Gorenjska, Primorska, and Ljubljana). To be included, family practices had at least 1,000 patients, a nurse with secondary-school training, and a qualified nurse with higher education (the diabetes care coordinator). This cluster sampling was chosen to give the best estimate for the Slovenian population of patients with DM type 2 not using insulin.

A computerised randomisation programme assigned patients to the interventional or the control group through a balanced randomisation process using the last four patients. Randomisation was carried out for all practices simultaneously, but not at the level of individual practices. Due to its design, the study could not be blinded; the staff at each practice was aware of patient allocation.

The randomisation process is presented in Figure 1.

The inclusion period was 3 months and the next criteria were the same for both groups:

- between the ages of 18 and 75;

- type 2 diabetes treated with non-pharmacological interventions or/and tablets (patients who are not using insulin);

- having Internet connection and access to a computer;

- having a mobile phone;

- sufficient Internet and e-mail skills (which were checked by a short questionnaire).

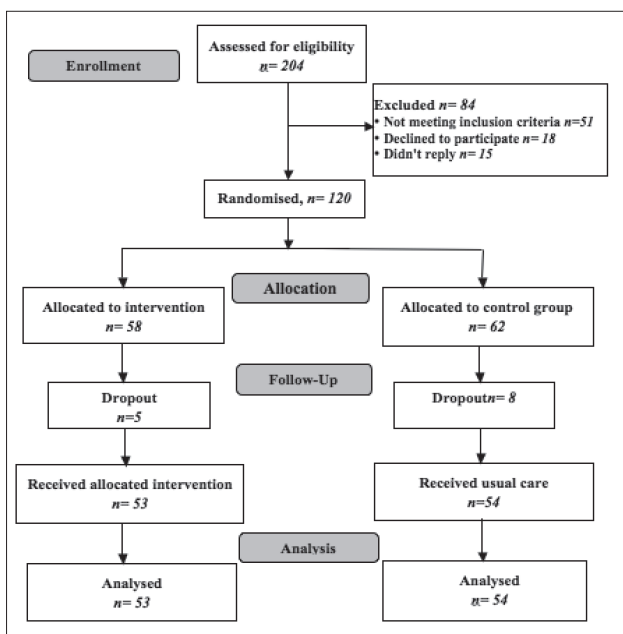The time frame for the follow-up of each patient was one year.

Figure 2. Flow diagram for the eDiabetes study.

2.2 Intervention

Patients randomised in the control group had the conventional care for diabetic patients, according to Slovenian professional guidelines. Patients in the interventional group had, in addition to conventional care, access to the eDiabetes application.

Nurse practitioners could comment about measurements made by patients in the interventional group and give advice about lifestyle. General practitioners gave advice about medications. Some medications, but not a significant number, were altered during the study period for both groups.

The comparison between the diabetes care offered to the control group and the interventional group is shown in Table 1.

Table 1. Comparison between conventional and eDiabetes care.

Parameters	Conventional diabetes care	eDiabetes care
No. of check-ups by nurse practitioner **in family practice**	2-4 times a year	2-4 times a year
No. of check-ups by family practitioner	2 times a year and for exacerbations	2 times a year and for exacerbations
Laboratory tests (HbA1c, FBG, creatinine, serum lipids, transaminases, albumin in urine)	1- 2 times a year	1- 2 times a year
Ophthalmologist examination	Once a year	Once a year
Internist and other specialists	For exacerbations	For exacerbations
e-consultation with nurse practitioner	NO	YES
e-consultation with family practitioner or specialists	NO	NO
SMS reminders	NO	YES
Access to eDiabetes application	NO	YES
Answering e-questionnaires	NO	Every two months

2.3 Software Description

The eDiabetes application, designed in collaboration with experienced ICT experts, consisted of a web portal for patients and health-care providers (26), with a patient-oriented interface for individualised care, and a web server for a repository and education material (http://eoskrba.si). The educational material included informational handouts, web addresses, articles, and instructions to help diabetic patients better manage their condition.

Every two weeks patients in the experimental group recorded data, including their body weight, blood pressure, diet, and physical activity. The last parameter was evaluated on a 7-point Likert scale. Every 6-8 weeks patients completed the COOP-WONCA charts. These are comprised of seven parameters designed to measure functional health status using words and pictures to represent and assess: physical fitness, feelings, daily

activities, social activities, change in health, overall health, and pain. These charts are rated using a five-point scale, with higher scores indicating a worse functional status (3, 4).

The application automatically sent users reminders by simple e-mail and SMS: "Please enter your blood sugar /or other parameters/ into the eDiabetes application". These reminders were sent if a user had not entered body weight, blood pressure, physical activity, and diet data within 2 weeks of the deadline or not completed the COOP-WONCA questionnaire within 8 weeks. Reminders were also e-mailed to the diabetes care coordinators.

In case of medical emergencies, a warning was issued to immediately contact the medical emergency services. More than 1000 SMS and e-mail reminders were sent during the study. E-mail communication between the patients and family practices was less common, with fewer than 100 such e-mails registered during the study. Nurse practitioners and physicians mostly commented directly with patients on the eDiabetes inputs during office visits.

2.4 Outcome Measures

The primary outcome measure was the change from baseline of HbA1c at 1 year. This outcome was calculated as the difference between baseline and final HbA1c for both groups.

The secondary outcome measures were the change from baseline of: (a) HbA1c at 6 months, (b) Body Mass Index (BMI) at 1 year, (c) Patients' Functional Health Status indicated by the COOP-WONCA Questionnaire at 6 months and 1 year, (d) blood lipids at 1 year, and (e) diastolic and systolic blood pressure at 6 month and 1 year.

The minimal clinically important difference (MCID) was set to one standard error of the mean in the outcome score (27, 28).

2.5 Power Calculation

A sample size of 60 patients per group was necessary to achieve 80% power at a two-sided 5% significance level and a hypothetical dropout rate of up to 15%.

No adjustment of the sample size was made for the potential clustering of scores within a single practice.

2.6 Data Analysis

The statistical analysis of data collected in the eDiabetes application and from the patient health record was performed using SPSS Statistics 21 and the EXCEL version of Microsoft Office 2010. The unequal variances t test was used to assess changes of the target interval outcomes between the two groups at baseline and within each group at 1 year. The Wilcoxon rank sum test was used to assess

differences in the COOP-WONCA results (29). Multivariate analysis was used to find factors that might be related to changes of HbA1c. The degree of statistical significance was defined as $p < 0.05$.

3 RESULTS

Twenty-two Slovene family practices applied to participate in the study, of which 15 enrolled at least one patient. Fifty-eight participants were randomly assigned to the interventional group and the remaining 62 to the control group. The first participant entered the study in April 2012 and the last consultation was completed in December 2013. Fifty-three participants in the interventional group and 54 in the control group completed the first office consultation, which included the study protocol's laboratory investigations. Participant characteristics are presented in Table 2.

Significant statistical differences ($p < 0.05$) were also not found for any parameter regarding age, education, smoking status, or medication use.

Table 2.   Baseline characteristics of participants.

Characteristic, number (percentage)	Inter-vention group	Control group	Total	Statistical diffe-rence (p)
Male, n (%)	36 (30)	37 (30.8)	73 (60.8)	<0.05
Female, n (%)	22 (18.3)	25 (20.8)	47 (39.1)	>0.05
Average age, years (SD)	56.3 (10.5)	54.7 (11.1)	55.5 (10.7)	>0.05
Education, n (%)				
Elementary school or less	4 (3.3)	5 (4.2)	9 (7.5)	>0.05
High school	13 (10.8)	13 (10.8)	26 (21.6)	>0.05
College or university	21 (17.5)	15 (12.5)	36 (30)	<0.05
Master, PhD or specialisation	8 (6.7)	11 (9.2)	19 (15.9)	<0.05
Unknown	12 (10)	18 (15)	30 (25)	<0.05
Diabetes duration in years (standard deviation)	5.1 (5.7)	5.7 (4.8)	5.5 (5.3)	>0.05
Only diet, n (%)	13 (10.8)	15 (12.5)	28 (23.3)	>0.05
Diet and oral antidiabetic medication, n (%)	21 (17.5)	20 (16.7)	41 (34.2)	>0.05
Diet, oral antidiabetic and other medication, n (%)	24 (20)	27 (22.5)	51 (42.5)	<0.05

Statistically significant differences (p<0.05) were not found between the initial or follow-up parameters of either group, or the average scores of the COOP-WONCA functional assessment charts. Total cholesterol was the only parameter with a significantly lower level in the control group (CHOL1, p=0.046), compared to the interventional group.

The paired sample t-test showed baseline glycated haemoglobin (HbA1c) as the only primary outcome measure in the interventional group having a statistically significant lower intermediate HbA1C (p=0.007, n=31) and final HbA1C (p=0.005, n=40) values compared to the initial one. Significant differences were not found between the intermediate HbA1c and final HbA1C values.

A secondary outcome measure, the intermediate average value of the COOP-WONCA score in the interventional group, was found to be statistically significantly lower compared to its initial average value (p=0.047, n=24).

Intermediate and final values of all other monitoring parameters (systolic and diastolic blood pressure, total cholesterol, triglycerides, low and high density lipoproteins, fasting blood glucose, body mass index, COOP-WONCA questionnaire score, body mass index, and moderate exercise level) were not significantly different compared to their initial values for either group. Descriptive statistics for baseline and final values of monitoring parameters, as well as of the four regularly self-recorded parameters, are presented in Table 3.

For the interventional group, the transient increase of the average COOP-WONCA score after 6 months (p=0.047, n=34) was caused mainly by elevated values of two of the seven sub-items: "feelings" (p=0.046) and "pain" (p=0.031).

Among the 58 participants in the interventional group, 49 used the application eDiabetes. During the observation period, forty-five participants entered at least once all the five self-monitoring parameters, which were weight (SELF-WT), systolic blood pressure (SELF-SBP), diastolic blood pressure (SELF-DBP), fasting blood glucose (SELF-FBG), and COOP-WONCA charts. The average number of these data entry per participant in the intervention group was: 13.26 for SELF-WT, 12.06 for SELF-SBP and SELF-DBP, 12.96 for SELF-BG, and 9.2 for COOP-WONCA.

The average intermediate level of the self-recorded blood glucose (SELF-FBG) was significantly lower in comparison to the initial average level (EFBG1, p=0.006, n=46), as well as to the final average level (EFBG3, p=0.033, n=42). Average values of the other three self-recorded parameters (SELF-SBP, SELF-DBP, and SELF-WT) did not vary significantly. Significant positive correlation was found between the final HbA1c and the self-measured diastolic blood pressure (p=0.01, n=37). A significant

Table 3. Baseline and final values of key monitoring parameters.

PARAMETER, unit	STUDY GROUP	MEAN (SD) BASELINE	MEAN (SD) FINAL
HbA1c, %	Interv.	7.1 (1.5)	6.4 (0.9)
HbA1c, %	Control	6.8 (1.2)	6.7 (1.5)
SBP, mm Hg	Interv.	138.4 (16.4)	137.0 (17.8)
SBP, mm Hg	Control	136.9 (17.4)	138.3 (18.4)
DBP, mm Hg	Interv.	84.5 (11.4)	84.6 (7.9)
DBP, mm Hg	Control	83.3 (10.5)	82.9 (9.4)
CHOL, mmol/l	Interv.	5.1 (1.3)	5.1 (1.4)
CHOL, mmol/l	Control	4.6 (1.1)	4.4 (1.1)
TG, mmol/l	Interv.	2.5 (1.4)	2.5 (1.4)
TG, mmol/l	Control	2.0 (1.1)	2.0 (1.1)
LDL, mmol/l	Interv.	3.0 (1.1)	3.0 (1.3)
LDL, mmol/l	Control	2.6 (1.0)	2.5 (1.0)
HDL, mmol/l	Interv.	1.1 (0.3)	1.1 (0.3)
HDL, mmol/l	Control	1.1 (0.4)	1.1 (0.3)
FBG, mmol/l	Interv.	8.1 (2.2)	8.0 (2.1)
FBG, mmol/l	Control	8.0 (2.6)	8.2 (2.6)
BMI, kg/m2	Interv.	32.6 (5.1)	32.0 (4.7)
BMI, kg/m2	Control	31.8 (4.9)	31.8 (5.1)
WONCA, score	Interv.	2.1 (0.7)	2.2 (0.5)
WONCA, score	Control	1.9 (0.6)	1.9 (0.7)
SELF-SBP, mm Hg	Interv.	135.0 (1.7)	134.03 (14.3)
SELF-DBP, mm Hg	Interv.	82.4 (10.2)	81.3 (7.3)
SELF-WT, kg	Interv.	97.9 (17.8)	96.1 (14.2)
SELF-FBG, mmol/l	Interv.	7.7 (2.2)	7.2 (1.5)

Legend: HbAc=glycated haemoglobin; SBP=systolic blood pressure; DBP=diastolic blood pressure; TG=triglycerides; LDL=low density lipoproteins; HDL=high density lipoproteins; FBG=fasting blood glucose; BMI=body mass index; WONCA=questionnaire about functional health status; SELF-SBP=self-measured systolic blood pressure; SELF-DBP=self-measured diastolic blood pressure; SELF-WT=self-measured weight; SELF-FBG=self-measured fasting blood glucose; interv=interventional; SD=standard deviation.

negative correlation was found between the number of inputs to the application and the average values of self-recorded systolic blood pressure (SELF-SBP, p=0.004, n=46), as well as to the EHbA1c-3 values (p=0.006, n=45). Significant correlation between the number of inputs and other self-measured parameters was not found.

Regression analysis showed four predictors of lower final values of HbA1c in the interventional arm. These were: lower baseline HbA1c (p<0.001, ß=0.802), lower average value of self-measured systolic blood pressure (p<0.001, ß=0.624), lower final value of total cholesterol (p=0.018, ß=-0.225), and lower value of self-measured fasting

blood glucose (p=0.005, ß=-0.384). R2 values showed that 81.1% of EHbA1c-3 variance was explained by the above-mentioned predictors (R=0.901, RSquare=0.811, Adjusted R Square=0.783 and Std. Error=0.4671).

4 DISCUSSION

4.1 Discussion about Methodology

In terms of the distribution by age, gender, medication and diabetes duration in years, the computerised randomisation process resulted in the almost ideal allocation of patients in both study arms (p>0.05). Despite some evidence about lower Internet use among less educated and older diabetic patients (9, 14, 19), these two sub-groups were adequately represented among those meeting the inclusion criteria. Statistically significant differences (p<0.05) between patients in interventional and control group were found in 2 groups with highest education. Statistically important differences were not found when merging participants from the "College or university" and "Master, PhD, or specialisation" subgroups in one group, which means that distribution of participants by level of education could not affect the results.

The main barriers to more extensive enrolment in the study and better adherence of enrolled patients were: low motivation of practitioners and nurses in some family practices, patients' lack of computer and/or access to the Internet (n=29), and patients' lack of sufficient e-skills (n=17). The importance of PHC provider adherence to different forms of web-based diabetic care is well documented in the literature (5, 13, 16-18, 20-22).

4.2 Discussion about the Main Results

The results of this research confirmed the hypotheses about improvement in treatment outcomes compared to usual healthcare, and rejected the presumption of eDiabetes application impact on the functional health status of patients with DM type 2.

A significant negative correlation found between the number of inputs to the application and the average values of self-recorded systolic blood pressure (p=0.004), as well as to the EHbA1c-3 values (p=0.006) showed that a higher number of inputs correlated with lower final HbA1c and SBP values. This can be understood as confirmation of the impact of application on the improvement of key parameters and, consequently, as the most important result of the study.

The result of the regression analysis – the list of four significant predictors that help explain 81.1% of the final HbA1c values – is also a valuable part of this study. The connections between the final and initial HbA1c values, as well as between self-measured blood glucose and final cholesterol levels, were expected.

The main limitation of this randomised controlled trial was poor adherence of some primary-care practices and, consequently, a smaller number of enrolled patients in both groups.

4.3 Comparing the Results with Previous Studies

However, the strong correlation (p<0.001) between the final HbA1c values and the average self-measured systolic and diastolic blood pressure values was surprising.

There were very few similar reports in the reviewed literature, although significant changes in serum lipids have often been reported (5, 6, 11, 12, 14, 20, 22).

Statistically significant reductions of the HbA1C level in the interventional group, at the first follow-up and the final check-up, were already reported in several previous meta-analyses and systematic reviews (5, 6, 11, 12, 14, 20, 30). However, the patient population of this trial had well-regulated diabetes with slightly elevated baseline HbA1c (7.1% for the interventional and 6.8% for the control group).

The findings of the lower HbA1c and self-measured fasting blood glucose (SELF-BG) for the interventional group, compared to initial values and to the control group, were consistent with previous studies (5, 11, 12, 19-22, 31).

Despite the improvement of laboratory results in the interventional group, there is no clear impact of separate factors, such as nurse practitioners or diabetes care coordinators, educational materials accessible from the application, SMS and e-mail remainders.

5 CONCLUSIONS

The significant reduction of HbA1c values in the interventional group confirmed the application's potential to improve the regulation of DM type 2 in patients who are not using insulin. A significant negative correlation between the number of inputs to the application and the values of either EHbA1c or average self-recorded systolic blood pressure values also suggests the impact of application on the improvement of some key health parameters in these patients.

It seems that the overall impact of the application was also greater engagement of patients with their own healthcare.

Coordinating the care of both groups of diabetic patients was the key part of this study. Nurse practitioners played this important roleas "diabetes care managers".

A better integration of new ICT applications for chronic conditions into well-established forms of healthcare remains a major challenge for primary care.

ETHICAL ISSUES

FUNDING AND STUDY REGISTRATION

ACKNOWLEDGEMENTS

AUTHOR DISCLOSURE STATEMENT

The authors declare they have no relationships, conditions or circumstances that present a potential conflict of interest with the material in this manuscript.

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SMOKING BEHAVIORS IN KOSOVA: RESULTS OF STEPS SURVEY
KADILSKO VEDENJE NA KOSOVU: REZULTATI ANKETE STEPS

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ABSTRACT

Keywords:
prevalence,
smoking, Kosova,
adults

Introduction. Tobacco use continues to be the leading global cause of preventable death. Most of these deaths occur in low and middle-income countries, and this trend is expected to widen further over the next several decades. The overall objective of the study is to describe and analyse the smoking behaviours of adults in Kosova.

Methods. According to the STEPs methodology, 6,400 respondents, aged 15 - 64 years, are selected randomly within each sex and 10-year age-group. Out of 6,400 participants, 6,117 were selected, which is approximately 95.6%.

Results. The prevalence of smoking was higher among males (37.4%) compared with females (19.7%). In all age groups, the prevalence of smoking was higher among males compared with females. Regarding the age group of 15 - 24 years, the prevalence of smoking was 16.0%, but in the age group of 25 - 34 years, it nearly doubled to the rate of 31.9%. We have a smaller increase in the age group of 35 - 44 years, and after the age of 45, it falls gradually.

Conclusions. The prevalence of smoking in Kosova is high compared with other countries in Eastern Europe. In future decades, Kosova will face a high probability of an increased burden of smoking-related diseases.

IZVLEČEK

Ključne besede:
prevalenca,
kajenje, Kosovo,
odrasli

Uvod. Uživanje tobaka je še vedno eden izmed glavnih vzrokov smrti, ki bi jih lahko preprečili. Večina teh smrti se zgodi v državah z nižjim in srednjim prihodkom, po pričakovanjih pa se bo ta trend v naslednjih nekaj desetletjih še povečal. Cilj te študije je opis in analiza kadilskega vedenja odraslih na Kosovu.

Metode. Glede na metodologijo STEPS je bilo naključno izbranih 6.400 anketirancev obeh spolov, starih med 15 in 64 let; razdeljeni so bili v starostne skupine po10 let. Izmed 6.400 anketirancev jih je bilo v študijo vključenih 6.117, kar je približno 95,6%.

Rezultati. Prevalenca kajenja je bila večja med odraslimi moškimi (37,4%) v primerjavi z ženskami (19,7%). V vseh starostnih skupinah je bila prevalenca kajenja višja med moškimi kot med ženskami. V starostni skupini med 15 in 24 let je bila prevalenca kajenja 16,9%, v starostni skupini med 25 in 34 let pa se je skoraj podvojila (31,9%). Prav tako je prisotno manjše povišanje v starostni skupini med 35 in 44 let, po 45. letu pa odstotek postopno pada.

Zaključki. Prevalenca kajenja na Kosovu je v primerjavi z ostalimi državami v Vzhodni Evropi visoka. V prihodnosti se bo Kosovo soočalo z visoko verjetnostjo povišanega bremena zaradi bolezni, povezanih s kajenjem.

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1 INTRODUCTION

Tobacco use continues to be the leading global cause of preventable death. It kills nearly 6 million people annually, and it causes hundreds of billions of dollars in economic damage worldwide. Most of these deaths occur in low and middle-income countries, and this trend is expected to widen further over the next several decades. If current trends continue, by 2030, tobacco will kill more than 8 million people worldwide each year (1). Smoking increases the risk of heart disease, cancer, stroke, and chronic lung disease. Environmental tobacco smoke has been demonstrated to increase the risk of heart disease and cancer among non-smokers. It has also been shown that non-smokers exposed to second hand smoke have a 25% to 35% increased risk of suffering acute coronary diseases, and increased frequency of chronic respiratory conditions (2). Cessations of smoking by current smokers reduce their risk of heart disease, cancer, stroke, and respiratory disease (3).

Tobacco use prevalence in Europe is characterized by large disparities, with Western nations reporting smoking rates generally below 25%, while Eastern nations have smoking rates usually above 30% (4). In total, in the European region, 45% of males and 24% females over 15 years old are smokers (5). Kosova is a country with some specifics, for example, Kosova's economic performance at the last assessment was evaluated as relatively weak as compared to Southeastern Europe. Kosova's economy would need to grow 10% to 12% per annum respectively for the next ten years to reach Albania's and Montenegro's income level (6). The total population in Kosova according to the census of 2011 is 1,739,825 inhabitants (7), Birth rate 15.7‰ and Total Mortality 3.2‰. The mean age of population is estimated to be 30.2 years and life expectancy at birth is 76.7 years: 79.4 years for females and 74.1 for males. In the years 2012 and 2013 the number one cause of death in Kosova were circulatory system diseases and the number two cause were neoplasm's (8). Due to lack of law on statistics and weak implementation of the health law as well as relevant existing by laws, health information flow remains fragmented and weak. Until recently, no reliable epidemiological data were available on the prevalence of smoking in Kosova adults. A study with school children (9) and first year medical students was available (10). In 2011 Kosova conducted the European School Survey Project on Alcohol and Other Drugs (ESPAD) on 15-16 years old school children (11). As this is the first representative population survey conducted in Kosova findings from this survey will help policymakers to develop future public health programmes and interventions. The overall objective of the study is to describe and analyze the smoking behaviors of adults in Kosova.

2 METHODS

A population-based survey for non-communicable diseases risk factors started in September 2010 by adopting the World Health Organization (WHO) STEPs Instrument (12), and the data collection was completed in March 2011. At that time the census of population in Kosova wasn't conducted, therefore the data for households according to the settlements from Statistical Agency of Kosova for 2008 were used (13), in total seven regions, 30 municipalities and 1464 settlements. The two-stage cluster random sampling was designed. Firstly, 120 enumeration areas were selected using probability proportional to size as the primary sampling units, followed by randomly selecting households from them as the secondary sampling units, using the proportion of households in urban and rural areas. Respondents aged 15-64 years old were selected randomly within each gender and 10-year age-group. One resident aged 15 to 64 years within each of the households was recruited for the survey using the Kish method, which provides tool for random selection of one individual from a household (12). The total sample size consisted of 6,400 men and women. The following assumptions for this cross-sectional study were used for sample size calculation: level of confidence 95%, margin of error 5%, baseline level of risk factors 50%, expected response rate 90% and the design effect of 1.5.

The WHO STEPs module is recommended for use on adults in the age group 25-64 years (12). The age group of 15-24 years, which is the optional age group in STEPs, were included in this study because according to the existing data, Kosova has a high percentage of young people in it's population (around 19.3% of population are in this age group) (7) .

2.1 Measurements

STEPs is a sequential process with three steps. Step 1 includes assessment of smoking behaviors, alcohol consumption, physical activity, and fruit and vegetable intake using a structured questionnaire. Step 2 includes physical measurements, i.e. weight, height, waist circumference, hip circumference, blood pressure and heart rate measurements. Step 3 includes blood sampling and blood sugar and cholesterol examination. In this study we present only data of smoking behavior from Step 1 and answers on the core questions: Do you currently smoke any tobacco products, such as cigarettes, cigars or pipes? Do you currently smoke tobacco products daily? How old were you when you first started smoking daily? On average, how many of the following (manufactured cigarettes; Hand-rolled cigarettes; Pipes full of tobacco; Cigars, cheroots, cigarillos) do you smoke each day?

Table 1.   Response proportions by gender.

Age Group (Year)	Men			Women			Both Sexes		
	Eligible	Responded		Eligible	Responded		Eligible	Responded	
	n	n	%	N	n	%	N	n	%
15-24	640	633	98.9	640	637	99.5	1280	1270	99.2
25-34	640	603	94.2	640	607	94.8	1280	1210	94.5
35-44	640	594	92.8	640	610	95.3	1280	1204	94.1
45-54	640	624	97.5	640	607	94.8	1280	1231	96.2
55-64	640	594	92.8	640	608	95.0	1280	1202	93.9
15-64	3200	3028	94.6	3200	3089	96.5	6400	6117	95.6
25-64	2560	2415	94.3	2560	2432	95.0	5120	4847	94.7

Current smokers were defined as persons who reported smoking any tobacco products, such as cigarettes, cigars, or pipes daily or non-daily irrespective of the quantity and current daily smokers if they smoked ≥1 cigarette per day (12).

2.2 Statistical Analysis

Statistical analysis was undertaken using SPSS version 22.0. As age and sex are strong determinants of smoking, descriptive results were presented for men and women separately and stratified by age group. Data are presented as percentage and 95% confidence interval. Chi-square test or Fisher exact test was performed to test the differences in proportions of qualitative variables between groups, Mann Whitney U test for testing the difference between quantitative variables when distribution was not normal and Student t-test when distribution was normal. The level $P<0.05$ was considered as statistically significant.

Out of 6,400 persons planned for research, 6,117 were included, which is approximately 95.6%. The response rate was slightly higher among females 96.5% compared with males 94.6%. The response rate has been higher among 15-24-year-old participants with 99.2% (Table 1). Of the total respondents, 49.5 % were men. Four in ten of them had primary or lower education (from one to eight years of education). 64.7% were currently married. The mean number of family members more than 18 years old, excluding a responder, was 4.7 (Table 2).

Table 2.   Distribution of the sample by gender, age, education, marital status and number of family members - Kosova STEPS survey 2011.

	N	%
Gender		
Male	3028	49.5
Female	3089	50.5
Age - group (year)		
15-24	1270	20.8
25-34	1210	19.8
35-44	1204	19.7
45-54	1231	20.1
55-64	1202	19.7
Education		
Primary or less	2438	39.9
Secondary	2345	38.3
Tertiary	1334	21.8
Marital status		
Never married	1912	31.3
Currently married	3960	64.7
Separated	14	0.2
Divorced	19	0.3
Widowed	163	2.7
Cohabitating	19	0.3
No answer	30	0.5
Nr. of family member more than 18 years except you		
Mean±SD	4.7±2.4	

3 RESULTS

In the age group 15-64 years old the prevalence of smoking was 28.4%. Prevalence of smoking was higher among men 37.4% compared with women 19.7%, with significant difference (P<0.001). In all age groups, the prevalence of smoking was higher among men compared to women.

Prevalence of smoking increases with age. After the age of 45 it falls gradually, probably due to starting quitting smoking for health reasons, and this trend of prevalence is noticed in both sexes (Table 3).

Table 3. Percentage of current smokers by gender - Kosova STEPS survey 2011.

Age Group (years)	Percentage of current smokers									
	Men			Women			Both Sexes			
	n	Current smoker		n	Current smoker		n	Current smoker		P-value*
		n	% (95% CI)		n	% (95% CI)		n	% (95% CI)	
15-24	633	127	20.7 (17.7 - 24.1)	637	76	11.6 (9.3 - 14.6)	1270	203	16.0 (14.1 -18.1)	0.000
25-34	603	255	42.3 (38.4 - 46.3)	607	131	21.6 (18.5 - 20.5)	1210	386	31.9 (29.3 -34.6	0.000
35-44	594	290	48.8 (44.8 - 52.8)	610	154	25.2 (22.0 - 28.8)	1204	444	36.9 (34.2 - 39.6)	0.000
45-54	624	254	40.7 (36.8 - 44.6)	607	139	22.9 (19.7 - 26.1)	1231	393	31.9 (29.4 - 34.6)	0.000
55-64	594	205	34.5 (30.7 - 38.3)	608	109	17.9 (15.1 - 21.2)	1202	314	26.1 (23.7 - 28.7)	0.000
15-64	**3028**	1131	**37.4 (35.6 - 39.1)**	**3089**	609	**19.7 (18.4 - 21.2)**	**6117**	**1740**	**28.4 (27.3 - 29.6)**	0.000
25-64	2415	1004	41.6 (39.6 - 43.6%)	2432	533	21.9 (20.3 - 23.6%)	4847	1537	31.7 (30.4 - 33.0%)	0.000

*Chi-square test or Fisher exact test

Among the current smokers of ages 15 – 64, current daily smokers were 90.1%. The rate of current daily smokers among men was 94.2% compared to women 82.4%. The lowest prevalence of daily smoking is recorded in the age-group 15-24 years with 82.8%. In all age-groups the daily smoking prevalence was higher among men compared with women (Table 4).

Table 4. Current daily smokers among current smokers - Kosova STEPS survey 2011.

Age Group (years)	Percentage of current smokers									
	Men			Women			Both Sexes			
	Current smoker (n)	Current daily smokers		Current smoker (n)	Current daily smokers		Current smoker (n)	Current daily smokers		P-value*
		n	% (95% CI)		n	% (95% CI)		n	% (95% CI)	
15-24	127	114	89.8 (83.3 - 93.9)	76	54	71.1 (60.0 - 80.0)	203	168	82.8 (77.0 - 87.3)	0.001
25-34	255	243	95.3 (92.0 - 97.3)	131	115	87.8 (81.1 - 92.3)	386	358	92.7 (89.7 - 94.9)	0.013
35-44	290	273	94.1 (90.8 - 96.3)	154	130	84.4 (77.9 -89.3)	444	403	90.8 (87.7 - 93.1)	0.001
45-54	254	240	94.5 (91.0 - 96.7)	139	113	81.3 (74.0 - 86.9)	393	353	89.8 (86.4 - 92.4)	0.000
55-64	205	195	95.1 (91.3 - 97.3)	109	90	82.6 (74.4 - 88.5)	314	285	90.8 (87.1 - 93.5)	0.001
15-64	**1131**	1065	**94.2 (92.6 - 95.4)**	**609**	502	**82.4 (79.2 - 85.2)**	**1740**	**1567**	90.1 (88.6 - 91.4)	0.000
25-64	1004	951	94.7 (93.2 - 95.9)	533	448	84.1 (80.7 - 86.9)	1537	1399	91.0 (89.5 -92.4)	0.000

*Chi-square test or Fisher exact test

Table 5.   Mean age of starting smoking by gender – Kosova STEPS survey 2011.

Age Group (years)	Percentage of current smokers						P-value
	Men		Women		Both Sexes		
	n	Mean age (95% CI)	n	Mean age (95% CI)	n	Mean age (95% CI)	
15-24	114	16.2 (15.7 - 16.7)	54	17.4 (16.8 - 18.0)	168	16.6 (16.2 - 17.0)	0.003
25-34	243	18.2 (17.7 - 18.7)	115	19.4 (18.5 - 20.3)	358	18.6 (18.1 - 19.0)	0.002
35-44	273	19.6 (19.0 - 20.3)	130	22.3 (21.1 - 23.5)	403	20.5 (19.9 - 21.1)	0.000
45-54	240	21.0 (20.0 - 21.9)	113	25.5 (23.8 - 27.1)	353	22.4 (21.5 - 23.3)	0.000
55-64	195	22.1 (20.9 - 23.4)	90	31.2 (28.8 - 33.6)	285	25.0 (23.8 - 26.2)	0.000
15-64	**1065**	**19.7 (19.3 - 20.1)**	**502**	**23.4 (22.6 - 24.2)**	**1567**	**20.9 (20.5 - 21.3)**	0.000
25-64	951	20.1 (19.7 - 20.5)	448	24.1 (23.3 - 24.9)	1399	21.4 (21.0 - 21.8)	0.000

*Mann Whitney U test or Student t-test

The mean age of starting smoking was 20.9 years. Among men the mean was 19.7 years, while among women the mean was 23.4 years, with significant difference (P<0.001), (Table 5).

Among the daily smokers aged 15-64 years, 93.6% smoke manufactured cigarettes, men 92.7% and women 95.6% (Table 6).

Table 6.   Manufactured cigarette smokers among daily smokers by gender - Kosova STEPS survey 2011.

Age Group (years)	Manufactured cigarette smokers among daily smokers									P-value*
	Men			Women			Both Sexes			
	Daily smokers (n)	Manufactured cigarette smokers		Daily smokers (n)	Manufactured cigarette smokers		Daily smokers (n)	Manufactured cigarette smokers		
		n	% (95% CI)		n	% (95% CI)		n	% (95% CI)	
15-24	114	108	94.7 (89.0 -97.6)	54	53	98.1 (90.2 - 98.1)	168	161	95.8 (91.7 - 98.0)	0.431
25-34	243	224	92.2 (88.1 - 94.9)	115	107	93.0 (86.9 - 96.4)	358	331	92.5 (89.2 - 94.8)	0.833
35-44	273	255	93.4 (89.8 - 95.8)	130	124	95.4 (90.3 - 97.9)	403	379	94.0 (91.3 - 96.0)	0.506
45-54	240	222	92.5 (88.5 - 95.2)	113	110	97.3 (92.5 - 99.1)	353	332	94.1 (91.1 - 96.1)	0.090
55-64	195	178	91.3 (86.5 - 94.5)	90	86	95.6 (89.1 - 98.3)	285	264	92.5 (89.0 - 95.1)	0.232
15-64	**1065**	987	**92.7 (91.0 -94.1)**	**502**	480	**95.6 (93.5 - 97.1)**	**1567**	**1467**	**93.6 (92.3 - 94.7)**	0.026
25-64	951	879	92.4 (90.6 - 93.9)	448	427	95.3 (92.9 -96.9)	1399	1306	93.4 (91.9 - 94.5)	0.050

*Chi-square test or Fisher exact test

The mean amount of manufactured cigarettes smoked during the day by smokers aged 15-64 years was 20.9 cigarettes, in men 23.9 cigarettes and in women 14.7 cigarettes. In all age groups men smoke more than women (P<0.0001), (Table 7).

Table 7. Mean amount of manufactured cigarettes used by daily smokers by gender - Kosova STEPS survey 2011.

| Age Group (years) | Mean amount of manufactures cigaretes used by daily smokers | | | | | | P-value* |
| | Men | | Women | | Both Sexes | | |
	n	Mean age (95% CI)	n	Mean age (95% CI)	n	Mean age (95% CI)	
15-24	108	18.4 (16.9 - 19.9)	53	12.9 (10.8 - 14.9)	161	16.6 (15.3 - 17.8)	0.000
25-34	224	21.6 (20.3 - 22.8)	107	11.9 (10.6 - 13.2)	331	18.4 (17.4 - 19.5)	0.000
35-44	255	24.2 (22.9 - 25.4)	124	14.0 (12.6 - 15.3)	379	20.8 (19.8 - 21.9)	0.000
45-54	222	26.8 (25.0 - 28.5)	110	16.1 (14.2 - 18.0)	332	23.2 (21.8 - 24.7)	0.000
55-64	178	26.0 (24.3 - 27.8)	86	18.5 (16.6 - 20.5)	264	23.6 (22.2 - 25.0)	0.000
15-64	**987**	**23.9 (23.2 - 24.6)**	**480**	**14.7 (13.9 - 15.5)**	**1467**	**20.9 (20.3 - 21.4)**	0.000
25-64	879	24.5 (23.8 - 25.2)	427	14.9 (14.1 - 15.7)	1306	21.4 (20.8 - 22.0)	0.000

*Mann Whitney U test or Student t-test

4 DISCUSSION

This is the first comprehensive population-based survey on risk factors of Non communicable diseases (NCDs) among adults in Kosova. Our study shows that Kosova is among the countries with high prevalence of smoking. 31.7% of respondents aged 25-64 years are current smokers. Findings of this survey confirmed that cigarette smoking was more prevalent among men than women in Kosova (41.6% vs. 21.9%: P<0.001).

The prevalence is similar with the prevalence of smoking among school children in Kosova (9). Students aged between 13 and 15 years reported smoking cigarettes with 37%. In Kosova, from the ESPAD survey on 15-16-year-old school children in 2011, the frequency of lifetime cigarette use was reported in 35.0 % (boys 48.0% vs. girls 25.0%), (11).

Another study (24) with 261 students from 4 secondary schools in Guilin, a town in south-east Kosova, found that 36% reported to have smoked cigarettes every day. Girls consumed more cigarettes, and the incidence of smoking was higher among students in their last year of high school studies.

In the study with the first year medical students, University of Prishtina, Kosova, (14) the prevalence of daily smokers was 8.9% (9.1% men vs. 8.7% women) for general medicine students and 5.8% (4.8% men vs. 6.5% women) for dentistry students. This shows that the medical students in Kosova smoke less compared with the general population.

The prevalence of smoking among Kosova adults is similar to the prevalence of smoking in most of Balkan countries (15). Compared to other studies from Balkan countries, Kosova has lower prevalence than Bosnia and Herzegovina (16, 17) and Albania (18, 19), but higher prevalence than Croatia (20, 21) and Slovenia (22, 23). In 2010, a face-to-face survey on smoking in 18 European countries of the population aged 15 years or older was conducted. Overall, 27.2% of the participants were current smokers (30.6% of men and 24.1% of women) (4). Our results show that the prevalence of current smokers in Kosova is higher than the European average, but lower than the prevalence in Bulgaria and Greece.

Similar studies (24) with adults aged over 18 years from 48 states which have reported their data, current daily smokers in the Middle-income country group among men was 34.1% and among women 10.8%. A current daily smoker in the Low-income country group was reported among men in 25.2%, and among women in 6%. In most countries, the prevalence of smoking is higher among

men, except in Sweden, where smoking prevalence is higher among women (25). The prevalence of smoking in Kosova adults is higher among men compared to women. According to the age group, the highest prevalence of smoking in Kosova was among 25-34yearolds (31.9%) and 35-44yearolds (36.9%) and 45-54yearolds (31.9%).

In the United States of America (USA), in 2014, nearly 17 of every 100 USA adults aged 18 years or older (16.8%) currently smoked cigarettes (men 18.8% vs. women 14.8%). Current cigarette smoking was higher among persons aged 25–44 years (20.0%), (26, 27).

In our study, among the smokers aged 15-64 years, 90.1% were daily smokers. The average number of cigarettes smoked during the day was 20.9 cigarettes, for men 23.9 cigarettes and for women 14.7 cigarettes. It is higher than in Germany (28), where the average number of cigarettes smoked per day is 10, and Greece (29) where the average number of cigarettes smoked per day is 19.8. Among the daily smokers aged 15-64 years, 93.6% smoked manufactured cigarettes. In 2012, in a study done in 187 countries (30), there were 75 countries where the average number of cigarettes per daily smoker was higher than 20 cigarettes per day.

There is evidence that comprehensive tobacco control programmes reduce smoking prevalence (31), and the implementation of those policies has decreased the prevalence of smoking,for example, in the USA, Canada, Ireland, Norway, The Great Britain and Iceland (32-37). At the time when the research was being conducted, there was no legislation on tobacco control in Kosova; there were only health education activities for quitting tobacco consumption and a few health warnings on boxes of tobacco. The law for tobacco control in Kosova came into force in May 2013. Therefore, these kind of studies (STEPs) need to be repeated in order to measure the effect of such actions to smoking prevalence, especially in places where the implementation of those measures is not satisfactory.

The limitation of the study is that, as the data were from a cross-sectional survey, a structured questionnaire was used to assess tobacco use by face-to-face interviews; this could have resulted in over-reporting or under-reporting of smoking. The age of smoking initiation may also be subject to recall bias. Although these limitations exist, our study offers valuable data for tobacco control and prevention in Kosova.

5 CONCLUSIONS

The prevalence of smoking in Kosova is high compared with other countries in Eastern Europe. In future decades, Kosova will face a high probability of an increased burden

of smoking-related diseases. A special attention should be paid to coordinated government- and community-based interventions, using the guidelines to implement and manage tobacco control, ratified by the WHO Framework Convention on Tobacco Control and proven measures to strengthen country level interventions in reducing cigarette smoking and smoking-related diseases and deaths among Kosova adults.

CONFLICTS OF INTEREST

No conflicts of interest are declared.

ETHICAL APPROVAL

Received from the Ethical Committee of the Medical Faculty, University of Prishtina, number 4483.

AUTHOR'S CONTRIBUTION

MB, SV, ADz and NR participated in design of the study, sample size, methodology and corrections of the manuscript. SG contributed to the design of the study, field work and statistical analysis. JK contributed in all phases and the correction of manuscript. MG compared the results with other studies. All authors have read and approved the final manuscript.

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THE ROLE OF ATTITUDES TO, AND THE FREQUENCY OF, DOMESTIC VIOLENCE ENCOUNTERS IN THE HEALTHCARE PROFESSIONALS' HANDLING OF DOMESTIC VIOLENCE CASES

VLOGA STALIŠČ IN POGOSTOSTI SREČEVANJA Z NASILJEM V DRUŽINI PRI UKREPANJU ZDRAVSTVENEGA OSEBJA

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ABSTRACT

Keywords:
domestic violence, attitudes, response, detection, health personnel

Background. Domestic violence is recognized as a public health problem with a high prevalence in the general population. Healthcare professionals play an important role in the recognition and treatment of domestic violence. Hence, conducting research on factors that facilitate or inhibit appropriate actions by healthcare professionals is of the upmost importance. The objective of the study was to examine the relationship between healthcare professionals' attitudes toward the acceptability of domestic violence and their responses when dealing with victims of domestic violence.

Methods. The sample consisted of 322 healthcare professionals (physicians, dentists, nursing staff and other healthcare workers; 85.2% female), who completed a questionnaire, assessing their attitudes towards domestic violence, experience, behaviour and perceived barriers in recognizing and treating domestic violence in the health care sector. The study was cross-sectional and used availability sampling.

Results. The results showed no significant differences in domestic violence acceptability attitudes when comparing groups of healthcare professionals who reported low or high frequency of domestic violence cases encounters. Furthermore, we found that domestic violence acceptability attitudes were negatively associated with action taking when the frequency of encounters with domestic violence cases was high and medium. However, the attitudes were not associated with action taking when the frequency of encounters with domestic violence cases was low.

Conclusions. The results highlight the important role of attitudes in action taking of healthcare professionals when it comes to domestic violence. This indicates the need for educational interventions that specifically target healthcare professionals' attitudes towards domestic violence.

IZVLEČEK

Ključne besede:
nasilje v družini, stališča, ukrepanje, prepoznava, zdravstveno osebje

Izhodišča. Nasilje v družini (NVD) je javnozdravstveni problem, ki ga označuje visoka prevalenca v splošni populaciji. Zdravstveno osebje ima pomembno vlogo pri prepoznavi in obravnavi NVD. Posledično je raziskovanje faktorjev, ki prispevajo k primernim odzivom zdravstvenega osebja ob prepoznanem NVD, ključnega pomena. Namen te študije je bil preveriti odnos med stališči zdravstvenega osebja o sprejemljivosti nasilja v družini in njihovimi odzivi ob obravnavi žrtev NVD.

Metoda. Končni vzorec je sestavljalo 322 strokovnjakov s področja zdravstva (zdravniki, zobozdravniki, osebje zdravstvene nege in ostali delavci v zdravstvu; 85,2 % žensk). Udeleženci so izpolnili vprašalnik, ki je ocenjeval njihova stališča do NVD, izkušnje, odzive in zaznane ovire pri obravnavi NVD v zdravstvu. Študija je bila prečna. Vključen je bil priložnostni vzorec.

Rezultati. Rezultati niso pokazali pomembnih razlik v stališčih o sprejemljivosti nasilja, ko smo primerjali skupine zdravstvenih delavcev, ki se z nasiljem srečujejo pogosto, ter tiste, ki se z obravnavo NVD srečujejo redko. Rezultati so pokazali tudi, da se stališča o sprejemljivosti NVD negativno povezujejo z ustreznimi odzivi zdravstvenega osebja pri obravnavi žrtev NVD. Ta odnos je bil najbolj izražen v primerih, ko se je zdravstveno osebje z žrtvami NVD srečevalo bolj pogosto. Stališča o sprejemljivosti NVD se z odzivi zdravstvenega osebja niso pomembno povezovala v primerih, ko je zdravstveno osebje poročalo o redkih oziroma neobstoječih stikih z NVD v njihovi praksi.

Zaključki. Rezultati nakazujejo na pomembno vlogo stališč o sprejemljivosti nasilja pri ustreznem odzivu zdravstvenega osebja ob obravnavi žrtev NVD. To nakazuje na potrebo po izobraževanjih, ki se specifično ukvarjajo s stališči zdravstvenega osebja do NVD.

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1 INTRODUCTION

Domestic violence is defined as "any use of physical, sexual, psychological or economic violence of one family member against the other family member and neglect of a family member, irrespective of a person's age, gender or any other personal circumstance of the victim or the perpetrator of violence" (1). In Slovenia, the prevalence of intimate partner violence is estimated to be anywhere from 15% to 17% (2-4).

Exposure to domestic violence can have many negative effects on the victim's health (5) and leads to an increased use of health care services (6). This provides healthcare professionals with an opportunity to access the victims of domestic violence and offer the appropriate support and help. However, studies show that healthcare professionals often miss the chance to help the victims of domestic violence (7). Reasons for this vary and can include problems with recognizing the victims of domestic violence and also inappropriate reactions when domestic violence is recognized. In line with that, studies show that clinicians recognize only one out of 20 victims of domestic violence on average (8). Even in those cases when the clinicians identify the victim of domestic violence, they often don't respond in an appropriate manner. According to the Family Violence Protection Act (1), adopted Slovenia in 2008, healthcare professionals are obligated to report any suspicions of domestic abuse. Therefore, conducting research on the factors that either inhibit or facilitate the appropriate actions of healthcare professionals in the case of domestic violence is of the upmost importance.

Next to well-developed protocols on a systemic level, working with domestic violence also requires a professional approach and compliance with moral and ethical norms on behalf of the individual working with victims of domestic violence. The attitudes towards domestic violence held by healthcare professionals therefore also play an important role in the treatment of domestic violence (9). In the literature, attitudes are defined as the combination of evaluations (10), emotions (11) and cognitions (12) in relation to different social situations and objects, that function as a permanent readiness to behave in a certain manner. They are usually stable over a longer period, but can also change over time (10). The theories of predicting individual's behaviour postulate that attitudes play an important role in a decision to act a certain way. Attitudes can, for example, serve as the motivation to act in a certain way by making individuals feel like they are capable of a certain behaviour (13). In a similar manner, the attitudes of healthcare professional can facilitate behaviours, due to a belief that it will lead to desired outcomes (14).

Attitudes are formed through interactions in social environments and have an effect on the behaviour of individuals (10). However, the relationship between attitudes and behaviour seems to be much more complicated, with the proposed causation running in both directions, i.e. - attitudes leading to behaviour and behaviour (experiences) leading to attitudes (15, 16). Despite the different theoretical postulations, there is a general consensus that there is a strong correlation between attitudes and behaviour (17). Therefore, we can assume that healthcare professionals' attitudes towards domestic violence importantly contribute to the way that healthcare professionals act when they recognize domestic violence victims.

Previous studies examining healthcare professionals' attitudes toward domestic violence showed that healthcare professionals have low levels of awareness, knowledge, competences and a lot of misconceptions and prejudges about domestic violence (18-20). However, most of the studies that examine the attitudes of healthcare professionals in relation to their actions when dealing with domestic violence victims only ask the participant to state their opinion about the possible barriers that negatively contribute to domestic violence recognition (21, 22). There are some recent studies that go beyond just asking the participants about their opinion on factors that contribute negatively to the treatment of domestic violence and measure the healthcare professionals' attitudes directly, however, they do not relate these measures to the measures of actions taken when dealing with domestic violence (23). For example, a study by Wong and colleagues (24) interviewed family doctors after completing a training program on partner abuse and found that, when asked about the importance of attitudes in their practice, the doctors seem to agree that this has an important role. However, the descriptive nature of qualitative data does not enable a detailed analysis of the relationships between these concepts. Due to the undeniable necessity of abovementioned studies, further studies that bridge this gap and relate measures of attitudes directly to the reported actions of healthcare professionals in the case of domestic violence are needed. The main objective of the study was to examine the relationship between healthcare professionals' attitudes toward the acceptability of domestic violence and their responses when dealing with victims of domestic violence. More specifically, we examined the association between actions taken in the case of domestic violence and healthcare professionals' attitudes about domestic violence and the frequency of encounters with domestic violence cases.

The specific hypotheses we tested were: (I) healthcare professionals' who encounter cases of domestic violence more frequently in their practice will perceive domestic violence as less acceptable, when compared to those who have rarely encountered domestic violence cases, (II)

the attitudes about domestic violence acceptability will be negatively associated with healthcare professionals' action taking for more frequent encounters with domestic violence cases and (III) the attitudes about domestic violence acceptability will not be associated with action taking for rare encounters with domestic violence cases.

2 METHODS

2.1 Participants

A total of 488 participants employed in the Slovenian health care sector were included in the broader study of the project Recognizing and treating victims of domestic violence in health care settings: Guidelines and training for health professionals (POND_SiZdrav; (25)). In the present study only participants who already encountered cases of domestic violence at their work were included, therefore the final sample consisted of 322 participants (refer to Results for demographic data).

2.2 Instruments

A questionnaire measuring different aspects of recognition and treatment of domestic violence for healthcare professionals was developed for the purposes of the broader study (25). The questionnaire was used to assess healthcare professionals' attitudes, experience, behaviour and perceived barriers in recognizing and treating domestic violence in health care sector. The participants used a 5-point scale (1 – I completely disagree, 5 – I completely agree), to complete the measures.

2.2.1 Attitudes towards Domestic Violence

The measure consists of 17 items assessing healthcare professionals' attitudes towards domestic violence (e.g., Domestic violence is a private matter). A principal component analysis was used to reduce the included items to a smaller set of variables (i.e., principal components). The results suggested a four-component solution, reducing the initial 17 items to four components measuring different aspects of attitudes towards domestic violence. The components were: attitudes linked to environment and culture, attitudes towards the characteristics of the family and their members, attitudes towards acceptability of domestic violence, and attitudes towards socioeconomic status in relation to domestic violence. In line with the postulated hypotheses of the study, our interest lied in one of the extracted components - the attitudes towards acceptability of domestic violence. This variable consisted of three items: (1) Domestic violence is a private matter, (2) Domestic violence is normal and (3) The victims of domestic violence are provoking the violence and are responsible for the violence they experience. The final score of the measure of attitudes towards acceptability of domestic violence was computed

by taking the average of the three items listed, resulting in a score from 1 to 5, where a higher score represents a stronger belief in the acceptability of domestic violence.

2.2.2 Experience and Behaviour when Encountering Victims of Domestic Violence in the Practice

The measure consists of 14 items assessing healthcare professionals' experience and behaviour when dealing with domestic violence cases. (e.g., I use the prescribed protocol for dealing with victims of domestic violence at my work.). To reduce the number of initial items to a smaller set of variables, a principal component analysis was conducted. The results suggested a three-component solution: behaviour related to the recognition of domestic violence, taking action when recognizing domestic violence, and response when recognizing domestic violence (such as offering support etc.). Again, as postulated in the hypotheses of the present study, we were interested in action taking when recognizing domestic violence from this part of a questionnaire. This component consisted of the following items: (1) I use the stipulated protocol for treating the victims of domestic violence, (2) If I recognize a victim of domestic violence I report this to the police, (3) If I recognize the victim of domestic violence I report this to social services, (4) If I recognize a victim of domestic violence I report this to the prosecution, (5) I have different information materials available and I forward those to the victim of domestic violence. The final score was computed by taking the average of the three items listed, resulting in a score from 1 to 5, where a higher score represents a more appropriate response in the case of an encounter with a domestic violence case.

2.2.3 Frequency of Encounters with Domestic Violence

This was assessed with the question: How often do you encounter cases of domestic violence at your work? Participants responded on 5-point scale (1 – very rarely or never, 5 – very often or always). A higher score represents a higher frequency of encounters with domestic violence.

2.3 Procedure and Statistical Analyses

Data collection was carried out from April to June 2015. The study was cross-sectional and used availability sampling. Participants were recruited through invitations published on various websites (the project website) and mailing lists. A total of 1581 individuals clicked on the link to the questionnaire, with 488 complete entries. This gives rise to a 31% response rate, which is comparable to the results of meta-analyses of response rates in email surveys (26).

The difference between domestic violence acceptability attitudes for those with high and low frequency of encounters with domestic violence cases was examined

using the Mann-Whitney U test for independent samples. The groups of high and low frequency of encounters with domestic violence cases (n_{low}=138, n_{high}=182) were created with the use of the median split.

The main effects of domestic violence acceptability attitudes and the frequency encounters with domestic violence and their interactions were examined in relation to taking action when recognizing domestic violence using hierarchical linear regression (27). Due to the statistically significant interaction we analysed the effects of domestic violence acceptability attitudes on action taking separately, for frequent (1 SD above the mean), medium (mean) and rare encounters (1 SD below the mean) with domestic violence cases, by examining simple slopes (28). Analyses were carried out with SPSS 22 (29) and R version 3.2.2015-06-07 (30).

3 RESULTS

3.1 Demographics of Participants

The sample included 322 participants (85.2% female, 14.8% male). The age of the participants ranged from 21 to 72 years (M=43.5±11.0). Sample consisted of physicians and dentists (56.4%), healthcare personnel (32.4%), and other employees in the health care sector (11.2%; e. g. psychologists, social workers, administrative staff). Most of the participants reported working in the field of family or general medicine (37.8%), followed by psychiatry (8.8%), pediatrics (8.2%), and gynaecology (6.0%). Employees from other fields were represented in the sample in less than six percent.

3.2 Descriptive Statistics

In the current study, we examined the relationship between attitudes about the acceptability of domestic violence, the frequency of encounters with domestic violence cases and action taking when domestic violence is recognized by healthcare professionals.

We examined the descriptive statistics for the three main variables of interest. The mean values for domestic violence acceptability attitudes, frequency of encounters with domestic violence cases and action taking were 1.72±55, 2.19±92 and 2.63±81, respectively. Attitudes about the acceptability of domestic violence were statistically significantly correlated with action taking (r=-.13, p<.05) but not with frequency of encounters (p>.05). The correlation between action taking and frequency of encounters was also statistically significant (r=.27, p<.01).

3.3 The Relationship between Attitudes, Frequency and Action Taking

The results showed no significant differences in domestic violence acceptability attitudes between those who

encounter domestic violence cases rarely (M=1.75±.58) as compared with those who encounter domestic violence cases in their practice often (M=1.68±.52); U=4786.50, p=.49.

The results of the regression analysis, examining the relationship between domestic violence acceptability attitudes, the frequency of encounters with domestic violence cases and action taking, are shown in Table 1.

Table 1. Results of hierarchical regression for action taking in domestic violence cases.

Predictor	ΔR^2	B	95 % CI for B	ß
Step 1	.09**			
Gender		.24	[- .03, .52]	.09
DV acceptability attitudes		- .36	[- .68, -.04]	- .12**
Frequency of DV cases		.30	[.19, .42]	.27***
Step 2	.02*			
Gender		.26	[- .02, .53]	.09
DV acceptability attitudes		- .41	[- .67, - .04]	- .12**
Frequency of DV cases		.30	[.18, .41]	.26***
Attitudes x frequency interaction		- .46	[- .86, - .08]	- .13*
R2	.11**			

Notes: DV=domestic violence
* p<05; ** p<.01; *** p<.001.

As expected, the interaction term was statistically significant (p<.05). The results of the follow-up simple slope analysis of the relationship between violence acceptability attitudes and action taking are presented in Figure 1.
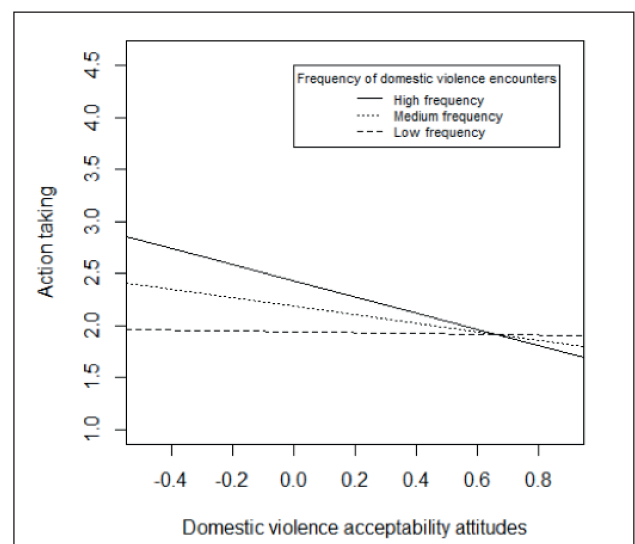

Figure 1. Regression slopes showing the predictive value of attitudes on action taking, separately for different frequencies of encounters with domestic violence.

The simple slopes analysis showed a significant negative association between the domestic violence acceptability attitudes and action taking for high and medium frequency of encounters with domestic violence cases (high: B=-.78, t(3)=-3.44, p=.001; medium: B=-.14, t(3)=-2.58, p=.01). For low frequency of encounters with domestic violence cases, the domestic violence acceptability attitudes were not associated with action taking (B=-.04, t(3)=-.18, p=.86).

4 DISCUSSION

The purpose of the present study was to examine the relationship between domestic violence acceptability attitudes and action taking in health care professionals. Specifically, we were interested in the role of domestic violence acceptability attitudes and the frequency of domestic violence cases in their practice in action taking. The results showed no significant differences in domestic violence acceptability attitudes, when comparing groups of healthcare professionals who reported low or high frequency of domestic violence cases encounters. Based on these results, the frequency of encounters with domestic violence does not play an important role in the healthcare professionals' attitudes about the acceptability of domestic violence. This is not in line with the expectations and theoretical postulations, as attitudes are expected to form and change with experience (15). This finding, however, must be interpreted with some methodological drawbacks in mind. Our data showed that, overall, the average value on the acceptability of domestic violence attitudes scale was low (see Results; Descriptive statistics). Considering the fact that the attitudes were measured on a scale from one to five, we can see that healthcare professionals, on average, do not consider domestic violence acceptable. Thus, it is possible that the lack of significant differences is also a reflection of the overall low variability of our data when looking at the domestic violence acceptability attitudes. With this in mind, we were interested in whether those subtle differences in attitudes play a role in the appropriate action taking by the healthcare professional when dealing with domestic violence cases. The results showed a very distinctive pattern for various frequencies of dealing with domestic violence cases. More specifically, we found that the healthcare professionals who believe that domestic violence is acceptable tend to respond in less appropriate ways when dealing with a victim of domestic violence. This is especially the case when these encounters with domestic violence victims are of medium or high frequency (see Figure 1). These results show that attitudes about domestic violence have a significant role in the way healthcare professionals act when coming across cases of domestic violence in their own practice. This finding is in line with the expectations and social psychology theories that postulate a relationship between attitudes and behaviours (in our case, action taking) (15, 16).

The results highlight the important role of attitudes and action taking of healthcare professionals when it comes to domestic violence. Our study showed that the role of attitudes on action taking increases with increasing the frequency of coming into contact with domestic violence cases. Nevertheless, considering the high prevalence of domestic violence cases, the majority of healthcare professionals are expected to come into contact with a victim of domestic violence during their professional career. Based on our data, the negative effects of domestic violence acceptability attitudes start showing at a relatively low frequency of encounters. More specifically, the effects were not significant only for the lowest frequency (i.e., those who reported absent or very rare encounters with domestic violence cases). If we combine this finding with the fact that the frequencies reported in our sample were fairly low (see Table 1), the importance of domestic violence acceptability attitudes when it comes to healthcare professionals' action taking can be emphasised even more. This indicates the need for educational interventions that specifically target healthcare professionals' attitudes towards domestic violence. This conclusion is also in line with the qualitative research done in the field of domestic violence that found that doctors can improve their awareness of partner abuse in daily practice if they also become more sensitised to the issue and more comfortable with exploring their own attitudes towards abuse (24).

4.1 Limitations

Our study had some limitations, which need to be accounted for when interpreting the results. Firstly, our sample is biased and not representative; therefore, the generalisation of our findings to a larger population of healthcare professionals is not possible. Secondly, the study was cross-sectional and based on self-report data, which also limits the reliability of our conclusions. Another drawback is the use of a questionnaire that is not validated and standardised. Due to the non-experimental nature of the study, we are also not able to infer any causality between the studied constructs. Experimental and longitudinal studies are necessary to examine these relationships in more detail. Studies which focus on exact evaluations of interventions that target the attitudes of healthcare professionals on their actions when dealing with domestic violence cases are also necessary.

5 CONCLUSION

Overall, the results of this study emphasise the important role of attitudes when it comes to action taking of healthcare professionals in cases of domestic violence. More specifically, seeing domestic violence as more acceptable relates to less appropriate action taking, with this relationship being particularly strong for higher frequency of encounters with victims of domestic violence. Since victims of domestic violence are frequent users of health care services, our results point to a strong need for educational programmes specifically designed for targeting the attitudes that healthcare professionals have about domestic violence.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

The research was realised in accordance with the terms of the "Declaration of Helsinki for recommendations guiding physicians in biomedical research involving human subjects" (http://www.cirp.org/library/ethics/helsinki/).

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NASOPHARYNGEAL CARRIAGE OF *STREPTOCOCCUS PNEUMONIAE* AND SEROTYPES INDENTIFIED AMONG NURSING HOME RESIDENTS IN COMPARISON TO THE ELDERLY AND PATIENTS YOUNGER THAN 65 YEARS LIVING IN DOMESTIC ENVIRONMENT

NOSILSTVO PNEVMOKOKA V NOSNEM ŽRELU IN IDENTIFIKACIJA SEROTIPOV MED OSKRBOVANCI DOMA STAREJŠIH OBČANOV V PRIMERJAVI S STAROSTNIKI IN MLAJŠIMI OD 65 LET, KI ŽIVIJO V DOMAČEM OKOLJU

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ABSTRACT

Keywords:
S. pneumoniae, nasopharyngeal carriage, serotype identification, retirement home residents, vaccination

Introduction. In Slovenia, there is little data available on pneumococcal vaccination rates and no data on asymptomatic NPCR and serotypes in the population of nursing home residents in comparison to the elderly living in domestic environment, therefore the goal was to gain these data.

Methods. A cross sectional epidemiological study was performed. Nasopharyngeal swabs from 151 nursing home residents, 150 elderly living in domestic environment, and 38 adults less than 65 years old were collected twice (in two consecutive years). The swabs were analysed for pneumococcal identification and serotyping. Patient data were collected from medical files and medical history.

Results. No statistically significant differences in NPCR were seen between compared groups in two consecutive years. An average NPCR in two consecutive years in nursing home residents was 1.45%, in the elderly living in domestic environment 0.85%, and in adults less than 65 years old 7.05%. Serotypes identified among nursing home residents were 6B and 9N, among the group of elderly living in domestic environment, 6A and among adults less than 65 years old, 35F, 18C and 3. Pneumococcal vaccination rates were low (3.3% in nursing home residents, 6% in the elderly from domestic environment and 0% in the group of adults less than 65 years old).

Conclusions. Our data suggests that NPCR and the proportion of people vaccinated with pneumococcal vaccine among the elderly are low. We identified different serotypes in all groups, only one person was a chronic carrier (serotype 35F).

IZVLEČEK

Ključne besede:
pnevmokok, nosilstvo v nosnem žrelu, identifikacija serotipov, oskrbovanci doma starejših občanov, cepljenje

Izhodišča. V Sloveniji je malo podatkov o stopnji precepljenosti s pnevmokoknimi cepivi in ni dostopnih podatkov o nosilstvu pnevmokoka v nosnem žrelu ter o serotipih med oskrbovanci doma starejših občanov (DSO) v primerjavi s starostniki, ki živijo v domačem okolju, zato je bil namen raziskave pridobiti te podatke.

Metode. Izvedli smo presečno epidemiološko raziskavo. Dvakrat (v dveh zaporednih letih) smo odvzeli brise 151 oskrbovancem DSO, 150 starostnikom, ki živijo v domačem okolju, in 38 odraslim, mlajšim od 65 let. Z analizo brisov smo identificirali pnevmokoke in jih serotipizirali. Podatke o bolnikih smo pridobili iz medicinske dokumentacije ter iz anamneze.

Rezultati. V nobeni od primerjanih skupin nismo ugotovili razlike v deležu nosilstva pnevmokoka v dveh zaporednih letih. Povprečni delež nosilstva v dveh zaporednih letih skupaj je bil med oskrbovanci DSO 1,45%, med starostniki, ki živijo v domačem okolju, 0,85% ter med odraslimi, mlajšimi od 65 let, 7,05%. Med oskrbovanci DSO smo identificirali serotipa 6B in 9N, med starostniki, ki živijo v domačem okolju, serotip 6A ter med odraslimi, mlajšimi od 65 let, stereotipe 35F, 18C in 3. Delež cepljenih s pnevmokoknim cepivom je bil nizek (3,3% med oskrbovanci DSO, 6% med starostniki, ki živijo v domačem okolju, in 0% med odraslimi, mlajšimi od 65 let).

Zaključki. Glede na naše izsledke sklepamo, da sta delež nosilcev pnevmokoka v nosnem žrelu ter delež oseb, cepljenih s pnevmokoknimi cepivi, med starostniki nizka. Identificirani serotipi v vseh skupinah so bili različni, odkrili smo le enega kroničnega nosilca (serotip 35F).

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1 INTRODUCTION

Elderly living in nursing homes represent 5% of the total elderly population in Slovenia (1). Among them respiratory tract infections are the second most prevalent and represent one of the most frequent causes of morbidity, mortality and hospital admissions (1-3). In this group, pneumonia is regarded a special category due to advanced age, numerous co-morbidities and non-specific, but often severe disease course, which all contribute to a high (30%) mortality rate (2). One of the main pathogens causing pneumonia in the group of elderly is *S. pneumoniae* (*Streptococcus pneumoniae*; 4-7).

S. pneumoniae is part of the normal nasopharyngeal microbial flora (8). Colonization occurs early in life, with prevalence of 40% in children and 15% in adults (9), transmission between individuals is via aerosol (8). Nasopharyngeal colonization is a risk factor for pneumococcal diseases: otitis media, pneumonia, sepsis, meningitis. Asymptomatic carriers are the main reservoir of pneumococci and the principal source of spread among new hosts (10). More than 20% of deaths associated with pneumococcal infection are supposed to occur among people older than 80 years, although nasopharyngeal pneumococcal carriage rate (NPCR) in this group is low (11, 12).

The estimated incidence of pneumonia among nursing home residents in the United States is 365/1000 residents per year and it is significantly higher in comparison to elderly living in domestic environment (20-40/1000) (13). Due to frequent and sometimes unjustified use of antibiotics, numerous antibiotic resistant pneumococcal strains develop (4, 13), representing an increasing problem worldwide (5, 14).

The incidence of invasive pneumococcal disease in Slovenia was 11.9/100,000 in year 2012 (most frequently pneumonia) (15). The highest rates were among children under 5 years of age (46.2/100,000) and among elderly over 65 years of age (27/100,000) (15). Among adults most prevalent serotypes, causing invasive pneumococcal disease, were 3, 9V, 14, 4, 1, 23F and 19F (15). Similar data was found in United States, German and Czech studies (16-18).

Although pneumococcal pneumonia is an important cause of morbidity and mortality among nursing home residents and represents great cost for the society (19), pneumococcal vaccination rates remain low (6, 13, 20). In situations where vaccination rates within a closed population, such as in a nursing home, are less than 5%, there is a greater risk for pneumococcal infection outbreak (6). Pneumococcal vaccination represents effective protection from pneumococcal pneumonia for an individual and vaccination of critical number of individuals can lead to herd immunity effect (6, 21).

So far, there is little data available on pneumococcal vaccination rates (20) and no data on asymptomatic NPCR and serotypes in the population of nursing home residents in comparison to adults living in domestic environment in Slovenia. Therefore the goal of this research is to gain these data.

2 METHODS

2.1 Type of a Study and Study Population

We performed a cross sectional epidemiological study, in which two swabs were taken from all the participants (one swab every year) in two consecutive years (February 2013 – November 2013 and February 2014 – November 2014).

The study included 151 nursing home residents from "Dom upokojencev center" in Ljubljana, 152 elderly living in domestic environment and 38 adults less than 65 years, all visiting General practitioners in the same region ("Zdravstveni dom Ljubljana Center"). Due to lack of data, 2 of the participants in the first year, both from the group of elderly living in domestic environment, and one participant in the second year, from the group of nursing home residents, were excluded from the analysis.

Inclusion criteria were i) no sign of acute respiratory infection, ii) living in a defined geographical region in a domestic environment or retirement home and iii) informed consent form signed by the patient or patient's legal representative.

Exclusion criteria were i) ongoing acute respiratory infection, ii) living outside defined geographical region, iii) refusal to sign informed consent form by patient or patient's legal representative, iv) the use of antibiotics in the two weeks prior to taking the swab, and v) immunocompromised patients (hematological malignancies, inherited immunodeficiency, HIV, post splenectomy status, cancer chemotherapy).

2.2 Data Collection

Recruitment of participants started in the nursing home. We asked all the residents from "unit Poljane" to participate. On-site recruitment approach, with the possibility to turn down the participation was used. This was previously identified as one of more successful approaches (22). 95 out of 168 decided to join the study. We continued in "unit Tabor", where the random number method was used until we included the expected number of participants. The same method was used to select the participants among elderly patients and adults less than 65 years from different General practitioner offices at "Zdravstveni dom Ljubljana Center". These were contacted by telephone.

Case report form was filled in for each participant. It included patient's identification number, gender,

age, preceding vaccination data against influenza and pneumococcal infections, preceding antibacterial therapy (from three months up to two weeks prior to taking the swab), data on preschool children contacts, corticosteroid or immunosuppressant treatment and data on chronic diseases. This data was collected by reviewing patient medical files and by taking patient history.

2.3 Nasopharyngeal Swab Collection

We used R Sterile Copan swab (Copan, Brescia, Italy) with a universal transport medium to take a sample from nasopharynx. Nasopharyngeal space is currently defined as the most appropriate spot for *S. pneumoniae* detection (23). The swab was inserted through a nostril about 10 cm deep into the nasopharynx, rotated there and removed after 5 seconds and inserted directly into the transport medium.

2.4 *Streptococcus Pneumoniae* Identification and Serotyping

The swabs were transferred to the National Laboratory of Health, Environment and Food, Centre for Medical Microbiology, Department for Public Health Microbiology, Laboratory for Public Health Bacteriology, Ljubljana, Slovenia no later than 24h after specimen collection, where the identification and serotyping of S. pneumonia was performed.

The cultures were grown on Columbia blood agar with 5% sheep blood and Blood agar with bovine blood, both manufactured at the laboratory, and incubated on 35±2 °C in the 5% CO_2 for 48h. The plates were checked for the presence of suspected *S. pneumoniae* colonies after 24 and 48h of incubation. All suspected colonies based on colony morphology and hemolysis were cultured on Columbia agar for 24h and then stained by Gram, tested for the presence of catalase, optochin sensitivity and bile solubility. An isolate was considered to be *S. pneumoniae* if the Gram stain morphology of the isolate showed gram-positive diplococci, cocci, single or in chains, was catalase negative, optochin sensitive and bile soluble. Serotyping was performed with the Neufeld-Quellung reaction, using specific pneumococcal typing antisera (Omni, pooled, group, type and factor) containing specific antibodies against pneumococcal capsular polysaccharide type antigens (Statens Serum Institute, Copenhagen, Denmark). To avoid misidentification of *S. pneumoniae* like viridians group streptococci, a Real-Time PCR Assay targeting Lyt A (autolysin) a gen specific for S. pneumoniae, has been used (24). The DNA isolation was done using the QIAamp DNA Mini Kit (Qiagen, Hilden, Germany).

2.5 Statistical Analysis

The collected data was analyzed with SPSS, version 20.0.0. Pearson Chi Square test was used to test the differences between different groups of participants. A value of p<0.05 was used as a limit to describe significant scientific differences between groups.

3 RESULTS

3.1 Description of the Groups

In the group of nursing home residents, the average age was 85.24 years (range 67-105 years), 120 (79.4%) were females and 31 (20.6%) were males.

In the group of elderly from domestic environment, the average age was 82.07 years (range 65-97 years), 115 (76.7%) were females and 35 (23.3%) were males.

In the group of adults less than 65 years the average age was 55.34 years (range 47-64 years), 19 (50%) were females and 19 (50%) were males.

3.2 Swab Results

NPCR were low in groups of elderly studied in two consecutive years. In the group of adults less than 65 years NPCR were higher, in the second year NPCR in this group was significantly higher, compared to others (p<0.05) (Table 1).

71 participants were eliminated from the study after the first year; 42 participants turned down the second swab (1 from nursing home residents, 38 elderly from domestic environment and 3 adults less than 65 years) and 29 due to death (20 nursing home residents, 8 elderly from domestic environment, 1 adult less than 65 years).

Table 1.   Number of positive swabs in different groups in two consecutive years.

	Nursing home residents	Elderly domestic environment	Adults < 65 years
First year	2 (1.3%) n=151	1 (0.7%) n=150	2 (5.3%) n=38
Second year	2 (1.6%) n=129	1 (1%) n=104	3 (8.8%) n=34*

* p<0.05

3.2.1 Characteristics of Participants with Positive Swab Results

There were five positive swab results in the first year (Table 2) and six in the second (Table 3). Serotype 6B and a non-typeable *S. pneumoniae* was identified in nursing home residents in the first year (Table 2), in the second year serotypes 6B and 9N were identified (Table 3). In the group of elderly from domestic environment a non-typeable

S. Pneumoniae was identified in the first year (Table 2) and 6A serotype in the second year (Table 3). In adults less than 65 years a non-typeable *S. pneumoniae* and 35F serotype were identified in the first year (Table 2) and 35F serotype (chronic carrier) and 18C and 3 in the second year (Table 3).

Table 2.   Characteristics of participants with positive swab result and *S. pneumoniae* serotypes in the first year.

	Participant Nr. 1	Participant Nr. 2	Participant Nr. 3	Participant Nr. 4	Participant Nr. 5
Age	88 years	78 years	80 years	47 years	58 years
Gender	Female	Male	Female	Male	Male
Group	Nursing Home	Nursing Home	Domestic Environment	Adults <65 years	Adults <65 years
Influenza vaccination[a]	No	Yes	No	No	No
Pneumococcal vaccination[b]	No	Yes	No	No	No
Antibiotics 3 months prior to swab	No	No	No	No	Yes
Preschool children contacts	No	No	No	No	Yes
Corticosteroid treatment[c]	No	Yes	No	No	Yes
1 chronic illness	/	/	/	No	Yes
2 chronic illnesses	/	/	Yes	No	/
≥ 3 chronic illnesses	Yes	Yes	/	No	/
***S. pneumoniae* serotype**	**NT**	**6B**	**NT**	**35F**	**NT**
Death after the first year	No	Yes	No	No	No
Second swab refusal	No	/	No	No	No

[a] in the previous season, [b] in the last 5 years, [c] in the last month, NT, non-typeable; /, not applicable

Table 3.   Characteristics of participants with positive swab result and *S. pneumoniae* serotypes in the first year.

	Participant Nr. 1'	Participant Nr. 2'	Participant Nr. 3'	Participant Nr. 4'	Participant Nr. 5'	Participant Nr. 6'
Age	86 years	77 years	80 years	47 years	58 years	60 years
Gender	Male	Female	Female	Male	Male	Female
Group	Nursing Home	Nursing Home	Domestic Environment	Adults <65 years	Adults <65 years	Adults <65 years
Influenza vaccination[a]	No	No	No	No	No	No
Pneumococcal vaccination[b]	No	No	No	No	No	No
Antibiotics 3 months prior to swab	No	No	No	No	Yes	No
Preschool children contacts	No	No	No	No	Yes	Yes
Corticosteroid treatment[c]	No	No	No	No	Yes	No
1 chronic illness	/	/	/	No	Yes	No
2 chronic illnesses	Yes	Yes	Yes	No	/	No
≥ 3 chronic illnesses	/	/	/	No	/	No
***S. pneumoniae* serotype**	**6B**	**9N**	**6A**	**35F**	**18C**	**3**

[a] in the previous season, [b] in the last 5 years, [c] in the last month; /, not applicable

3.2.2 Characteristics of Participants with Negative Swab Results

The rate of influenza vaccination was significantly lower in the group of adults less than 65 years, compared to both groups of elderly, the rate of influenza vaccination was significantly higher in the group of nursing home residents, compared to elderly from domestic environment (Table 4). The rate of pneumococcal vaccination was low in all the groups, there was no statistically significant difference (Table 4). There was also no difference considering preschool children contacts and immunosuppressant therapy. Antibiotic consumption rate was significantly higher in both groups of elderly, compared to adults less than 65 years and the number of comorbidities (≥ 3) was significantly higher in the group of nursing home residents, compared to others. Death incidence was significantly higher among nursing home residents, compared to the other two groups, whereas the rate of second swab refusal, was significantly higher in the group of elderly living in domestic environment, compared to others.

Table 4. Characteristics of participants with negative swab results in two consecutive years.

		Nursing home residents		Elderly domestic environment		Adults <65 years	
		First year	Second year	First year	Second year	First year	Second year
Influenza vaccinationa	Yes	50 (33.6%)*	23 (18.1%)	31 (20.8%)	20 (19.4%)	2 (5.6%)	2 (6.4%)
	No	99 (66.4%)	63 (49.6%)	118 (79.2%)	56 (54.4%)	34 (94.4%)*	28 (90.3%)
	Unknown	/	41 (32.3%)	/	27 (26.2%)	/	1 (3.3%)
Pneumococcal vaccinationb	Yes	4 (2.7%)	4 (3.1%)	9 (6%)	8 (7.8%)	0	/
	No	145 (97.3%)	123 (96.9%)	139 (93.3%)	94 (91.2%)	36 (100%)	31 (100%)
	Unknown	/	/	1 (0.7%)	1 (1%)	/	/
Antibiotics 3 months prior to swab	Yes	43 (28.9%)*	37 (29.1%)	19 (12.8%)*	12 (11.7%)	5 (13.9%)	4 (12.9%)
	No	106 (71.1%)	90 (70.9%)	130 (87.2%)	91 (88.3%)	31 (86.1%)	27 (87.1%)
	Unknown	/	/	/	/	/	/
Preschool children contacts	Yes	29 (19.5%)	26 (20.5%)	38 (25.5%)	28 (27.2%)	14 (38.9%)	12 (38.7%)
	No	119 (79.9%)	100 (78.7%)	111 (74.5%)	75 (72.8%)	22 (61.1%)	19 (61.3%)
	Unknown	1 (0.6%)	1 (0.8%)	/	/	/	/
Corticosteroid treatmentc	Yes	9 (6%)	6 (4.7%)	6 (4%)	4 (3.9%)	0	/
	No	140 (94%)	121 (95.3%)	143 (96%)	99 (96.1%)	36 (100%)	31 (100%)
	Unknown	/	/	/	/	/	/
1 chronic illness	Yes	38 (25.5%)	35 (27.6%)	64 (43%)	43 (41.7%)	11 (30.6%)	10 (32.3%)
2 chronic Illnesses	Yes	50 (33.6%)	42 (33.1%)	43 (28.9%)	28 (27.2%)	5 (13.9%)	4 (12.9%)
≥ 3 chronic illnesses	Yes	47 (31.6%)*	38 (29.9%)	21 (14.1%)	14 (13.6%)	4 (11.1%)	3 (9.7%)
Death after the first year	Yes	19 (12.8%)*		8 (5.4%)		1 (2.8%)	
	No	130 (87.2%)		141 (94.6%)		35 (97.2%)	
Second swab refusal	Yes	1 (0.7%)		38 (25.6%)*		3 (11.2%)	
	No	148 (99.3%)		111 (74.4%)		32 (88.8%)	

a in the previous season, b in the last 5 years, c in the last month, *, p<0.05 – see discussion

4 DISCUSSION

Swab analysis in two consecutive years in nursing home residents showed a NPCR of 1.45% on average, which is similar to the data found in the United States study among retirement community residents (25). Some characteristics of nursing home residents in our study, such as a higher number of patients with two or more comorbidities in the group of nursing home residents and a more common use of antibiotics in this group, were similar to the data found in studies by Lee and Sundvall (26, 27). An average NPCR in the group of elderly living in domestic environment in two consecutive years was 0.85%, which also correlates to some studies conducted among the elderly, where NPCR were 0.32% and 5.3%, respectively (28, 12). Most of the pneumococi isolated were serotyped, some of them were non-typeable, which means they did not have the polysaccharide capsule.

6B and 9N serotypes are present, along with other serotypes, in the 23-valent polysaccharide pneumococcal vaccine (PPV23); moreover, 6B is also present in the 13-valent conjugate pneumococcal vaccine (PCV13). The one *S. pneumoniae* carrier, who was vaccinated with PPV23 vaccine, carried a 6B serotype. Vaccination with this type of vaccine only prevents invasive pneumococcal disease, whereas vaccination with PCV13 vaccine also prevents nasopharyngeal colonization (29). A 6A serotype, which was identified in the participant from the group of the elderly from domestic environment, may have a potential to cause micro-epidemics in closed communities; it is present in the PCV13 vaccine (30).

Although NPCR among the elderly are low, this group represents a high risk population for invasive pneumococcal disease. This might implicate that long-term pneumococcal carriage among the elderly is rare, and that newly acquired pneumococci are responsible for invasive pneumococcal disease (31, 32). Seasonality also affects pneumococcal carriage rates - pneumococci are transmitted better during cooler and drier months (33).

The nasopharyngeal swab analysis among adults less than 65 years old showed that pneumococcal carriage rates were higher in this group in comparison to the elderly population – 5.3% in the first year and 8.8% in the second year. This may be because the participants from this group have more preschool children contacts (39.5%), compared to the groups of the elderly, although statistically significant difference was not confirmed in this case. Adults less than 65 years old carried 35 F (chronic carrier), 18C, 3 and a non-typeable serotype. None of the participants were vaccinated with either of pneumococcal vaccines.

The strong side of this study is that it is the first study addressing the topic of pneumococcal carriage and serotype identification among nursing home residents and the elderly living in domestic environment in Slovenia, and that the results of this study (low NPCR and serotype diversity) are consistent with foreign studies (34). There are also some limitations to this study. The first is that the sample is not representative, since it includes only participants from one nursing home and one community health center in the same region, and as the number of participants is not very high. The second limitation is that the study was not conducted in the coolest and driest months of the year, which might have influenced our results.

Although the NPCR among nursing home residents are low, the incidence of pneumonia (3) and the mortality rate in this population are significantly higher in comparison to the group of the elderly living in domestic environment (30% vs.16.7%) (2). In 2012, 81% of invasive pneumococcal infections in the population >65 years of age in Slovenia were caused with serotypes included in the PCV13 vaccine and 95% with serotypes included in the PPV23 vaccine (15). Pneumococcal vaccines are important means of invasive disease prevention, and are related to a lower mortality rate from pneumococcal pneumonia (6); nevertheless, the vaccination rates remain low also according to our data (3.3% in nursing home residents and 6% in the elderly from domestic environment). It is necessary to increase the number of vaccinated elderly.

5 CONCLUSIONS

Our data suggests that NPCR among the elderly are low and not significantly different in nursing home residents, compared to the elderly living in domestic environment. We identified different serotypes in all groups, only one person was a chronic carrier (serotype 35F). Our data also shows that pneumococcal vaccination rates are low in all compared groups, despite the benefits the vaccination brings.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

The Committee of the Republic of Slovenia for medical ethics approved the study on 19.12.2011, Nr. 72/11/11.

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KNOWLEDGE ABOUT BLOOD-BORNE PATHOGENS AND THE PREVALENCE OF NEEDLE STICK INJURIES AMONG MEDICAL STUDENTS IN SERBIA

POZNAVANJE PATOGENOV, KI SE PRENAŠAJO S KRVJO, IN RAZŠIRJENOST POŠKODB Z INJEKCIJSKIMI IGLAMI MED ŠTUDENTI MEDICINE V SRBIJI

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ABSTRACT

Keywords:
Hepatitis B vaccine, knowledge, medical students, needlestick injuries, Serbia

Introduction. Medical students are mainly exposed to needle stick and sharp object injuries in the course of their clinical activities during studying. They are at high risk due to their undeveloped skills, restricted clinical experience, lack of knowledge and risk perception. The objectives of this study were to determine the prevalence of needle stick injuries of the fourth and final year medical students, and to estimate their knowledge about blood-borne pathogens disease transmission and standard precautions.

Methods. This cross-sectional study was conducted at the Faculty of Medicine, in February 2014. The students were invited to self-administer a questionnaire of 26 closed questions prepared for this study.

Results. The questionnaire was filled in and returned by 637 students. The prevalence of needle sticks and sharp object injuries was 29.5%. Needle stick injuries were the most common type of accidents, more frequent among the fourth compared to the sixth year students (p=0.002). The majority of accidents occurred in patient rooms (53%) and the emergency department (15%). 54% of participants reported an accident to the responsible person. Students without accidents had a significantly better perception of risk (3.79 vs. 3.35; p<0.05). Out of the total participating students, only 16.6% (106/637) received all three doses of Hepatitis B vaccination, while 16.2% were partially vaccinated.

Conclusions. There is a need for additional theoretical and practical education of our students on blood exposure via accidents, raising the awareness of the necessity of hepatitis B vaccination, and introducing the unique/comprehensive procedure for accident reporting for students and healthcare workers in the entire country.

IZVLEČEK

Ključne besede:
cepivo za hepatitis B, znanje, študenti medicine, poškodbe z injekcijskimi iglami, Srbija

Uvod. Študentje medicine so v okviru kliničnih dejavnosti med študijem izpostavljeni predvsem vbodnim poškodbam z iglami ter urezninam z ostrimi predmeti. Zaradi še nerazvitih kliničnih veščin, skromnih kliničnih izkušenj in omejenega znanja je tveganje za poškodbo pri njih višje. Cilj te raziskave je bil zato ugotoviti razširjenost poškodb z iglami in ostrimi predmeti v medicini med študenti četrtega in zadnjega letnika medicine ter oceniti njihovo znanje o boleznih, ki se prenašajo s krvjo, in poznavanje standardnih varnostnih ukrepov.

Metode. Februarja 2014 smo izpeljali presečno raziskavo na Medicinski fakulteti Univerze v Beogradu. Študentje so bili povabljeni, naj izpolnijo vprašalnik, sestavljen iz 26 vprašanj zaprtega tipa, pripravljenih za to študijo.

Rezultati. Vprašalnik je izpolnilo 637 študentov. Razširjenost poškodb z iglami in ostrimi predmeti je bila 29,5-odstotna. Poškodbe z iglami so bile najpogostejša vrsta poškodb nasploh in pogostejša med študenti četrtega letnika v primerjavi s študenti šestega letnika (p=0,002). Večina poškodb se je pojavila v bolniških sobah (53%) in na urgentnih oddelkih (15%). Odgovorni osebi je nezgodo sporočilo 54% udeležencev. Študenti brez poškodb so bistveno bolje zaznavali tveganje (3,79 vs. 3,35; p<0,05). Le 51% sodelujočih študentov je bilo v celoti cepljenih proti hepatitisu B.

Zaključek. Obstaja potreba po dodatnem teoretičnem in praktičnem izobraževanju naših študentov o izpostavljenosti krvi zaradi poškodb z iglami in ostrimi predmeti, po dvigu zavesti o nujnosti cepljenja proti hepatitisu B in uvajanju celovitega postopka za poročanje o poškodbah z iglami in ostrimi predmeti za študente in zdravstvene delavce v celotni državi.

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1 INTRODUCTION

The World Health Organization (WHO) estimated that approximately 3 million Health Care Workers (HCWs) experience percutaneous exposure to blood-borne pathogens each year due to needle stick and sharp instruments injuries (1). Occupational accident can be defined as any unintended contact with blood and/or body fluids during a medical intervention. Although most of these accidents are without adverse outcomes, a number of blood-borne pathogens (BBP), such as hepatitis B and C viruses (HBV and HCV) or human immunodeficiency virus (HIV), can be transmitted through needle stick and other sharp injuries (2, 3). Medical students, as the HCWs, are exposed mainly to needle stick and sharp object injuries in the course of their clinical activities during studying due to their undeveloped skills, restricted clinical experience, lack of knowledge and risk perception (4-12). This study is one of the limited number of studies especially in the eastern part of Europe, about medical students' knowledge, practice, and attitudes toward occupational accidents.

The aims of this study were: [1] to determine the prevalence of needle stick injuries of fourth and final year medical students and [2] to estimate their knowledge about blood-borne pathogens (BBP) disease transmission and standard precautions.

2 METHODS

2.1 Study Design and Participants

This cross-sectional study was conducted at the Faculty of Medicine, University of Belgrade in February 2014. The participans were students of the fourth and sixth year of the faculty (first and final year clinical study). At our faculty, students have an introductory module for clinical practice in first grade, but they start their real practical sessions in the first semester of the fourth year, during study subject of the internal medicine, when they had daily student clinical practice and contacts with doctors, nurses and other staff in the hospital. All students in fourth and sixth study year were invited to complete a questionnaire at the end of their lectures. They did not feel pressured to fill out the questionnaire, because the participation in the survey was voluntary and anonymous. A self-administered anonymous questionnaire was prepared for the purpose of this study according to literature data.

Draft version of the questionnaire was given to a group of 15 students to determine whether the questions were understandable, whether the choice of responses was compatible with the experience of the respondents, whether all respondents understood the questions in the same manner and whether the questions measured what they needed to measure. The questionnaire was revised after the pretest and the final version was prepared. The students filled the questionnaire at the end of regular exercises

The questionnaire contained 26 closed questions that included: demographic characteristics (age, sex and type of finished secondary school), the number of accidents during previous year and during complete clinical schooling (fourth to sixth year of Medical faculty), place and circumstances of the accidents. Accidents were divided by nature of accidents on: a) needle stick injury (a sharp, penetrating stab wound from a needle that may result in exposure to blood or other body fluids); b) accident after handling with a contaminated sharp device; c) sharp injury after handling with the broken glass device (broken blood collection tubes, ampoules, thermometers etc.); d) accident after contact with a patient's blood through health care worker's damaged skin, and e) accident after contact with a patient's blood through HCW's conjunctiva/mucose membranes. Further, needle stick injuries are divided according the circumstances when an accident is occurring on: needle stick injury before using a needle (accident which occurred before needle contact with patient's blood or body fluids), needle stick injury after using a needle (accident made by any needle after exposure to the patient's blood of body fluids), accidents during needle recapping and during needle disposition in sharp containers. The level of knowledge was scored - the total score was 12 for knowledge of blood-borne diseases, 10 for knowledge of standard precautions and 8 for risk perception. The overall mean score for all three parties was taken for this survey.

2.2 Statistical Analysis

A descriptive analysis was performed. Continuous variables were presented as mean values with standard deviation (SD). Categorical values were summarized in terms of absolute frequencies and percentages. All variables were normally distributed. Fisher's chi-square test or Student's t-test was used as appropriate. Differences with a $p<0.05$ (two-tailed) were considered to be statistically significant. Two prevalence rates were calculated: the prevalence rate of students with accidents in previous year and prevalence rate of all accidents. The first one was calculated as the percentage of students who had reported at least one accident during the 12 months preceding the study. The second rate was calculated as the ratio between the number of all accidents during schooling and the number of students interviewed. We compared students' demographic characteristics and knowledge students' score about accidents between two groups of students (without accidents and with at least one accident). For the knowledge scores, one point was awarded for each correct answer and incorrect answer with a score of zero for a maximum aggregate knowledge

score of thirty points. Analysis of the database was done by SPSS 17.0 software package for Microsoft Windows.

3 RESULTS

Out of 769, a total of 637 students filled in and returned questionnaire. The response rate was 83% (89.4% in the fourth year and 73.8% in the final year of study). Demographic characteristics of students are given in Table 1. The majority of the students were female (68%), and two-thirds of all (68%) have graduated from a medical secondary school. Out of total participated students, only 16.6% (106/637) received all three doses of Hepatitis B vaccination, while 16.2% were partially vaccinated.

The reasons for not completing the course were that they forgot about the vaccination (77%), they were not at risk (11%), they believed that vaccine was not safe (4%), they already had antibodies towards Hepatitis B (1%). 8% of all students did not respond.

Table 1. Demographic characteristics of 4th and 6th year students, Medical school, University of Belgrade, Serbia, 2014 (N=637)[1].

	Frequency	(%)
Academic year		
Fourth	397	(62.3)
Sixth	240	(37.7)
Gender		
Male	201	(31.6)
Female	436	(68.4)
Finished secondary school		
Medical	434	(68.1)
Other	203	(31.9)
Taken Course on Occupational Exposure		
No	157	(24.6)
Yes	468	(73.4)
Hepatitis B vaccination		
No	428	(67.2)
Partially vaccinated	103	(16.2)
Vaccinated with 3 doses	106	(16.6)

[1]Missing data were not included in some analyses

In total, 60 students had at least one accident during the previous twelve months, which corresponds to a prevalence of 9.4%, (95% CI=7.3-12.0), (10.1% in fourth year students and 8.3% in sixth year students; p=0.466). Eleven of 16 students who had multiple accidents were

fourth year students. There were a total of 188 episodes of accidents (ranging from 1 to 8). The prevalence rate of all accidents was 29.5% (95% CI=26.0-33.2). Needle stick injuries were the most common type of accidents, and they were more frequent among fourth compared to sixth year students (p=0.002). Those accidents happened before and after using hollow bore needles, during recapping or disposing of needles into sharp containers. The majority of episodes of accidents happened during performing procedures in patient's room (46%). Further, it was found that students in sixth year have statistically significant more often mucocutaneous exposure to blood and body fluids through non-intact skin and conjunctiva (p=0.033 and p=0.003, respectively) (Table 2). The majority of accidents occurred in the patient's rooms (53%) and emergency department (15%). Only 31 (54%) participants who had an accident reported it to the responsible person, regardless of the academic year. The two major reasons were the beliefs that it was not the type of exposition during which a student could be infected (32%), and the belief that the patient had not been infected (17%). Further, students failed to report because they did not know to whom to report (12%), or because they believed that it was not necessary to report (7%).

Table 2. Nature of accidents by the circumstances when the accidents occurred of 4th and 6th year students, Medical school, University of Belgrade, Serbia, 2014.

	n=60 Academic year No. (%)		P
	Fourth	Sixth	
Needle stick injury	32 (53.3)	8 (13.3)	0.002
Before using needle	1 (1.7)	2 (3.3)	0.209
After using needle	5 (8.3)	7 (11.7)	0.040
Needle recapping	12 (20.0)	4 (6.7)	0.409
During needle disposition in sharp container	9 (15.0)	0 (0)	0.018
Handling with contaminated sharp devices	12 (20.0)	2 (3.3)	0.084
Handling with broken glass devices (broken blood collection tubes, ampoules, thermometers etc.)	9 (15.0)	1 (1.7)	0.086
Contact with blood through damaged skin	0 (0)	5 (8.3)	0.003
Contact with boold through conjuctiva/mucose membranes	0 (0)	3 (5.0)	0.033

* P - according to Chi-square test or Fisher test

Factors possibly associated with an accident are presented in Table 3.

Table 3. Factors possibly associated with the accidents among Medical school students, University of Belgrade, Serbia, 2014.

	Students		
	Without accidents	With at least one accident	P
Academic year			
Fourth	357 (89.9)	40 (10.1)	0.466
Sixth	220 (91.7)	20 (8.3)	
Gender			
Male	177 (88.1)	24 (11.9)	0.139
Female	400 (91.7)	36 (8.3)	
Finished secondary school			
Medical	399 (91.9)	35 (8.1)	0.087
Other	178 (87.7)	25 (12.3)	
Mean Scores of:			
knowledge on BBD transmission	8.59±2.08	8.44±2.51	0.606
knowledge on standard precautions	6.05±2.08	6.35±2.19	0.281
risk perception	3.79±1.66	3.35±1.56	0.049
Total score	18.44±3.92	18.15±4.44	0.597

* P - according to Chi-square test, Fisher test or Student`s t-test

There were no statistically significant differences between students who had and who did not have any accident, regarding the year of study, sex and type of finished secondary school. The overall mean score on blood borne diseases (BBD), separated in three categories (knowledge on BBD transmission, knowledge on standard precautions and risk perception) was 18.41±3.97, with a score range from 0 to 30. The mean score of knowledge on BBD transmission was 8.58±2.13 (with a range of 0-12); on standard precaution 6.08±2.09 (with range of 0-10), and 3.75±1.66 (with range of 0-8) on risk perception. Students without accidents during the past year had a slightly better perception of risk (3.79 vs. 3.35; p<0.05). The statistical analysis did not reveal significant differences regarding other scores between the two groups of students.

Students who have taken the course on occupational exposure had a higher prevalence of accidents (needle stick injuries and sharp objects injuries) (10.9% vs. 5.1%; p=0.013) and a better protection against hepatitis B virus; they were the ones who received all three doses of the vaccine (18.4% vs. 12.9%) (p=0.114). But there was no statistical significance between students who have taken

the course on occupational exposure and those who have not, in relation to knowledge scores about BBD transmission (8.55±2.1 vs. 8.64±1.9; p=0.307).

The majority of all students (74%) expressed their needs about additional education on needle stick and sharp devices accidents.

4 DISCUSSION

The results of this study indicate that the prevalence of students with at least one accident was the prevalence obtained among students in developed countries, (6, 14, 15) but lower than the prevalence in some less developed countries (15, 16). The overall accidents were less frequent in the sixth year students than in younger students. Needle stick injuries and injuries with sharp and broken glass devices were less common in these students too. This can be explained by a higher theoretical education and better practical skills of older students. Other authors also revealed that final year students had a smaller number of accidents (13, 17). On the contrary, Zhang at al. found the highest rate of accidents in the fifth academic year (18). In a recently published study, which included students in the final year of education from 11 medical universities in Austria, Germany, and the United Kingdom, it is revealed that 34% of these students suffered at least one accident during medical school training with significant differences among countries (19). The authors postulated that the medical curricula in Austria and Germany included training and practice of blood collection. A higher workload regarding blood collection resulted in a higher rate of accidents in Austria and Germany. Higher lifetime prevalence in the final academic year was also noted in other studies (13). Although there were no significant differences regarding the level of knowledge on BBD transmission and standard precautions, our results revealed that the lower score of risk perception was present in students who experienced at least one accident. In a study conducted in the UK, Austria and Germany (5), the authors concluded that improved knowledge due to the training and implementation of the guidelines resulted in a significant reduction of needle stick injuries over the time (5). Both our student groups showed a relatively low knowledge level, although the lectures on occupational exposure to blood and body fluids are compulsory in some subjects during studying at the faculty. Even though there is a lack of safety devices (such as safety yellow biohazard containers, protective disposable goggles, masks, gloves and aprons, which should exist not only for health care work, but also for students during their practical training) in our country, it is important to improve students' theoretical knowledge and practical skills regarding needle stick and sharp device injuries, as it has been done in other countries (20).

Approximatelythree-quartersof our students expressed their needs and determination for additional education on occupational injuries.

Underreporting of accidents observed both in healthcare workers and students still remains a widespread public health problem. Kessler et al. noted underreporting from 14.8% to 97% in their review of literature (21). About half of our student did not report the accident in our study. The major reasons for not reporting were the lack of knowledge about proper reporting procedures and perceived low risk. Our country does not possess a comprehensive guide for blood exposure reporting. Therefore, underreporting in healthcare workers, in Serbia, was observed in the research conducted by Jovic-Vranes et al. (22).

Although vaccination against HBV for HCW's and medical students in secondary medical schools is mandatory, according to the Rulebook about immunisation and hemiprofilactic protective treatment of the Republic of Serbia, made by doctors and specialists selected by the Serbian Government, not enough HCW's and medical students have been vaccinated before they started their school or professional practice.

In our study, about 33% of medical students were immunised, with half of them receiving complete vaccination with three doses. It is particularly concerning that only 10% of the fourth year students, who begin their clinical practice and are exposed to blood borne viruses, have been vaccinated. The importance of immunisation is covered early in the medical training at our faculty, as early as in the second year and, in more detail, in the fourth year. Even though such education contributes to a higher percentage of those who get vaccinated in the senior years of their studies (47% of the sixth year students), that percentage is still much smaller compared to the percentage of medical students who get vaccinated in other countries (13, 15).

5 CONCLUSION

We can conclude that there is a need for additional theoretical and practical education of our students on blood exposure via accidents, raising the awareness of the necessity of hepatitis B vaccination, and introducing the unique/comprehensive procedure for accident reporting for students and healthcare workers in the entire country.

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CONFLICTS OF INTEREST

All authors confirm that no conflict of interests exists in this research article.

I confirm that this manuscript is not under simultaneous consideration by any other journal, and that it has not been previously published.

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ETHICAL APPROVAL

This type of research didnot require an ethical approval, but it complies with all ethical and moral standards. Participants were not being forced to participate in this research or to fill in questionnaires. They completed questionnaires at the end of their lecture in epidemiology.

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SURVIVAL OF NODE-NEGATIVE BREAST CANCER PATIENTS TREATED AT THE UNIVERSITY MEDICAL CENTRE MARIBOR IN THE PERIOD 2000-2009

PREŽIVETJE BOLNIC Z RAKOM DOJK BREZ ZASEVKOV V BEZGAVKAH, ZDRAVLJENIH V UNIVERZITETNEM KLINIČNEM CENTRU MARIBOR V OBDOBJU OD LETA 2000 DO LETA 2009

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ABSTRACT

Keywords:
breast cancer,
survival,
time trends,
regional
differences,
Slovenia

Introduction. Breast cancer is increasingly diagnosed in the early stages without regional nodal involvement. The aim of the present study was to determine the 5-year overall (OS) and breast cancer specific survival (BCSS) for patients with node-negative breast cancer treated at the University Medical Centre Maribor, and compare it with survival at the national level.

Methods. Medical records were searched for information on patients with lymph node-negative invasive breast cancer who received primary treatment at the University Medical Centre Maribor in the period 2000-2009. Information on all Slovenian node-negative breast cancer patients diagnosed in the same period was obtained from the Cancer Registry of Republic of Slovenia. Time trends in survival were assessed by comparing the periods 2000-2004 and 2005-2009.

Results. The 5-year OS and BCSS of patients treated in Maribor in the period 2000-2009 were 92.3% (95% CI, 90.5%-94.1%) and 96.4% (95% CI, 95.2%-97.6%), respectively, and did not differ from the corresponding OS and BCSS for Slovenian patients. Although the improvement in OS for patients from Maribor diagnosed in the period 2005-2009 compared to 2000-2004 did not reach statistical significance (HR 0.73; 95% CI, 0.51-1.05; p=0.086), BCSS significantly improved over the same time periods (HR 0.53; 95% CI, 0.30-0.94; p=0.028).

Conclusions. Survival of node-negative breast cancer patients treated at the University Medical Centre Maribor is comparable to survival of corresponding patients at the national level. The rising number of long-term breast cancer survivors places additional importance on survivorship care.

IZVLEČEK

Ključne besede:
rak dojk,
preživetje,
časovni vzorci,
regionalne
razlike,
Slovenija

Uvod. *Raka dojk vse pogosteje odkrijemo v zgodnjih stadijih, ko regionalne bezgavke še niso prizadete. Namen te raziskave je bil ugotoviti petletno celokupno in specifično preživetje bolnic z rakom dojk brez zasevkov v bezgavkah, zdravljenih v Univerzitetnem kliničnem centru Maribor, in ga primerjati s preživetjem na ravni Slovenije.*

Metode. *Podatke o bolnicah z invazivnim rakom dojk brez zasevkov v bezgavkah, ki so bile primarno zdravljene v Univerzitetnem kliničnem centru Maribor v obdobju 2000-2009, smo pridobili iz medicinske dokumentacije. Podatke o vseh slovenskih bolnicah z invazivnim rakom dojk brez zasevkov v bezgavkah, odkritim v istem obdobju, smo pridobili iz Registra raka Republike Slovenije. Za analizo časovnih vzorcev preživetja smo primerjali dve petletni obdobji odkritja bolezni: 2000-2004 in 2005-2009.*

Rezultati. *Petletno celokupno preživetje bolnic, zdravljenih v Univerzitetnem kliničnem centru Maribor v letih 2000-2009, je znašalo 92,3 % (95-odstotni interval zaupanja 90,5-94,1 %), specifično preživetje pa 96,4 % (95-odstotni interval zaupanja 95,2-97,6 %). Preživetje bolnic, zdravljenih v Univerzitetnem kliničnem centru Maribor, se ni pomembno razlikovalo od ustreznih preživetij vseh slovenskih bolnic. Opazno je bilo izboljšanje celokupnega preživetja pri bolnicah, primarno zdravljenih v obdobju 2005-2009, v primerjavi s tistimi, zdravljenimi v obdobju 2000-2004, čeprav trend ni dosegel statistične značilnosti (Maribor: razmerje tveganj 0,73; 95-odstotni interval zaupanja 0,51-1,05; p=0,086; Slovenija: razmerje tveganj 0,77; 95-odstotni interval zaupanja 0,66-0,89; p<0,001). Izboljšanje specifičnega preživetja v istih obdobjih diagnoze je bilo statistično značilno pri obeh skupinah bolnic (Maribor: razmerje tveganj 0,53; 95-odstotni interval zaupanja 0,30-0,94; p=0,028; Slovenija: razmerje tveganj 0,66; 95-odstotni interval zaupanja 0,54-0,81; p<0,001).*

Zaključki. *Preživetje bolnic z rakom dojk brez zasevkov v bezgavkah, zdravljenih v Univerzitetnem kliničnem centru Maribor, je primerljivo s preživetjem vseh podobnih bolnic v Sloveniji. Zaradi vse večjega števila žensk z dolgotrajnim preživetjem po zdravljenju raka dojk, pri katerih se pojavljajo specifične zdravstvene težave in tveganja, postaja vse pomembnejša njihova celostna in dolgoročna obravnava.*

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1 INTRODUCTION

Breast cancer is the most common cancer in women whose incidence continues to grow in most parts of the world, largely due to the aging population. In Slovenia, crude breast cancer incidence has increased from 94.3/100.000 women in 2000 to 110.7/100.000 women in 2009 (1). Breast cancer remains the leading cause of cancer-related death in Slovenia (2) as well as in Europe (3) despite the remarkable improvements in survival achieved over the last decades (2, 4, 5). Breast cancer screening programmes have been implemented in many countries across Europe since the 1990s (6). These have been shown to improve breast cancer specific survival rates by approximately 20%, mostly due to earlier diagnosis (7-9). In Slovenia, national breast cancer screening programme DORA has begun with biannual organised screening of women aged 50-69 in the Ljubljana region in 2008 and has been gradually expanding so that it now includes 72% of the target population in Slovenia (10). A slight shift towards earlier diagnosis has been already noted in Slovenia before widespread organised breast cancer screening (11, 12), probably due to a considerable amount of "opportunistic" mammography testing and rising public awareness. In 2013, 55.5% of breast cancers in Slovenian women were diagnosed in a localised stage without regional nodal involvement (2). This number is expected to rise further in the following years.

Irrespective of such a large proportion of patients with localised disease, Slovenian data on survival of this prognostically favourable group of patients are scarce. In addition, separate survival data for patients treated at the University Medical Centre Maribor, a combined secondary/tertiary care centre treating breast cancer patients from the north-eastern region of Slovenia, have never been published. We performed this retrospective study to determine the 5-year overall and breast cancer specific survival for patients with node-negative breast cancer who received primary treatment at the University Medical Centre Maribor in the period 2000–2009. As a quality control measure, we compared the survival of our patients with that of patients with the same characteristics at the national level.

2 METHODS

Medical records were searched for information on patients with lymph node-negative invasive breast cancer without distant metastases who received primary treatment at the University Medical Centre Maribor, Slovenia, between January 1 2000 and December 31 2009. Exclusion criteria were systemic treatment or radiotherapy before primary surgery and more than one primary cancer. Information on date of diagnosis, patient age, primary treatment, possible disease recurrence, date and cause of death was

obtained from hospital medical records. Information on possible date and cause of death for the patients who did not regularly attend follow-up visits was obtained from the Cancer Registry of Republic of Slovenia. The cause of death for these patients was double-checked with their family physicians. All patients were followed for a minimum of 5 years until December 31, 2014.

The study group was compared with all female permanent residents of Slovenia who were diagnosed with invasive breast cancer without lymph node or distant metastases in the period 2000-2009 who were primarily treated with surgery and did not receive preoperative systemic treatment or radiotherapy. All data for this group of patients were obtained from the Cancer Registry of Republic of Slovenia (1). In order to make this group as similar to the study group as possible and because the Cancer Registry did not yet have information on cause of death for patients who died in 2015 and 2016, December 31, 2014, was chosen as the cut-off date for survival analyses for these patients, as well.

All patients received either lumpectomy with sentinel lymph node biopsy followed by radiotherapy or modified radical mastectomy as locoregional treatment. Adjuvant systemic therapy was given according to the relevant clinical practice guidelines and the decision made by the multidisciplinary tumour board. In general, all patients with hormone receptor positive tumours were offered adjuvant hormone therapy, and most patients with hormone receptor negative tumours were offered adjuvant chemotherapy. Adjuvant chemotherapy in addition to adjuvant hormone therapy was offered to high-risk patients with hormone receptor positive tumours. Adjuvant trastuzumab in combination with chemotherapy was offered to most patients with HER2 positive tumours treated in the period 2005–2009 and to a few selected high-risk patients in the period 2000–2004.

To analyse the time trends in survival, patients were divided in two groups based on the year of diagnosis: 2000–2004 and 2005–2009. Overall survival (OS) was calculated from the date of diagnosis until the date of death from any cause. Breast cancer specific survival (BCSS) was calculated from the date of diagnosis until the date of death from breast cancer. Kaplan-Meier method was used to calculate survival curves and univariate Cox regression was used to assess the hazard ratios (HR). To control for some other clinically important variables apart from treatment period, multivariate analyses were performed by applying the multivariate Cox proportional hazards model. All tests were performed at a significance level of $p=0.05$ and a confidence interval (CI) of 95%. All p values were two-sided. Statistical analysis was performed using the SPSS software package v. 22 (IBM, Armonk, NY, USA).

3 RESULTS

In the period 2000–2009, 858 node-negative invasive breast cancer patients without distant metastases were treated at the University Medical Centre Maribor. This represented 18.1% of the 4740 corresponding node-negative patients who were treated in Slovenia in the same period. The characteristics of patients in both groups are shown in Table 1.

Table 1. Characteristics of node-negative breast cancer patients treated at the University Medical Centre Maribor (N=858) and in Slovenia (N=4740) in the period 2000–2009.

	Maribor N (%)	Slovenia N (%)
Time period		
2000-2004	373 (43.5)	2253 (47.5)
2005-2009	485 (56.5)	2487 (52.5)
Age		
<40 years	37 (4.3)	208 (4.4)
≥40 and <70 years	561 (65.4)	3316 (70.0)
≥70 years	260 (30.3)	1216 (25.6)
Postoperative radiation therapy		
no	439 (51.2)	2504 (52.8)
yes	419 (48.8)	2236 (47.2)
Adjuvant systemic therapy		
no	71 (8.3)	839 (17.7)
yes	787 (91.7)	3901 (82.3)

Overall survival analysis was based on 163 events in the group of patients treated in Maribor, and 943 events in all Slovenian patients. The 5- and 10-year OS probabilities of patients who underwent primary treatment at the University Medical Centre Maribor in the period 2000–2009 were 92.3% (95% CI, 90.5%–94.1%; 66 events, 44 censored cases) and 80.1% (95% CI, 77.0%–83.2%; 133 events, 479 censored cases), respectively. The 5-year OS probabilities of the patients diagnosed in the periods 2000–2004 and 2005–2009 were 89.2% (95% CI, 86.1%–92.3%) and 94.6% (95% CI, 92.6%–96.6%), respectively (HR 0.73; 95% CI, 0.51–1.05; p=0.086; Figure 1). In the group of all Slovenian patients, the 5- and 10-year OS probabilities of patients diagnosed in the period 2000–2009 were 91.3% (95% CI, 90.5%–92.1%; 413 events, no censored cases) and 79.6% (95% CI, 78.2%–81.0%; 809 events, 2179 censored cases), respectively. For these patients, OS was significantly better for patients diagnosed in the period 2005–2009, compared to those diagnosed in the period 2000–2004 (HR 0.77; 95% CI, 0.66–0.89; p<0.001; Figure 2).
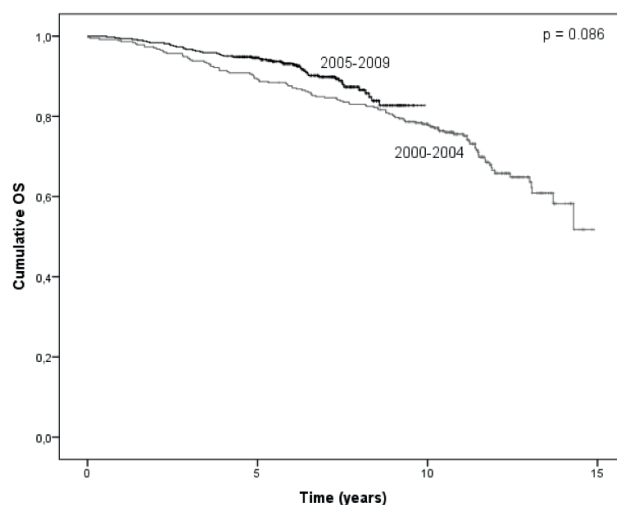

Figure 1. Kaplan-Meier plot of overall survival (OS) probability for node-negative breast cancer patients treated at the University Medical Centre Maribor, according to the period of diagnosis (N=858). The difference in OS between the two periods of diagnosis is not statistically significant (p=0.086).
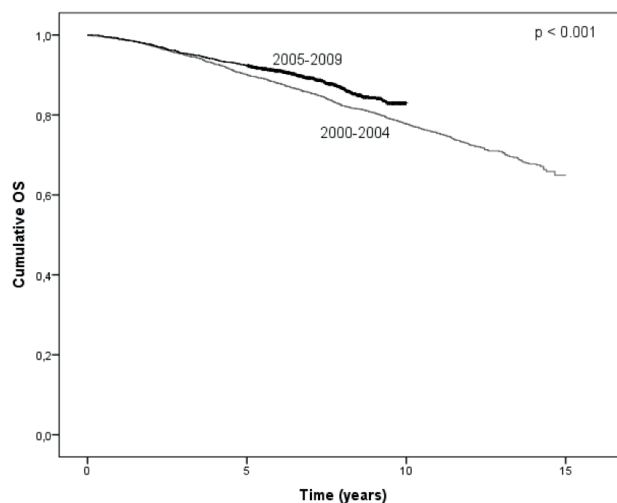

Figure 2. Kaplan-Meier plot of overall survival (OS) probability for all Slovenian node-negative breast cancer patients according to the period of diagnosis (N=4740). OS was significantly better for patients diagnosed in the period 2005–2009, compared to those diagnosed in the period 2000–2004 (p<0.001).

A comparison of 1-, 3- and 5-year OS probabilities according to the period of diagnosis and site of treatment is presented in Table 2. No difference in overall survival was observed between the patients treated at the University Medical Centre Maribor and all Slovenian patients (HR 1.07; 95% CI, 0.91–1.27; p=0.413; Figure 3).

Table 2. Comparison of 1-, 3- and 5-year overall survival (OS) probabilities for node-negative breast cancer patients treated at the University Medical Centre Maribor (N=858) and in Slovenia (N=4740) in the period 2000-2009. The only statistically significant OS difference was observed between the two periods in Slovenian patients (p<0.001).

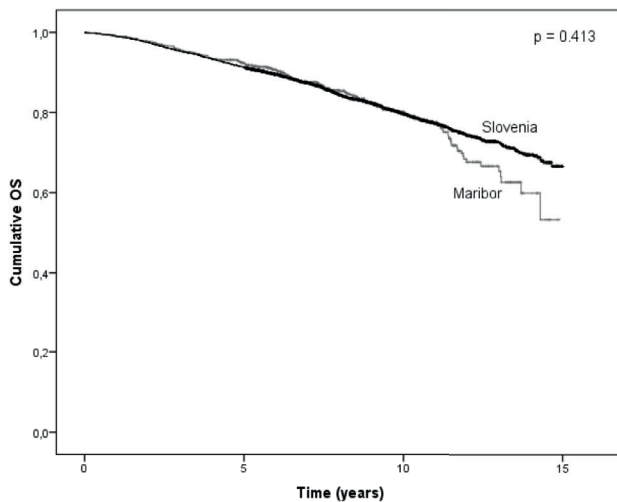| OS	Maribor				Slovenia			
	2000-2004		2005-2009		2000-2004		2005-2009	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
1-year	98.7	97.5-99.9	99.4	98.6-100	98.9	98.5-99.3	99.0	98.6-99.4
3-year	94.3	91.9-96.7	96.7	95.1-98.3	95.2	94.2-96.2	95.5	94.7-96.3
5-year	89.2	86.1-92.3	94.6	92.6-96.6	90.1	88.9-91.3	92.4	91.4-93.4

Figure 3. Kaplan-Meier plot of overall survival (OS) probability for node-negative breast cancer patients treated at the University Medical Centre Maribor (N=858), compared to all Slovenian node-negative breast cancer patients (N=4740) diagnosed in the period 2000-2009. No difference in OS was observed (p=0.413). The final part of the line representing the Maribor data is less reliable, because of the small number of patients at risk.
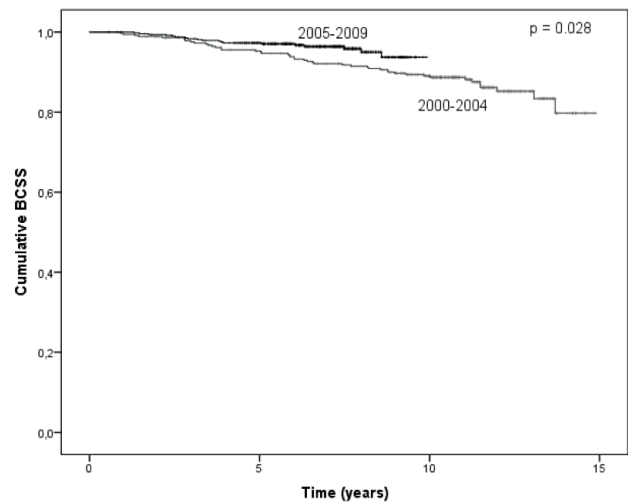

Figure 4. Kaplan-Meier plot of breast cancer specific survival (BCSS) probability for node-negative breast cancer patients treated at the University Medical Centre Maribor, according to the period of diagnosis (N=858). BCSS was significantly better for patients diagnosed in the period 2005-2009, compared to the patients diagnosed in the period 2000-2004 (p=0.028).

Breast cancer specific survival analysis was based on 65 events in the group of patients treated in Maribor, and 458 events in all Slovenian patients. The 5- and 10-year BCSS probabilities of patients who underwent primary treatment at the University Medical Centre Maribor in the period 2000-2009 were 96.4% (95% CI, 95.2%-97.6%; 30 events, 69 censored cases) and 91.1% (95% CI, 88.7%-93.4%; 57 events, 556 censored cases), respectively. The corresponding 5- and 10-year BCSS probabilities in all

Slovenian patients were 95.1% (95% CI, 94.5%-95.7%; 413 events, 183 censored cases) and 89.5% (95% CI, 88.5%-90.5%; 415 events, 2573 censored cases), respectively. Improved BCSS was noted in patients diagnosed in the period 2005-2009, compared to the period 2000-2004 for patients treated in Maribor (HR 0.53; 95% CI, 0.30-0.94; p=0.028; Figure 4), as well as for all Slovenian patients (HR 0.66; 95% CI, 0.54-0.81; p<0.001; Figure 5).
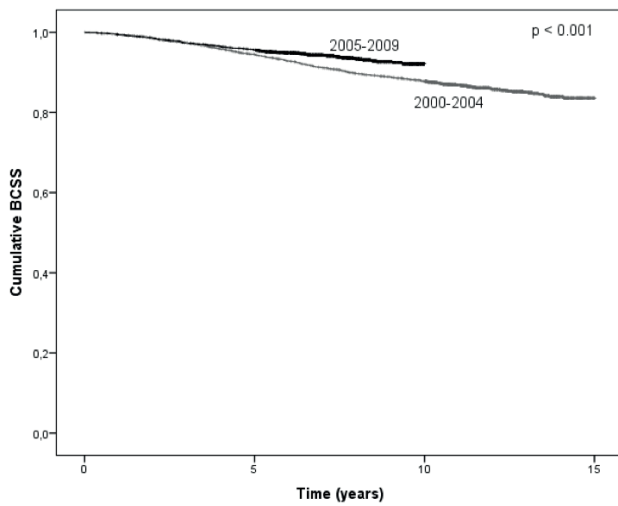
Figure 5. Kaplan-Meier plot of breast cancer specific survival (BCSS) probability for all Slovenian node-negative breast cancer patients according to the period of diagnosis (N=4740). BCSS was significantly better for patients diagnosed in the period 2005-2009, compared to those diagnosed in the period 2000–2004 (p<0.001).
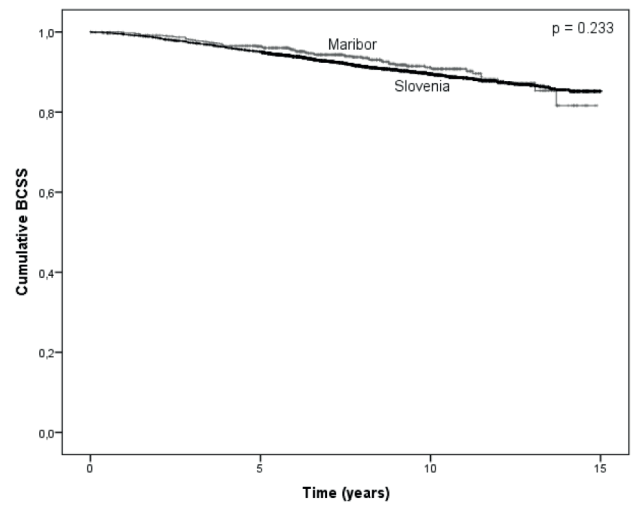

Figure 6. Kaplan-Meier plot of breast cancer specific survival (BCSS) probability for node-negative breast cancer patients treated at the University Medical Centre Maribor (N=858), compared to all Slovenian node-negative breast cancer patients (N=4740) diagnosed in the period 2000–2009. No difference in BCSS was observed (p=0.233).

No difference in breast cancer specific survival was observed between the patients treated at the University Medical Centre Maribor and all Slovenian patients (HR 0.85; 95% CI, 0.66–1.11; p=0.233; Figure 6). Table 3 shows a comparison of 1-, 3- and 5-year BCSS probabilities according to the period of diagnosis and site of treatment.

Table 3. Comparison of 1-, 3- and 5-year breast cancer specific survival (BCSS) probabilities for node-negative breast cancer patients treated at the University Medical Centre Maribor (N=858) and in Slovenia (N=4740) in the period 2000–2009. Statistically significant BCSS differences were observed between the two periods in patients treated in Maribor (p=0.028) and in all Slovenian patients (p<0.001). No differences were observed according to the site of treatment (p=0.233).

BCSS	Maribor				Slovenia			
	2000-2004		2005-2009		2000-2004		2005-2009	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
1-year	99.5	98.7-100	100	99.6-100	99.4	99.0-99.8	99.4	99.0-99.8
3-year	97.5	95.9-99.1	98.3	97.1-99.5	97.3	96.7-97.9	97.3	96.7-97.9
5-year	95.3	93.1-97.4	97.3	95.9-98.7	94.5	93.5-95.5	95.6	94.8-96.4

The results of multivariate analyses of OS and BCSS are presented in Tables 4 and 5.

Table 4. Multivariate analysis of factors influencing overall survival (OS) and breast cancer specific survival (BCSS) in node-negative breast cancer patients treated at the University Medical Centre Maribor in the period 2000-2009 (N=858).

Factor	OS		BCSS	
	HR (95% CI)	p	HR (95% CI)	p
Treatment period				
(2005-2009 vs. 2000-2004)	0.63 (0.44-0.90)	0.011	0.51 (0.29-0.91)	0.021
Adjuvant radiotherapy				
(yes vs. no)	0.36 (0.22-0.57)	<0.001	0.41 (0.22-0.76)	0.005
Adjuvant chemotherapy				
(yes vs. no)	0.56 (0.36-0.85)	0.007	0.39 (0.20-0.78)	0.007
Age		<0.001		0.105
<40 years vs. ≥70 years	0.55 (0.22-1.42)	0.217	2.17 (0.77-6.13)	0.142
40-70 years vs. ≥70 years	0.33 (0.23-0.49)	<0.001	0.80 (0.45-1.42)	0.442

Table 5. Multivariate analysis of factors influencing overall survival (OS) and breast cancer specific survival (BCSS) in node-negative breast cancer patients treated in Slovenia in the period 2000-2009 (N=4740).

Factor	OS		BCSS	
	HR (95% CI)	p	HR (95% CI)	p
Treatment period				
(2005-2009 vs. 2000-2004)	0.76 (0.66-0.88)	<0.001	0.67 (0.55-0.82)	<0.001
Adjuvant radiotherapy				
(yes vs. no)	0.60 (0.51-0.71)	<0.001	0.65 (0.52-0.81)	<0.001
Adjuvant chemotherapy				
(yes vs. no)	0.75 (0.65-0.87)	<0.001	0.77 (0.62-0.96)	0.019
Age		<0.001		<0.001
<40 years vs. ≥70 years	0.37 (0.26-0.54)	<0.001	0.86 (0.57-1.30)	0.475
40-70 years vs. ≥70 years	0.30 (0.26-0.34)	<0.001	0.47 (0.38-0.58)	<0.001

4 DISCUSSION

Despite some limitations as pertains the comparability of the groups due to the differences in data collection, we believe that our results show clearly enough that overall and breast cancer specific survival of early stage breast cancer patients treated at the University Medical Centre Maribor do not differ from the survival of all Slovenian patients with similar characteristics. This expected result serves as important evidence that the quality of treatment of early breast cancer patients in our centre is not inferior to Slovenian average. Of course, this result will also encourage us to try to further improve our patient care.

Improvement of survival was noted over two five-year periods of diagnosis, 2000-2004 and 2005-2009. In multivariate analyses, controlling for other clinically important variables, statistically significant improvement of both OS and BCSS persisted, irrespective of patient age and adjuvant treatment. One of the reasons for this improvement is probably the increasing proportion of small nonpalpable tumours detected by screening. The other major reason for improved survival is undoubtedly the improvement of both adjuvant systemic treatment and treatment of metastatic breast cancer, as exemplified by the use of trastuzumab in HER2-positive disease (13).

In general, a marked improvement of 5-year relative survival rates of all breast cancer patients has been noted in most of the European countries in the first decade of the 21st century (14). In Slovenia, 5-year relative survival for breast cancer patients has risen from 81.8% for those diagnosed in the period 2000-2004 to 88.1% in the period 2005-2009 (15). However, some data suggest that the larger part of survival improvement in developed countries has been seen in higher-stage, node-positive disease, while little or no improvement has been noted in the prognostically more favourable group of node-

negative patients (16). In contrast, strong improvement of survival rates over time has been observed in node-negative breast cancer patients in some less developed countries, for example, in Malaysia, where an increase of 5-year overall survival probability from 79% in the period 1993–1997 to 94% in 1998–2002 has been reported in a single-institution study (17).

The other factors associated with better survival in multivariate analyses of both the Maribor and the Slovenian cohort were adjuvant radiotherapy and adjuvant systemic therapy. These findings are consistent with large reviews of the literature (18, 19). However, firm conclusions about the effects of adjuvant treatment cannot be drawn based on our study, because we did not have exact information on important confounding prognostic factors that influence adjuvant treatment decisions. Additionally, age was a significant factor in our multivariate analyses as well. Expectedly, patients aged 70 and above were at an increased risk of dying of any cause, compared to younger patients. In the larger Slovenian cohort, these patients also had worse BCSS, compared to patients aged 40–70 years, but no worse than patients under 40. Similar trends have been reported in other countries (20).

The results of our study confirm excellent 5-year survival rates in breast cancer patients without lymph node metastases throughout the study period. BCSS of patients treated at the University Medical Centre Maribor in the period 2000–2009 was 96.4%, and the corresponding BCSS of all Slovenian patients was 95.1%. These numbers are similar to the reported 96.9% 5-year cause-specific survival of node-negative breast cancer patients treated in Sweden in the period 2000-2004 (21). A CONCORD high-resolution study that compared breast cancer survival data across seven US states and twelve European countries, including Slovenia, reported 92–98% 5-year age-standardised net survival of node-negative patients with small (T1) tumours, and 84–93% 5-year age-standardised net survival of node-negative patients with larger (T2-3) tumours for patients diagnosed in the period 1994–1999 (22).

Due to these high and further rising survival rates, it is essential to emphasise the need for coordinated survivorship care. Patients may face long-term medical issues, such as cardiac issues, bone health problems, lymphedema and thromboembolic events as a consequence of their disease or its treatment. In addition to follow-up for breast cancer recurrence, it is important to keep in mind that these patients are at an increased risk for second primary malignancies. Furthermore, survivorship care should routinely incorporate advice on a healthy diet and an active lifestyle (23).

5 CONCLUSIONS

We have shown that overall and breast cancer specific survival of node-negative breast cancer patients treated at the University Medical Centre Maribor are not inferior to survival of patients treated elsewhere in Slovenia. Although survival rates of these patients who now constitute more than half of all Slovenian breast cancer patients are already very high, there was still a clear trend of improvement over two time periods, both in Maribor and in Slovenia. The rising number of long-term breast cancer survivors places an additional importance on survivorship care.

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CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

Received from the Republic of Slovenia National Medical Ethics Committee, approval No. 55/11/13.

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7. Hickner J, Barry HC, Ebell MH, Ettenhofer T, Eliot R, Sugden K et al. Suicides and non-suicidal deaths in Slovenia: molecular genetic investigation. In: 9th European Symposium on Suicide and Suicidal Behaviour. Warwick: University of Oxford, 2002: 76.

example for master theses, doctor theses:

8. Bartol T. Vrednotenje biotehniških informacij o rastlinskih drogah v dostopnih virih v Sloveniji: doktorska disertacija. Ljubljana: Biotehniška fakulteta, 1998.

example for electronic sources:

9. Mendels P. Textbook publishers extend lessons online. Available Sept 23, 1999 from: http://www.nytimes.com/library/tech/99/09.

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Type on the place in the text where they belong. Tables should be composed by lines and columns which intersect in fields. Number tables consecutively. Each table should be cited in the text and supplied with a brief title. Explain all the abbreviations and non-standard units in the table.

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Illustrations should be professionally drawn. When preparing the illustrations consider the black-and-white print. Illustration material should be prepared in black-and-white (not in color!). Surfaces should have no tone-fills, hatchings should be chosen instead (in case of bar-charts, so called pie-charts or maps). In linear graphs the individual lines should also be separated by various kinds of hatching or by different markers (triangles, asterisks ...), but not by color. Graphs should have white background (i. e. without background).

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Should be in accordance with International System of Units (SI).

ABBREVIATIONS

Avoid abbreviations, with the exception of internationally valid signs for units of measurement. Avoid abbreviations in the title and abstract. The full term for which an abbreviation stands should precede its first use in the text, abbreviation used in further text should be cited in parentheses.

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The received manuscript is submitted by the editor to three international professional reviewers. After the reviewing process, the contribution is sent to the author for approval and consideration of corrections. The final copy is than again submitted to the Editorial Office. During the editorial process, the secrecy of the contribution content is guaranteed. All the articles are language edited. Author receives in consideration also the first print, but at this stage corrigenda (printing errors) only are to be considered. Proofreading should be returned in three days, otherwise it is considered that the author has no remarks.

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NAVODILA AVTORJEM

Revija: **Zdravstveno varstvo (ZV)** ISSN 0351-0026 (tiskana izdaja) / **Slovenian Journal of Public Health (SJPH)** ISSN 1854-2476 (elektronska izdaja)

Navodila so v skladu z Uniform Requirements for Manuscripts Submitted to Biomedical Journals. Popolna navodila so objavljena v N Engl J Med 1997; 336: 309-15 in v Ann Intern Med 1997; 126: 36-47 in na spletni strani http://www.icmje.org.

ETIČNI STANDARDI

Uredništvo sprejema v obdelavo le članke s širšo mednarodno javnozdravstveno tematiko, ki še niso bili in ne bodo objavljeni drugje. Dele članka, ki so povzeti po drugi literaturi (predvsem slike in tabele), mora spremljati dovoljenje avtorja in založnika prispevka, da dovoli naši reviji reprodukcijo.

Oddan rokopis morajo prebrati vsi avtorji in se z njegovo vsebino strinjati.

Raziskave na ljudeh (vključno s človeškimi materiali in osebnimi podatki) morajo biti izpeljane v skladu s Helsinško deklaracijo in potrjene s strani nacionalne etične komisije. V izjavi na koncu rokopisa morajo avtorji podati izjavo o etiki raziskav na ljudeh, ki mora vsebovati ime etične komisije in referenčno številko obravnave. Poročanje o raziskavah na ljudeh brez potrdila etične komisije zahteva dodatno razlago v poglavju o metodah dela. Na zahtevo Uredništva je avtor dolžan predložiti vso dokumentacijo o obravnavi raziskovalne etike njegovega rokopisa. Uredništvo si pridržuje pravico, da kontaktira etično komisijo.

Prav tako morajo avtorji, ki poročajo o ljudeh ali posredujejo javnosti njihovo slikovno gradivo, pridobiti dovoljenja vseh sodelujočih, da se z vključitvijo v raziskavo strinjajo (v primeru otrok so to starši ali skrbniki). Izjavo o pridobitvi teh dovoljenj morajo avtorji podati v poglavju o metodah dela. Uredništvo si pridržuje pravico vpogleda v to dokumentacijo.

Raziskave na živalih morajo biti izpeljane v skladu z navodili "Animal Research: Reporting In Vivo Experiments" (ARRIVE) in potrjene s strani nacionalne etične komisije. V poglavju o metodah dela in v izjavi na koncu rokopisa morajo avtorji podati izjavo o etiki raziskav na živalih z veljavno številko dovoljenja.

V izjavi na koncu rokopisa morajo biti zapisani morebitni finančni ali drugi interesi farmacevtske industrije ali proizvajalcev opreme ter inštitucij, povezani z objavo v ZV/SJPH.

Avtorji morajo na koncu rokopisa zapisati sledeče izjave:

CONFLICTS OF INTEREST (The authors declare that no conflicts of interest exist.)

FUNDING (The study was financed by ...)

ETHICAL APPROVAL (Received from the... ali opis etičnega vidika raziskave)

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Po uspešni prijavi izpolnite vsa zahtevana strukturirana polja. Potrdite izjavo, da vaš prispevek še ni bil objavljen ali poslan v objavo kakšni drugi reviji, da so prispevek prebrali in se z njim strinjajo vsi avtorji, da so raziskave na ljudeh oz. živalih opravljene v skladu z načeli Helsinško-Tokijske deklaracije oz. v skladu z etičnimi načeli.

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Polje 'Comments' je namenjeno vašim dodatnim razlagam, navedete lahko tudi predlog recenzentov z imeni, nazivi, e-naslovi in zaposlitvijo.

Podatke o avtorju in soavtorjih vnesite kar se da natančno in popolno. Naveden naj bo korespondenčni avtor (s polnim naslovom, telefonsko številko in elektronskim naslovom), ki bo skrbel za komunikacijo z uredništvom in ostalimi avtorji.

Jezik prispevka je angleščina. Objavljamo izvirne znanstvene članke, sistematične pregledne znanstvene članke, metodologije raziskav in vabljene uvodnike. Pri izvirnih, metodoloških in sistematičnih preglednih znanstvenih prispevkih morajo biti naslov, izvleček in ključne besede prevedeni tudi v slovenščino.

Naslov, ključne besede in izvleček se oddajajo dvojezično v angleščini in slovenščini v strukturirana polja. Posebno polje za zapis v drugem jeziku obstaja le za izvleček, preostale podatke vnesite v obeh jezikih v ustrezno isto polje. Prvi izvleček je vselej v angleškem jeziku (do 250 besed - sistem vam besede sproti šteje), drugi pa v slovenskem jeziku (razširjen izvleček - do 400 besed).

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Sistem najbolje deluje, če uporabljate zadnjo različico Acrobata.

Če pri oddajanju rokopisa naletite na nepremostljive težave, se za pomoč obrnite na naslov uredništva: zdrav.var@nijz.si.

V nadaljevanju podajamo še nekaj natančnejših napotkov.

ROKOPIS

Besedila naj bodo napisana z urejevalnikom Word for Windows 97-2003. Robovi naj bodo široki najmanj 25 mm. Znanstveni članki naj imajo naslednja poglavja: uvod, metode, rezultati, razpravljanje in zaključek. Uvodniki in sistematični pregledni članki so lahko zasnovani drugače, vendar naj bo razdelitev na poglavja in podpoglavja jasno razvidna iz velikosti črk naslovov. Poglavja in podpoglavja naj bodo številčena dekadno po standardu SIST ISO 2145 in SIST ISO 690 (npr. 1, 1.1, 1.1.1 itd.).

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Naslov v angleškem in slovenskem jeziku naj bo kratek in natančen, opisen in ne trdilen (povedi v naslovih niso dopustne). Navedena naj bodo imena piscev z natančnimi akademskimi in strokovnimi naslovi ter popoln naslov ustanove, inštituta ali klinike, kjer je delo nastalo. Avtorji morajo izpolnjevati pogoje za avtorstvo. Prispevati morajo k zasnovi in oblikovanju oz. analizi in interpretaciji podatkov, rokopis morajo intelektualno zasnovati oz. ga kritično pregledati, strinjati se morajo s končno različico rokopisa. Samo zbiranje podatkov ne zadostuje za avtorstvo.

IZVLEČEK IN KLJUČNE BESEDE

Izvleček v angleškem in slovenskem jeziku naj bo pri znanstvenem in metodološkem članku strukturiran in naj ne bo daljši od 250 besed v angleščini in 400 besed v slovenščini, izvlečki ostalih člankov so lahko nestrukturirani. Izvleček naj vsebinsko povzema in ne le našteva bistvene vsebine dela. Izogibajte se kraticam in okrajšavam. Napisan naj bo v 3. osebi.

Izvleček znanstvenega članka naj povzema namen dela, osnovne metode, glavne izsledke in njihovo statistično pomembnost ter poglavitne sklepe (struktura IMRC - Introduction, Methods, Results, Conclusions).

Navedenih naj bo 3-10 ključnih besed, ki nam bodo v pomoč pri indeksiranju. Uporabljajte izraze iz MeSH - Medical Subject Headings, ki jih navaja Index Medicus.

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Kategorijo prispevka predlaga z vnosom v ustrezno polje avtor sam, končno odločitev pa sprejme urednik na osnovi predlogov recenzentov. Objavljamo izvirne znanstvene članke, metodološke članke, sistematične pregledne znanstvene članke in vabljene uvodnike.

REFERENCE

Vsako navajanje trditev ali dognanj drugih morate podpreti z referenco. Reference naj bodo v besedilu navedene po vrstnem redu, tako kot se pojavljajo. Referenca naj bo navedena na koncu citirane trditve. Reference v besedilu, slikah in tabelah navedite v oklepaju z arabskimi številkami ((1), (2, 3), (4-7)). Reference, ki se pojavljajo samo v tabelah ali slikah, naj bodo oštevilčene tako, kot se bodo pojavile v besedilu. Kot referenc ne navajajte izvlečkov in osebnih dogovorov (slednje je lahko navedeno v besedilu). Seznam citirane literature dodajte na koncu prispevka. Literaturo citirajte po priloženih navodilih, ki so v skladu s tistimi, ki jih uporablja ameriška National Library of Medicine v Index Medicus. Uporabljajte numerično citiranje. Imena revij krajšajte tako, kot določa Index Medicus (popoln seznam na naslovu URL: http://www.nlm.nih.gov).

Navedite imena vseh avtorjev, v primeru, da je avtorjev šest ali več, navedite prvih šest avtorjev in dodajte et al.

PRIMERI ZA CITIRANJE LITERATURE

primer za knjigo:

1. Premik M. Uvod v epidemiologijo. Ljubljana: Medicinska fakulteta, 1998.
2. Mahy BWJ. A dictionary of virology. 2nd ed. San Diego: Academic Press, 1997.

primer za poglavje iz knjige:

3. Urlep F. Razvoj osnovnega zdravstva v Sloveniji zadnjih 130 let. In: Švab I, Rotar-Pavlič D, editors. Družinska medicina. Ljubljana: Združenje zdravnikov družinske medicine, 2002: 18-27.
4. Goldberg BW. Population-based health care. In: Taylor RB, editor. Family medicine. 5th ed. New York: Springer, 1999: 32-6.

primer za članek iz revije:

5. Barry HC, Hickner J, Ebell MH, Ettenhofer T. A randomized controlled trial of telephone management of suspected urinary tract infections in women. J Fam Pract 2001; 50: 589-94.

primer za članek iz revije, kjer avtor ni znan:

6. Anon. Early drinking said to increase alcoholism risk. Globe 1998; 2: 8-10.

primer za članek iz revije, kjer je avtor organizacija:

7. Women's Concerns Study Group. Raising concerns about family history of breast cancer in primary care consultations: prospective, population based study. Br Med J 2001; 322: 27-8.

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8. Shen HM, Zhang QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994; 102(Suppl 2): 275-82.
9. Payne DK, Sullivan MD, Massie MJ. Women's psychological reactions to breast cancer. Semin Oncol 1996; 23(Suppl 2): 89-97.

primer za članek iz zbornika referatov:

10. Sugden K, Kirk R, Barry HC, Hickner J, Ebell MH, Ettenhofer T et al. Suicides and non-suicidal deaths in Slovenia: molecular genetic investigation. In: 9th European Symposium on Suicide and Suicidal Behaviour. Warwick: University of Oxford, 2002: 76.

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Tabele v angleškem jeziku naj bodo v besedilu prispevka na mestu, kamor sodijo. Tabele naj sestavljajo vrstice in stolpci, ki se sekajo v poljih. Tabele oštevilčite po vrstnem redu, vsaka tabela mora biti citirana v besedilu. Tabela naj bo opremljena s kratkim angleškim naslovom. V legendi naj bodo pojasnjene vse kratice, okrajšave in nestandardne enote, ki se pojavljajo v tabeli.

SLIKE

Slike morajo biti profesionalno izdelane. Pri pripravi slik upoštevajte, da gre za črno-beli tisk. Slikovno gradivo naj bo pripravljeno:

- črno-belo (ne v barvah!);
- brez polnih površin, namesto tega je treba izbrati šrafure (če gre za stolpce, t. i. tortice ali zemljevide);
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Vsaka slika mora biti navedena v besedilu. Besedilo k sliki naj vsebuje naslov slike in potrebno razlago vsebine. Slika naj bo razumljiva tudi brez branja ostalega besedila. Pojasniti morate vse okrajšave v sliki. Uporaba okrajšav v besedilu k sliki je nedopustna. Besedila k slikam naj bodo napisana na mestu pojavljanja v besedilu.

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Kraticam in okrajšavam se izogibajte, izjema so mednarodno veljavne oznake merskih enot. V naslovih in izvlečku naj ne bo kratic. Na mestu, kjer se kratica prvič pojavi v besedilu, naj bo izraz, ki ga nadomešča, polno izpisan, v nadaljnjem besedilu uporabljano kratico navajajte v oklepaju.

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