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VALIDATION OF THE CROATIAN VERSION OF WORK ABILITY INDEX (WAI) IN POPULATION OF NURSES ON TRANSFORMED ITEM-SPECIFIC SCORES

OVREDNOTENJE HRVAŠKE RAZLIČICE INDEKSA DELOVNE SPOSOBNOSTI V POPULACIJI MEDICINSKIH SESTER NA PREOBLIKOVANIH REZULTATIH, SPECIFIČNIH ZA POSAMEZNO POSTAVKO

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ABSTRACT

Aim: To assess the psychometric properties of the Croatian version of a Work Ability Index Questionnaire (WAIQ-CRO) in the population of nurses by using a specific methodological approach.

Methods: A cross-sectional survey was conducted in a sample of 711 Croatian nurses in 2018 in Zagreb, Croatia. The instrument's internal consistency was assessed by using Cronbach's alpha coefficient (α). The factor structure was verified by confirmatory (CFA) and exploratory factor analysis (EFA), with the assumption of a single-factor structure. To ensure the equality of importance of items in the assessment, the item-specific scores were transformed.

Results: The internal consistency of the instrument was satisfactory (α=0.71). CFA showed poor first model (Model-1) compatibility data (p<0.001, CFI=0.85, GFI=0.93, RMSEA=0.13). The modificated indexes suggested the introduction of correlation parameters residual variances of results from WAIQ-CRO Item-1 and Item-2. After introducing these covariances, the index model assentation (Model-2) showed desirable assentation measures (p<0.001, CFI=0.95, GFI=0.97, RMSEA=0.08). Comparison showed better compatibility of Model-2 (p<0.001). The implementation of EFA has identified three factors. Replication of this model in CFA resulted in relatively good model assentation approaches with data (p<0.001, CFI=0.96, GFI=0.98, RMSEA=0.07). Comparison of this model (Model-3) with Model-2 showed a significantly better compatibility of Model-3 (p<0.001).

Conclusion: The WAIQ-CRO proved to be a reliable and valid instrument which can be used in research among Croatian nurses. The results suggest that it would be better to consider a three-factor structure than a single-factor structure, as a three-factor structure can direct decision-makers to which segment to locate interventions.

Keywords:
psychometric properties, work ability index questionnaire, validation, nurses, occupational health

IZVLEČEK

Namen: *Ovrednotiti psihometrične lastnosti hrvaške različice vprašalnika indeksa delovne sposobnosti (WAIQ-CRO) v populaciji medicinskih sester ob uporabi posebnega metodološkega pristopa.*

Metode: *Presečna raziskava je bila opravljena na vzorcu 711 hrvaških medicinskih sester leta 2018 v Zagrebu, Hrvaška. Notranja skladnost instrumenta je bila ocenjena z uporabo Cronbachovega koeficienta alfa (a), za ovrednotenje njegove faktorske strukture pa sta bili uporabljeni tako konfirmativna (CFA) kot eksplorativna (EFA) faktorska analiza s predpostavko eno-faktorske strukture. Da bi zagotovili enakost pomembnosti postavk pri vrednotenju, so bili rezultati, specifični za posamezno postavko, preoblikovani.*

Rezultati: *Notranja konsistentnost instrumenta je bila zadovoljiva (a = 0,71). Rezultati prvega modela CFA (Model-1) niso bili ugodni (p < 0,001; CFI = 0,85; GFI = 0,93; RMSEA = 0,13). Preoblikovane vrednosti so nakazale uvedbo kovarianc pri postavkah 1 in 2. Po njihovi uvedbi so se rezultati v drugem modelu (Model-2) močno izboljšali (p < 0,001, CFI = 0,95, GFI = 0,97, RMSEA = 0,08). Rezultati EFA so nato pokazali trifaktorsko strukturo. Ponovitev tega modela v CFA je pokazala relativno dobre rezultate (p < 0,001, CFI = 0,96, GFI = 0,98, RMSEA = 0,07). Primerjava tega (Model-3) z Modelom-2 je pokazala, da je Model-3 bistveno boljši (p < 0,001).*

Zaključek: *WAIQ-CRO se je izkazal kot zanesljiv in veljaven instrument, ki ga lahko uporabljamo pri raziskavah med hrvaškimi medicinskimi sestrami. Rezultati kažejo, da bi bilo bolje razmisliti o tri- kot eno-faktorski strukturi instrumenta, saj lahko trifaktorska struktura pomaga pri presoji, v kateri segment naj odločevalci usmerijo intervencije.*

Ključne besede:
psihometrične lastnosti, vprašalnik indeksa delovne sposobnosti, validacija, medicinske sestre, poklicno zdravje

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1 INTRODUCTION

Due to aging of the workforce, work demands, stress, occupational hazards and other workplace challenges it is important to take action in the preservation of health and work ability (WA) among the working population. Poor organisation at work, lack of leadership, work overload, work under pressure and stress, and exposure to occupational hazards can have a negative impact on workers' health and their WA causing work-related illness, early retirement and death (1).

In the early 1980s, Finnish Institute of Occupational Health (FIOH) researchers developed a WA concept (2) based on the Finnish Longitudinal Study on Municipal Employees (FLAME), defining it as the balance between human resources and the demands of work (3). They illustrated it as a four-floor house. The first and second floors consist of individual resources, the third consists of values, attitudes and motivation, while the fourth represents work, work arrangements, work community and work leadership (3).

Nurses are constantly exposed to various occupational hazards - biological (e.g. infectious patients' excretions), chemical (e.g. toxic substances), physical (e.g. radiation and noise), biomechanical (e.g. lifting patients and high levels of workload) and psychological (e.g. shift work, overtime work, performing of complex tasks in critical situations, and verbal abuse and violence) (4-7). Several studies have identified also a high level of occupational stress among them (4,8-11). It is therefore very important to constantly monitor WA in this professional group in order to ensure timely reaction.

For measuring different aspects of WA, e.g. prediction of long-term sickness absence, work disability and retirement (2, 12, 13), the Work Ability Index Questionnaire (WAIQ) was developed by the FIOH (14, 15). WAIQ is a widely used instrument all over the world (3). Its reliability and validity have been tested in various working populations so far (16-27), including among nurses, where it proved to be a very predictive instrument (17).

Occupational stress is present also among Croatian nurses (28-30). Six major groups of occupational stressors were identified: organization of work and financial issues, public criticism, workplace hazards, workplace interpersonal conflicts, shift work, and professional and intellectual demands, indicating that hospital managers should develop strategies to address and improve the quality of working conditions for Croatian nurses (28).

The WAIQ was already translated into Croatian (WAIQ-CRO) by using the standard procedure (forward translation by two independent translators, synthesis of the results and back translation by a certified translator) about a decade ago in the frame of a research project of Ministry of Science, Education and Sports of the Republic of Croatia entitled Health at work and healthy environment (code 108-1080316-0300; project duration 2007-2012), and led by Andrija Stampar of the School of Public Health, School of Medicine, University of Zagreb (31). However, we could not find any explicit reporting on validation results, although it was used in several studies so far (28, 32, 33). Consequently, the aim of the present study was to assess the psychometric properties of the WAIQ-CRO in Croatian nurses, with inclusion of a specific methodological approach.

2 MATERIALS AND METHODS

2.1 Study Design, Timeframe and Study Population

This cross-sectional study, which was a part of a larger research project on the impact of a sense of coherence on WA in nurses, was carried out from December 2017 to June 2018 at the University Hospital Centre Sisters of Mercy (UHCSM) in Zagreb, Croatia.

The total population of 1465 nurses employed in UHCSM was considered for inclusion in the study. However, due to various absences (sick, annual or study leave), it was possible to deliver the questionnaire to 1300 nurses.

2.2 Procedure

An initial meeting was held with the head nurses of the hospital where the study aim/objectives and the procedure were presented. Afterwards, the WAIQ-CRO was distributed to all departments. Written informed consent was obtained from each participant, gathered separately from completed questionnaires. Questionnaires were marked by the same identiWfication code for each participant. Participants were given the possibility to take the questionnaire home, fill it in and return it back at the workplace. All questionnaires were returned anonymously in sealed envelopes to protect the nurses' privacy.

2.3 Questionnaire

The WAIQ consists of 10 questions arranged in 7 items (15) (Table 1). All questions are closed-ended with a different number of answers. The measure provided by the WAIQ is a summary score Work Ability Index (WAI), obtained by summing the values of individual responses to all items, ranging from 7-49 points, with higher values indicating better WA. Scores ranging from 7-27 indicate poor WA, 28-36 moderate WA, 37-43 good WA, and 44-49 excellent WA (15).

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Table 1. Work Ability Index Questionnaire items and scoring (15).

Item		Number of questions	Scoring (min-max)
Item-1	Current work ability compared with the lifetime best	1	0–10
Item-2	Work ability in relation to the demands of the job	2	2–10
Item-3	Number of current diseases diagnosed by a physician	1	1–7
Item-4	Estimated work impairment due to diseases	1	1–6
Item-5	Sick leave during the past year (12 months)	1	1–5
Item-6	Own prognosis of work ability 2 years from now	1	1,4,7
Item-7	Mental resources	3	1–4

2.4 Psychometric Validation

The instrument's reliability was assessed using the internal consistency method. Cronbach's alpha coefficient (α) was applied.

To assess the factor structure of the instrument, first the confirmatory factor analysis (CFA) with the assumption of one factor in the background, as proposed by the authors of the instrument (15), was performed. As input data, item-specific scores were used. Since these scores are measured on a different scale, before the implementation of the factor analysis, each of the seven scales was transformed to a range of 0-1. Specifically, the scores of Item-1 were collected on a scale of 0-10 so the transformation implied the partition of each result with 10; the scores of Item-3 varied in the range of 1-7 so that each score was deducted 1 (consequently scores ranged 0-6) and this new score was divided by six; etc. Consequently, we obtained two summary scores: one on the raw item-specific scores (the larger-scale groups are of greater importance in the overall assessment of the WA), and the other on transformed item-specific scores (each item is equally important in the assessment of WA). With prior checking of the factor structure, the assumptions for the factor analysis implementation were verified, primarily those of the multivariate normality of the distribution of item-specific scores. Mardia's multivariate normality tests were used. The robust maximum likelihood estimator was applied. The criteria for the fit measures were a relative chi-square (χ^2) 2.0-5.0 (34), a comparative fit index (CFI) ≥0.95 (35,36), a goodness-of-fit index (GFI) ≤0.95 (37), and a root mean squared error of approximation (RMSEA) 0.06-0.07 (34). Finally, the exploratory factor analysis (EFA) (a common factor model with limited number of factors) was applied in order to check whether the full exploratory approach could replicate the obtained factor structure.

The data were processed with MATLAB and JASP programmes.

2.5 Ethical Considerations

The study was carried out in accordance with the ethical principles of the Helsinki Declaration. All respondents gave their informed consent to participate in the study, which was approved by the UHCSM (code EP–7811/16-19).

3 RESULTS

3.1 Study Participants' Characteristics

The study ultimately involved the participation of 711/1300 nurses (response rate 54.7%) (630 (88.4%) females; 81 (11.4%) males; mean age 38.4±12.5 years.

The mean value of the total WAI score was 40.5±5.6 points.

3.2 Psychometric Validation

3.2.1 Reliability

Cronbach's alpha coefficient showed satisfactory internal consistency (α=0.71).

3.2.2 Factor Structure

The correlation between raw and transformed scores was very high (r=0.988, p<0.001).

Table 2 shows the intercorrelations between the scores of seven items. All coefficients were statistically highly significant (p<0.001). A close look at the correlation matrix did not reveal a systematic relationship and grouping of individual indicators, with the exception of the relatively low relationship of Item-7 with the rest of the indicators, suggesting that in the background of Item-7 probably stood a factor that is common throughout the entire WAIQ-CRO. Multivariate normality tests showed significant deviation of the observed multivariate distribution in terms of asymmetry ($\chi^2(84)$=1790.83, p<0.001) and flattening (z=35.28), meaning that sampled indicators did not satisfy the assumption of multivariate normality.

Table 2. Intercorrelations between the scores of seven items of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

	Item-1	Item-2	Item-3	Item-4	Item-5	Item-6	Item-7
Item-1	1.000						
Item-2	0.636	1.000					
Item-3	0.279	0.208	1.000				
Item-4	0.416	0.408	0.444	1.000			
Item-5	0.183	0.160	0.271	0.298	1.000		
Item-6	0.383	0.341	0.309	0.393	0.218	1.000	
Item-7	0.257	0.374	0.127	0.272	0.126	0.276	1.000

In the CFA, two models were defined and tested. The first model (Model-1) showed poor compatibility ($\chi^2(14)=174.41$, $p<0.001$, CFI=0.85, GFI=0.93, RMSEA=0.13). This basic model implied assessment of the factor saturations of seven items by one factor. The modification indices suggested the introduction of correlation parameters residual variances of scores of Item-1 and Item-2. After the introduction of this covariance, the index model assentation (Model-2) showed desirable assentation measures ($\chi^2(13)=72.78$, $p<0.001$, CFI=0.95, GFI=0.97, RMSEA=0.08). The comparison of the original model (Model-1) and the model with the allowed covariance residual of the two measurement indicators (Model-2) showed a better compatibility of the latter model ($\chi^2(1)=101.63$, $p<0.010$). Consequently, the accepted model was Model-2 with one latent factor that estimated factor saturation and one covariance of the residual indicators. The parameters of this model are shown in Table 3. The saturation of all indicators was significant, whereby the highest saturation has been noted in Item-4, and the lowest in Item-5 (Table 3). The residual correlation between Item-1 and Item-2 was r=0.470 ($p<0.001$). This correlation was somewhat expected given that Item-1 and Item-2 reflect explicit self-assessment of WA (Item-1 reflects current WA compared with the lifetime best, while Item-2 measures WA in relation to the demands of the job).

The implementation of the EFA has identified three factors (Table 4). From the factor saturation, it is apparent that Factor-1 was defined by Item-1 and Item-2 (corresponding to self-assessment of WA), Factor-3 by Item-7 (corresponding to general mental state), and Factor-2 by the remaining items (Item-3, Item-4, Item-5 and Item-6) (corresponding to general health problems). Table 5 shows the correlations of three factors identified by EFA.

Table 3. Factor saturation estimated by confirmatory factor analysis of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

Indicator	b	se	p	ß
Item-1	1.000	0.000		0.577
Item-2	0.916	0.061	<0.001	0.554
Item-3	1.940	0.187	<0.001	0.535
Item-4	1.326	0.110	<0.001	0.733
Item-5	1.000	0.123	<0.001	0.386
Item-6	1.426	0.130	<0.001	0.582
Item-7	0.773	0.091	<0.001	0.407

Legend: b=non-standardized saturation; se=saturation estimation error; p=significance of saturation; ß=standardized saturation

Table 4. Factor saturation estimated by exploratory factor analysis of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

Indicator	Factor-1	Factor-2	Factor-3
Item-1	0.784		
Item-2	0.803		
Item-3		0.693	
Item-4		0.614	
Item-5		0.446	
Item-6		0.380	
Item-7			0.997

Table 5. Correlations of factors identified by exploratory factor analysis of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

	Factor-1	Factor-2	Factor-3
Factor-1	1.000		
Factor-2	0.697	1.000	
Factor-3	0.436	0.317	1.000

The attempt to replicate this model in the CFA resulted in relatively good model assentation approaches with data ($\chi^2(12)=55.48$, $p<0.001$, CFI=0.96, GFI=0.98, RMSEA=0.07). A comparison of this model (Model-3) with the previously described one-factor model (Model-2) found by CFA showed a significantly better compatibility of Model-3 ($\chi^2(1)=17.3$, $p<0.001$). Table 6 shows the factor saturation of the three factors and the indicators which were used.

Table 6. Factor saturation estimated by confirmatory factor analysis of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

Factor	Indicator	b	se	p	ß
Factor-1	Item-1	1.000	0.000		0.785
	Item-2	0.986	0.064	<0.001	0.811
Factor-2	Item-3	1.000	0.000		0.551
	Item-4	0.683	0.058	<0.001	0.754
	Item-5	0.510	0.063	<0.001	0.393
	Item-6	0.699	0.066	<0.001	0.570
Factor-3	Item-7	1.000	0.000		1.000

Legend: b=non-standardized saturation; se=saturation estimation error; p=significance of saturation; ß=standardized saturation

The correlation assessments of three factors in the CFA are shown in Table 7. All three factors were in significant positive correlations, with the high correlation between the first two factors.

Table 7. Correlations of factors identified by exploratory factor analysis of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

	Factor-1	Factor-2	Factor-3
Factor-1	1.000		
Factor-2	0.669	1.000	
Factor-3	0.400	0.358	1.000

The arithmetic means of the three factors are shown in Table 8. It is important to note that not all the items are expressed in the same scales. The result for each participant is calculated as the sum of results on the items belonging to each factor.

Table 8. Arithmetic mean and standard deviation of the three factors of the Croatian version of the Work Ability Index Questionnaire in Croatian nurses (n=711).

Typical value	Factor-1	Factor-2	Factor-3
Arithmetic mean	16.76	20.40	3.31
Standard deviation	2.81	4.05	0.77

When the total transformed WAI score was divided by the number of items on which the factors were obtained, we obtained the result for Factor-1 of 8.38, and for Factor-2 5.10, while for Factor-3 it remained 3.31 because it was based on only one item.

4 DISCUSSION

The results of our study showed that the WAIQ-CRO is a valid instrument which can be used in occupational health research among the Croatian nurse population.

The internal consistency of WAIQ-CRO was satisfactory and its Cronbach's alpha very similar to the overall Cronbach's alpha (α=0.72) in the study of Radkiewicz et al. (17). However, in the same study some country-specific coefficients were lower (Slovakia 0.54; Belgium 0.68; Italy 0.68), some were similar (France 0.70; Poland 0.70; Netherlands 0.72), while others were higher (Norway 0.74; Germany 0.78; Finland 0.79) (17). Cronbach's alpha was higher also among Brazilian nurses (α=0.80) (19), Argentinian primary care workers (α=0.80) (20), and among Iranian nurses/healthcare workers (α=0.79) (21).

Factor structure analysis revealed a three-factor structure of the WAIQ-CRO with good fit. These results are partially consistent with the results of other similar studies. The study among nurses from different European countries found a single-factor structure in Germany and Finland, but a two-factor structure in Belgium, France, Italy, Norway, Netherlands, Poland and Slovakia (Factor-1: subjective assessment of ability to work and one's own mental resources, Factor-2: objective information concerning one's own health and absenteeism due to diseases) (17). However, there was some overlapping of two factors from our study with one factor from this study. A two-factor structure was found also in the Brazilian study (19), while in the Argentinian study among primary care workers a three-factor structure was confirmed (20). A three-factor structure was confirmed also in Iranian nurses/healthcare

workers with factors being very similar to the factors in our study (Factor-1: self-perceived WA, Factor-2: mental resources, Factor-3: presence of disease and health related limitation) (21). Comparisons were also made using the results of studies that did not include nursing/healthcare personnel. The study among German workers confirmed a two-factor structure (Factor-1: subjective WA and resources, Factor-2: health related factor) (26), while the study among Brazilian electrical company workers confirmed a three-factor structure (Factor-1: mental resources, Factor-2: self-perceived WA, Factor-3: presence of diseases and health-related limitations) (18). Recently, a three-factor structure was also confirmed among Iranian workers in petrochemical and car manufacturing industries (25). Again, these factors are very similar to the factors in our study. Basing on previous and present knowledge it would make sense to consider in futher analyses the three-factor structure, especially in Croatia. However, it is also evident that we can use the overall result on the WAIQ as well, and explain moderate to high correlations between the factors. This is a common and quite powerful argument for using the overall result of the questionnaire, although there a multi-factor structure was detected.

We can also make a rough comparison of the WAI summary score mean value obtained in our study. Similar results (median value 39) were found in the study of Sorić et al. (33), both assessing WA of Croatian nurses as good.

This study has potential limitations. First, our study involved participants from only one health institution, which is specific regarding its working conditions. However, this institution is a large healthcare facility where a large number of nurses performing various tasks are employed. Consequently, this allows a detailed assessment of WA related to the nurses' workplace, which is a strength rather than a limitation. Second, one could argue the transformation of raw scores which was implemented in our study. However, one of the prerequisites for implementing the factor analysis is that all the items are measured on the same scales (38). Also, this transformation does not change the form of distribution, the correlation between the analyzed variables, and the correlation of the analyzed variables with any third variable. Importantly, this transformation changes variance and covariant variables. Variables measured at different scales will result in different variance, in a way that the particles measured on the scales with a larger range generally have a larger variance and consequently larger covariates; e.g. a variable measured on a scale from 0 to 10 has a larger range and thus a larger variance of the same variable measured on a scale of 1-5. Since the input data in the factor analysis are variances and covariances, it is important to ensure that the results of the factor analysis don't arise from the methodological characteristics of the questionnaire such as the type of scale that was used. In the case of the WAIQ, Item-1, measured on an 11-degree scale (0-10), would almost certainly have a greater variance than Item-7, measured on a scale 1-4, and consequently have greater importance in factor analysis. Thus the outcome of factor analysis is somewhat predictable before the implementation of the analysis itself. Previous verification of WAIQ factor structure did not take into account these characteristics of the questionnaire. It is important to note that the result that would be consistent with previous findings does not justify the implementation of factor analysis on crude results (without transformation of all variables on the same scale) - factor saturation will almost certainly not be the same although the factor analysis on transformed and untransformed results would find an equal number of factors (e.g. one common factor). Next, one could argue that no method of measurement of stability of the instrument over time, e.g. the test-retest method, was used in the present study. However, the reliability of any self-reported outcome measure can be evaluated using measurement stability and/or measurement equivalence methods. The latter were developed for situations in which it is not possible to perform repeated measurements reliably because the measured phenomenon could change over time (39). Since we assumed, based on the results of previous studies (28-30), that the phenomenon measured in our study could change over time, due to specifics of the workplace of the observed group, only the measures of equivalence were used (39). Finally, one could argue the low response rate, however, there is no agreed-upon standard for acceptable response rates (40). According to Babbie, cited by Draugalis et al., 50% is regarded as an acceptable response rate in social research postal surveys (40). Consequently, we assumed that the response rate achieved in our study still permits reliable conclusions.

The study has also some important strenghts. First, implementation of transformed scores for factor analysis could be seen as a very important strength since it makes the study results more reliable, with greater power of applicability. Next, the study offers to our knowledge the first published psychometric properties of WAIQ-CRO. Finally, the results of this study could be applicable not only in Croatia but much wider - in several countries of former Yougoslavia where WAIQ-CRO could be used due to similarity of languages, all of them also facing the similar transition in departing from a common healthcare system.

Basing on the results of our study we can already draw some rough implications for public health in Croatia. The results in WAI scoring are not in accordance with our expectations. According to the relative means of transformed scores, the highest result was shown for Factor-1, then Factor-2, while the least mean was for Factor-3. This could imply that nurses in our study had the best result in self-assessment of WA and worst in general

mental state. However, taking into account that our participants were mostly middle-aged nurses this result is understandable – in this age group major health problems are not present yet. However, the results of Factor-2 and Factor-3 indicate that the problems exist, but are not so influential as to reflect on their WA. On the other hand, the question is how long employees in such a demanding profession as clinical nursing can compensate for potential physical and/or mental disabilities in carrying out their work. This means that if certain interventions are not taken, these difficulties will, in time, affect their WA. According to the study of Milošević et al. Croatian nurses are faced with inadequate resources to work with, an inadequate working environment, complex administration and patients' waiting lists, insufficient funds for normal everyday work, a shortage of registered nurses and high workload (41). Similar was also confirmed by the study of Golubic et al. which highlighted that Croatian healthcare workers were exposed to poor organisation of work, insufficient financial resources and inadequate working environment (28). These factors can contribute to a worsening of nurses' health and decreased WA. Therefore, permanent monitoring of WA with a valid and reliable instrument is of enormous importance. According to Carel et al., the WAI instrument enables early identification of poor WA and consequently identification of nurses needing intervention for prevention of unfavourable consequences, including early retirement (42).

Further in-depth examination of the structure of the questionnaire is required in order to more firmly confirm whether it is better to take into account the total WAI score or evaluate each factor separately. Also, it would be necessary to conduct similar studies in other occupational groups within the population of Croatian workers.

5 CONCLUSION

The WAIQ-CRO demonstrated satisfactory psychometric properties and can therefore be used in the assessment of WA among the Croatian nurse population. From the results of our study it is evident that it would be better to consider a three-factor than single-factor structure, as a three-factor structure can direct decision makers to which segment to locate interventions - in motivation for work, in improving working conditions, or in improving health through workplace health-promotion programmes.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING

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ETHICAL APPROVAL

The study was carried out in accordance with the ethical principles of the Helsinki Declaration. All respondents gave their informed consent to participate in the study, which was approved by the UHCSM (code EP–7811/16-19).

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ASSOCIATION BETWEEN ORAL HEALTH-RELATED AND HEALTH-RELATED QUALITY OF LIFE

POVEZAVA MED ORALNIM IN SISTEMSKIM ZDRAVJEM V ZVEZI S KAKOVOSTJO ŽIVLJENJA

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ABSTRACT

Objectives: To investigate the correlation between the four dimensions of Oral Health-Related Quality of Life (OHRQoL) and Health-Related Quality of Life (HRQoL) constructs in a dental patient population.

Methods: A cross-sectional study carried out at HealthPartners, Minnesota, USA. This study is a secondary data analysis of available adult dental patients' data. The instruments used to assess the OHRQoL and HRQoL constructs were the Oral Health Impact Profile–version with 49 items (OHIP-49) and Patient-Reported Outcome Measures Information System (PROMIS) measures v.1.1 Global Health instruments Patient Reported Outcome Measures (PROMs), respectively. We used Structural Equation Modeling to determine the correlation between OHRQoL and HRQoL.

Results: Two thousand and seventy-six dental patients participated in the study. OHRQoL and HRQoL scores correlated with 0.56 (95%CI:0.52-0.60). The OHRQoL and Physical Health dimension of HRQoL correlated with 0.55 (95%CI:0.51-0.59). The OHRQoL and Mental Health dimension of HRQoL correlated with 0.51 (95%CI:0.47-0.55). When adjusted for age, gender, and depression, the correlation coefficients changed only slightly and resulted in 0.52 between OHRQoL and HRQoL Physical Health, and 0.47 between OHRQoL and HRQoL Mental Health. Model fit statistics for all analyses were adequate and indicated a good fit.

Conclusions: OHRQoL and HRQoL overlap greatly. For dental practitioners, the OHRQoL score is informative for their patients' general health status and vice versa. Study results indicate that effective therapeutic interventions by dentists improve patients' OHRQoL as well as HRQoL.

Keywords:
oral health, health, quality of life, self report, surveys and questionnaires, depressive disorder, public health, structural equation modeling, correlation of data, evidence-based dentistry

IZVLEČEK

Namen: *Določiti korelacijo med štirimi dimenzijami konstrukta z oralnim zdravjem povezana kakovost življenja (ang. Oral Health-Related Quality of Life ali krajše OHRQoL) in konstruktom z zdravjem povezana kakovost življenja (ang. Health-Related Quality of Life ali krajše HRQoL) pri zobozdravstvenih pacientih.*

Metode: *Podatki zobozdravstvenih pacientov so bili v tej presečni raziskavi pridobljeni s klinike HealthPartners, Minnesota, ZDA. Ta študija je sekundarna analiza podatkov o razpoložljivih podatkih o zobozdravnikih za odrasle. Za oceno konstruktov OHRQoL in HRQoL sta bila uporabljena instrumenta Oral Health Impact Profile, ki sestoji iz 49 vprašanj (OHIP-49) in Patient-Reported Outcome Measures Information System (PROMIS) v.1.1 Global Health. Korelacija med konstruktoma je bila izračunana na podlagi modeliranja strukturnih enačb.*

Rezultati: *V raziskavo je bilo vključenih 2.076 zobozdravstvenih pacientov. Korelacijski koeficient med konstruktoma OHRQoL in HRQoL je znašal 0,56 (95 % CI:0,51-0,59). Korelacijski koeficient med oceno telesnega zdravja po OHRQoL in HRQoL (ang. HRQoL Physical Health) je znašal 0,55 (95 % CI:0,51-0,59). Korelacijski koeficient med oceno duševnega zdravja OHRQoL in HRQoL (ang. HRQoL Mental Health) je znašal 0,51 (95 % CI:0,47-0,55). Ob upoštevanju motečih dejavnikov, kot so starost, spol in depresija, je korelacijski koeficient med OHRQoL in telesnim zdravjem znašal 0,52 ter med OHRQoL in duševnim zdravjem 0,47. Pokazatelji stopnje prileganja modelov so bili ustrezni in so pokazali dobro prileganje.*

Zaključek: *Konstrukta OHRQoL in HRQoL se zelo prekrivata. Zobozdravstveni delavci lahko na osnovi pacientove ocene OHRQoL pridobijo tudi koristne informacije o njihovem sistemskem zdravju, drugi zdravstveni delavci pa informacije o njihovem oralnem zdravju. Rezultati raziskave dokazujejo, da učinkovito zobozdravniško zdravljenje ne izboljša samo pacientove z oralnim zdravjem povezane kakovosti življenja, ampak tudi s sistemskim zdravjem povezano kakovost življenja.*

Ključne besede:
oralno zdravje, zdravje, kakovost življenja, samoocena, ankete in vprašalniki, depresivna motnja, javno zdravje, modeliranje strukturnih enačb, korelacija podatkov, z dokazi podprto zobozdravstvo

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1 INTRODUCTION

Environmental, behavioral, and personal factors influence both oral and general health, and oral health is also considered a "window" to overall health (1, 2). The overlap between oral health and general health can be assessed with the constructs Oral Health-Related Quality of Life (OHRQoL) (3,4) and Health-Related Quality of Life (HRQoL) (5,6), respectively, that is, how much OHRQoL data could explain HRQoL, and vice versa (1, 2, 7). Knowing the magnitude of the OHRQOL-HRQOL relationship would enable a more patient-centered treatment approach for patients in general and dental patients, specifically.

Studies have shown different magnitudes of the association between OHRQoL and HRQoL. In one cohort of first-year students, it was found that OHRQoL and HRQoL have various determinants suggesting that these two constructs are unrelated in this healthy population (8). In contrast, two studies using two patient-reported outcome measures (PROMs), specifically Oral Health Impact Profile (OHIP) and Short Form Survey (SF) in German dental patients, identified a high correlation between OHRQoL and HRQoL (9, 10). Zimmer et al. derived a correlation between OHIP-14 and SF-12 scores of 0.31-0.32 (9), while Reissmann et al. reported a slightly higher correlation of 0.40 between OHIP-49 and SF-36 scores (10). Ranfl and Zeletel-Kragelj assessed the association between self-rated dentate status and self-rated general health and concluded that poor self-rated health was associated with a higher number of self-reported missing teeth (11).

Single-item or multi-item PROMs can theoretically measure both constructs, but the number of items also influences the reliability, validity, and overall precision of measurement. HRQoL PROMs designed for medical conditions, e.g. dyspnea (12), are used for evaluation of how disease impacts patients HRQoL (13, 14). The Patient-Reported Outcomes Measurement Information System (PROMIS) provides such PROMs (15). With more than 300 individual PROMIS PROMs, it is possible to comprehensively evaluate physical, mental, and social health components in general and patient populations (15).

Several theoretical models exist that aim to explain the OHRQoL construct (16). A new four-dimensional OHRQoL structure was proposed in 2014 (17, 18), providing dentists and researchers with a solid theoretical background for the development of measures for OHRQoL assessment (17–21). It was also demonstrated that this four-dimensional OHRQoL structure could be measured with the most extensively applied dental PROMs (22,23), i.e. longer and shorter OHIP versions (24–28), which assess the patient's self-perception of oral health. Investigation of the measurement precision of different OHIP versions has provided evidence that even the ultra-short OHIP version, i.e. OHIP-5 (28), precisely measures all four dimensions (29).

The aim of this study was to identify the magnitude of overlap between oral health and general health. Thus the objective of this study was to investigate the correlation between the four-dimensional OHRQoL and HRQoL constructs in a dental patient population.

2 METHODS

2.1 Study Subjects and Data Collection

Adult dental patients' data came from a cross-sectional study carried out at HealthPartners (HP), Minnesota, USA. Our study is a secondary data analysis of available data. A consecutive sample of English and Spanish-speaking dental patients was targeted to recruit 2,000 patients. Study participants were patients attending HP dental clinics for dental interventions or follow-ups and having 40% or less missing information (N=2,076, response rate 55%) about their OHRQoL or HRQoL as measured with the 49-item OHIP and the PROMIS v.1.1 Adult Global Health, respectively. Patients were asked to complete a printed battery of self-administered PROMs and informed consent at home. Data were collected from July 2014 to April 2016. The study was reviewed and approved by the Institutional Review Board of the HealthPartners Institute (Study Number A11-136).

2.2 Patient Reported Outcome Measures and Items Included in Structural Equation Modeling

A battery of PROMs about broad self-perceived oral and general health indicators, more specifically, Oral Health Impact Profile version with 49 items (OHIP-49) (24) and PROMIS v.1.1 Adult Global Health (30), were administered to each participant. Both instruments were developed in English and thoroughly psychometrically tested in English (15, 24) and Spanish language versions (31, 32).

2.2.1 Oral Health Impact Profile Questionnaire

The OHIP-49 questionnaire is based on five response options, where "0" indicates the absence of any problem, while higher OHIP scores represent more impaired patients' OHRQoL (24). OHIP-49 summary scores range from zero to 196. To give the construct OHRQoL the same direction in comparison to the construct HRQoL regarding their correlation estimation, we reversely coded OHIP items so that higher summary scores represented better OHRQoL. With reversely coded OHIP items, a positive correlation between OHRQoL and HRQoL scales indicated that better OHRQoL is associated with better HRQoL.

We characterized the OHIP summary scores based on the four dimensions of OHRQoL (17, 18), i.e., Oral Function, Orofacial Pain, Orofacial Appearance, and Psychosocial

Impact, which are composed of ten, seven, six, and 18 OHIP items, respectively, and derived from the 41 OHIP items that were identified in the previous exploratory (17) and confirmatory factor analyses (CFA) (18) when OHIP-49 structure was thoroughly investigated.

2.2.2 Patient Reported Outcome Measurement Information System v.1.1 – Global Health Questionnaire

PROMIS v.1.1 – Global Health questionnaire (12, 30) measures self-reported general health with ten items. The instrument is composed of two components or dimensions, namely Physical Health and Mental Health. Each component comprises four items. The remaining two items assess overall HRQoL. The values of the response to each question for a given respondent are summed. The PROMIS v.1.1 – Global Health PROM was recently addressed as "a retired" measure (30). For this reason, we converted the scores from PROMIS v.1.1 – Global Health PROM into the latest PROMIS v.1.2 Global Health.

2.2.3 Patient Reported Outcome Measurement Information System v.1.0 Emotional Distress - Depression Questionnaire

The PROMIS v.1.0 Emotional Distress - Depression questionnaire (33) measures the level of depression by evaluating self-reported negative mood, views of self, and social cognition. It consists of 28 items with five response options. In this study, a higher depression score indicated more severe depression. The score range is 28 to 140, and the higher score represents more severe depression.

2.3 Statistical Analysis

We performed all statistical analyses with Mplus Statistical Software, version 8 (Muthén & Muthén, Los Angeles, CA, USA). This software uses by default a Full Information Maximum Likelihood (FIML) (34) estimation approach to handle missing values. Study subjects who did not complete 40% or more of the 46 non-dental items of OHIP-49, PROMIS v.1.1 Global Health, and v.1.0 Emotional Distress - Depression were excluded from the study. Ninety-eight percent of patients in the analysis sample were missing less than 5% of 46 OHIP items, and 96% were missing less than 5% of the ten global health items. For the Depression score, the average item score from non-missing responses was imputed for these patients missing less than 40% of items; 93% of patients were not missing any Depression items, and 97% were missing less than 5% of 28 Depression items.

We analyzed the following three models with Structural Equation Modeling (SEM) methodology.

Model 1: We measured HRQoL with the two HRQoL factors, i.e., Physical Health and Mental Health. In this model, only the Physical and Mental Health of HRQoL were used because PROMIS documentation does not indicate a global HRQoL factor that combines the two HRQoL factors.

We measured OHRQoL with four first-order factors, i.e., the dimensions of OHRQoL. We introduced a second-order OHRQoL factor comprising the four first-order factors. We determined two correlation coefficients for the HRQoL-OHRQoL association: one for HRQoL Physical Health – OHRQoL and one for HRQoL Mental Health – OHRQoL.

Model 2: Even if the PROMIS authors do not suggest forming a global factor for PROMIS v.1.1 Global Health PROM, we added a second-order global HRQoL factor in Model 2 because we wanted to derive a single correlation coefficient characterizing the association between OHRQoL and HRQoL constructs. Model 2 is otherwise identical to Model 1.

Model 3: To be comparable with previous analysis (10), three independent variables, i.e. age, gender, and level of depression, were included in Path Analysis (35). Age and gender were self-reported by the patients. This model allows us to compute the association between OHRQoL and HRQoL controlled for potential confounders. We first approached the path analysis model by adding the three independent variables to Model 2. However, we encountered problems fitting the second model, and have, therefore, added the three independents to Model 1 composed of one global OHRQoL factor and two HRQoL Physical and Mental Health factors, which we regressed upon patients' age, gender, and depression score.

SEM-based second-order confirmatory factor analysis was used to test the model fit scale of OHIP and both PROMIS PROMs and to assess correlations between the global OHRQoL factor and its four dimensions with HRQoL Physical and Mental Health dimensions. In addition, correlation coefficients between OHRQoL dimensions were also estimated from the SEM second-order confirmatory factor analysis model.

Two model fit indices that account for model complexity are the Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI). For both indices, an index value higher than 0.95 indicates a good fit of the model to the data. The Root Mean Square Error of Approximation (RMSEA) of less than 0.08 indicates a good fit (36). More recently, RMSEA (37) of less than 0.06 or a stringent upper limit of 0.07 is the current consensus for a good fit (38). The Weighted Root-Mean-Square Residual (WRMR) uses a variance-weighted approach (39). The WRMR statistic of less than 1.0 indicates a good fit. We judged the magnitude of correlation coefficients according to Cohen (40), where the effect size of 0.1 is considered small, 0.3 medium, and 0.5 large.

3 RESULTS

3.1 Demographic and Clinical Characteristics

In total, 2,076 dental patients completed OHIP and PROMIS v.1.1 Global Health PROMs (Table 1). Patients had a mean age of 54.7 (16.2) years. The number of patients who also completed PROMIS v.1.0 Emotional Distress - Depression was 2,049 dental patients (mean age (SD): 54.8 (16.2)), of which 1,239 were females (59.7%).

Table 1. Dental patients' demographic and clinical characteristics.

Dental patients (n=2,076)	mean (SD) or %
Demographics	
Gender (female)	59.7
Age (years)	54.7 (16.2)
Language	
English	84.5
Spanish	15.5
Ethnicity	
Hispanic or Latino	12.3
Unknown	87.7
Self-reported oral health	
Excellent	6.5
Very good	24.1
Good	35.2
Moderate	25.6
Poor	8.5
Self-reported general health	
Excellent	10.3
Very good	36.8
Good	38.4
Moderate	13.0
Poor	1.3
OHIP summary scores	
OHIP-49	32.0 (32.3)
OHIP-14	7.7 (9.4)
OHIP-5	3.4 (3.7)
OHIP-49 dimensional scores	
Oral Function	6.4 (7.6)
Orofacial Pain	6.0 (5.7)
Orofacial Appearance	6.9 (7.0)
Psychosocial Impact	7.8 (12.0)
PROMIS v.1.1 Global Health dimensional scores	
Physical Health	15.3 (2.9)
Mental Health	15.1 (3.0)

Legend: SD=standard deviation; OHIP=Oral Health Impact Profile; PROMIS=Patient-Reported Outcomes Information System

3.2 Model 1

For this model, all correlation coefficients displayed in Table 4 were positive and significant ($p<0.05$). The correlation between the OHRQoL score and the two HRQoL scores was "large," as reported by Cohen, i.e. 0.55 and 0.51 for Physical Health and Mental Health, respectively (Figure 1, Table 2).

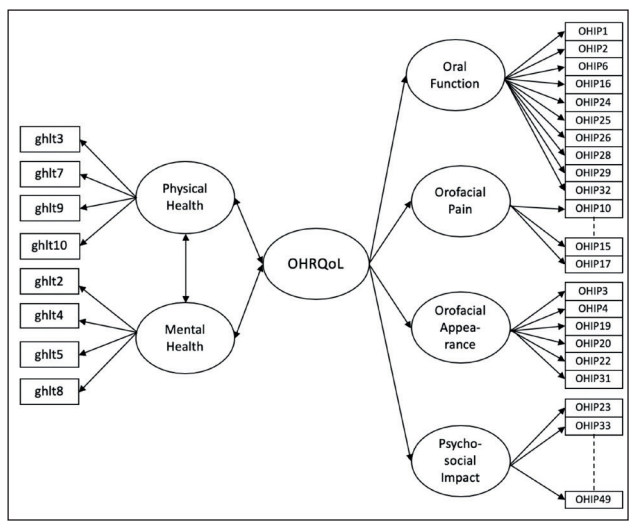

Figure 1. Structural equation modeling confirmatory factor analysis for correlations of one second-ordered global OHRQoL measure (OHIP-49) and two first-ordered HRQoL measures (PROMIS v.1.1 Global Health).

Note: Circles reflect latent constructs, and rectangles represent measured variables.

The two HRQoL factors, i.e. Physical and Mental Health, correlated almost perfectly (r=0.98). All four first-order OHRQoL scores correlated very strongly to almost perfectly with the second-order OHRQoL score (r=0.81-0.98). The four first-order OHRQoL scores strongly correlated with each other (r=0.67-0.81).

Table 2. Model 1 estimated correlation matrix for first and second-order OHRQoL and HRQoL factors from structural equation modeling confirmatory factor analysis.

Factors	Physical Health	Mental Health	OHRQoL	Oral Function	Orofacial Appearance	Orofacial Pain	Psychosocial Impact
Physical Health	1.00						
Mental Health	0.89	1.00					
OHRQoL	0.55	0.51	1.00				
Oral Function	0.45	0.41	0.81	1.00			
Orofacial Appearance	0.49	0.45	0.88	0.72	1.00		
Orofacial Pain	0.46	0.42	0.83	0.67	0.73	1.00	
Psychosocial Impact	0.54	0.50	0.98	0.79	0.86	0.81	1.00

Note: The highlighted correlations are the only correlations that are specified by Model 1. All other correlations between all latent variables and dimensions were generated but were not specified by the model.

The proportion of variance in the Physical and Mental Health of HRQoL explained by OHRQoL was R^2 for Physical Health of HRQoL and equaled 0.30. The R^2 for the Mental Health of HRQoL equaled 0.26. We present the Model Fit statistics for Model 1 in Table 3.

Table 3. Model Fit Indices of Model 1, Model 2, and Model 3.

Model Fit Indices	Model 1	Model 2	Model 3
		Index value	
Comparative Fit Index (CFI)	0.96	0.96	0.94
Tucker-Lewis Index (TLI)	0.95	0.95	0.94
Standardized Root Mean Square Residual (RMSEA)	0.06 (95%CI:0.063-0.065)	0.06 (95%CI:0.063-0.065)	0.06 (95%CI:0.061-0.063)
Weighted Root Mean Square Residual (WRMR)	3.14	3.14	3.16

Note: The highlighted correlations are the only correlations that are specified by Model 1. All other correlations between all latent variables and dimensions were generated but were not specified by the model.

3.3 Model 2

Compared to Model 1, Model 2 contains an overall HRQoL factor (Figure 2).

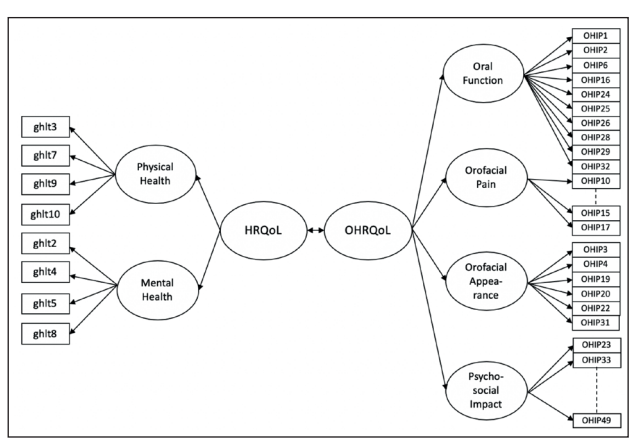

Figure 2. Structural Equation Modeling Path Analysis for correlations of one second-ordered global OHRQoL measure (OHIP-49) and two first-ordered HRQoL measures (PROMIS v.1.1 Global Health).

Note: Circles reflect latent constructs, and rectangles represent measured variables.

In this model, HRQoL and OHRQoL are represented by their two or four dimensions, respectively. We present the model fit statistics for Model 2 in Table 3. The added level of complexity with a second-order global HRQoL factor did not alter the exactness of the model fit. In line with Cohen's r guidelines, the correlation of 0.56 between OHRQoL and HRQoL scores was "large." All correlation coefficients for Model 2 are displayed in Table 4.

Table 4. Estimated correlation matrix for first and second-order factors from structural equation modeling confirmatory factor analysis for Model 2.

Factors	HRQoL	Physical Health	Mental Health	OHRQoL	Oral Function	Orofacial Appearance	Orofacial Pain	Psychosocial Impact
HRQoL	1.00							
Physical Health	0.98	1.00						
Mental Health	0.90	0.89	1.00					
OHRQoL	0.56	0.55	0.51	1.00				
Oral Function	0.46	0.45	0.41	0.81	1.00			
Orofacial Appearance	0.50	0.49	0.45	0.88	0.72	1.00		
Orofacial Pain	0.47	0.46	0.42	0.83	0.67	0.73	1.00	
Psychosocial Impact	0.55	0.54	0.50	0.98	0.79	0.86	0.81	1.00

Note: The highlighted correlations are the only correlations that are specified by Model 2. All other correlations between all latent variables and dimensions were generated but were not specified by the model.

3.4 Model 3

The SEM path model was specified for Model 2 with the global HRQoL and OHRQoL second-order factors regressed on the patients' age, gender, and depression score. The strong correlation between Physical Health and global HRQoL (0.98 in Model 2) resulted in linear dependency between these two factors when we included additional variables in the model. Therefore, we used the model conceptualizing HRQoL with two factors and OHRQoL with four factors, and an overall OHRQoL factor (Figure 3).

We presented the Model Fit statistics in Table 3. Patients' older age was significantly ($p<0.001$) associated with increased OHRQoL and decreased Physical Health factor scores and was not significantly associated with Mental Health. Female gender was associated with significantly lower Physical and Mental health scores but was not significantly associated with the OHRQoL score. Increased depression score (more depression) was significantly associated with decreased OHRQoL, Physical, and Mental Health factor scores (Table 5).

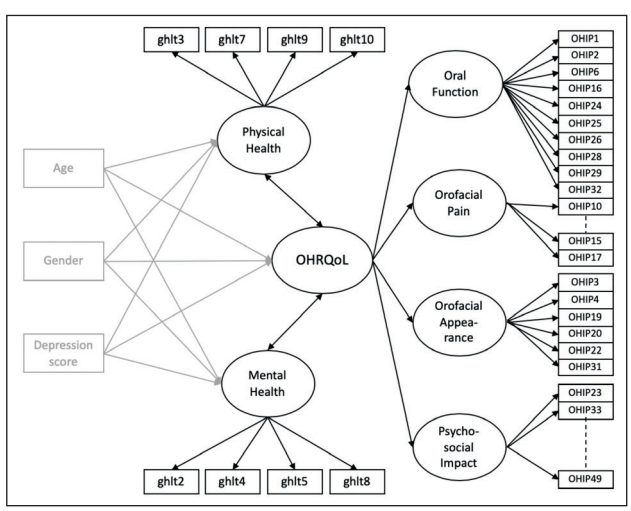

Figure 3. Structural Equation Modeling Path Analysis for correlations of one second-ordered global OHRQoL measure (OHIP-49) and two first-ordered HRQoL measures (PROMIS v.1.1 Global Health). Note: Circles reflect latent constructs, and rectangles represent measured variables.

Note: Circles reflect latent constructs, and rectangles represent measured variables.

Table 5. The structural equation modeling path analysis model estimated standardized regression coefficients (SE). Standardized estimates are for the mean change in factor score for one standard deviation increase in the independent variable.

Independent variables	Factors					
	OHRQoL		Physical Health		Mental Health	
	Estimate (SE)	p-value	Estimate (SE)	p-value	Estimate (SE)	p-value
Age	0.052 (0.023)	0.024	-0.167 (0.022)	<0.001	0.007 (0.018)	0.704
Female	-0.029 (0.023)	0.195	-0.101 (0.022)	<0.001	-0.055 (0.018)	0.003
Depression score	-0.410 (0.019)	<0.001	-0.520 (0.018)	<0.001	-0.663 (0.012)	<0.001

Legend: SE=standard error; OHRQoL=Oral Health-Related Quality of Life.

The magnitude of correlations between the factors in this model was significant ($p<0.05$) and similar to those of Model 1. According to Cohen's r, the association between the two HRQoL scores (Physical and Mental Health) of 0.87 was "large," as well as correlations of all four first-order OHRQoL scores with the second-order global OHRQoL score which ranged from 0.83 to 0.97, and with each other ranging from 0.68 to 0.86. The correlation between the global OHRQoL score and the two HRQoL scores was "large," i.e., 0.52 and 0.47 for Physical Health and Mental Health, respectively (Table 6).

Table 6. Estimated correlation matrix for first and second-order factors adjusted for age, gender, and depression score for Model 3.

Factors	Physical Health	Mental Health	OHRQoL	Oral Function	Orofacial Appearance	Orofacial Pain	Psychosocial Impact
Physical Health	1.00						
Mental Health	0.87	1.00					
OHRQoL	0.52	0.47	1.00				
Oral Function	0.43	0.39	0.83	1.00			
Orofacial Appearance	0.46	0.42	0.88	0.73	1.00		
Orofacial Pain	0.43	0.39	0.83	0.68	0.73	1.00	
Psychosocial Impact	0.50	0.46	0.97	0.80	0.86	0.80	1.00

Note: The highlighted correlations are the only correlations that are specified by Model 3. All other correlations estimates were generated but were not specified by the model.

The proportion of variance in Physical and Mental Health explained by OHRQoL, adjusted for effect of age, gender, and depression were R^2 for the Physical Health of HRQoL and equaled 0.27. The R^2 for Mental Health of HRQoL equaled 0.22.

4 DISCUSSION

The magnitude of the correlation between the four-dimensional OHRQoL and HRQoL constructs was large in our dental patient population. This is the first study in which PROMIS PROMs for HRQoL evaluation was used to assess self-reported general health in a dental patient population. The included dental patients are representative of the full range of patients attending dental practices. OHIP-49 and PROMIS v.1.1 Global Health are psychometrically sound and valid PROMs.

Zimmer and co-authors explained that about 10% of the OHRQoL information is incorporated into HRQoL (9). Nevertheless, they did not take into account that measurement error can weaken a correlation evaluated with short PROMs. Reissmann and co-authors found a higher correlation coefficient compared to the previous study (10), explaining 29% of the information contained in HRQoL. While our dental patient population is similar

to the subjects Reissmann and co-authors investigated, our measurement tools capturing OHRQoL and HRQoL constructs differ from their study. Reissmann et al. used OHIP-49 and SF-36 PROMs, while we used OHIP-49 and PROMIS v.1.1 Global Health PROMs. Similarly, the study by Ranfl and Zaletel-Kragelj used single items for the evaluation of the connection between dentate status and self-assessed general health on a large sample of general population subjects (11). Like us, they also considered the possibility of variation in data when adjusted for confounders such as age, gender, educational level, type of work, and self-classified social class (11).

Because the stomatognathic system is an essential component of the body, from a biological point of view, OHRQoL is embedded in the HRQoL construct. From a conceptual perspective, the HRQoL construct is broad, general, and not linked to body elements or organs. Also, the high correlation between Mental Health and Physical Health in our study indicates that in typical dental patients, the two scores measure the same underlying construct, i.e. the HRQoL construct. Oral disorders may have different outcomes. When patients perceive "physical" impacts in the OHRQoL area, their functional and psychosocial oral health deteriorate. This also worsens their HRQoL, but to a minor degree. This is of importance in clinical dentistry as well as in oral public health studies. For example, temporomandibular disorders (41) impact a patient's oral health and may also influence overall health substantially. In other instances, oral disorders may also present as part of systemic disease. Dementia can affect patients' oral health (42). A patient with oral cancer and resected mandible certainly has oral health-related psychosocial impacts, but mental health is also affected (43). Thus OHRQoL and HRQoL PROMs should be able to represent such information. A substantial overlap between OHRQoL and HRQoL should be detected if dental patients' present both oral impairments and systemic effects, oral impairments with systemic effects, or a more general element, e.g. health behavior, that can influence oral and systemic diseases (44–46). On the contrary, the correlation should be small in a dental patient population with a localized oral disease not associated with systemic disease.

A limitation of the study could be the oversampling of Spanish-speakers, and we have not provided separate analyses for the two language groups. However, we did not see a reason why the OHRQoL-HRQoL relationship in those patients would differ. In contrast to modeling HRQoL or OHRQoL with its indicators, i.e. items, we used the depression instrument's items and derived a summary score to be included in the SEM. While Mplus can handle missing data for the HRQoL and OHRQoL in the analysis, we imputed missing depression items to include patients with sufficient depression information. Overall, the amount of missing data was low, generating a limited potential to change the observed results. Especially for the two quality of life latent variables, we had sufficient information to characterize them. Adjustment by age, gender, and depression did not change the HRQoL-OHRQoL relationship substantially. Therefore, it seems unlikely that the small amount of missing depression information would alter the observed results substantially. We conceptualized OHRQoL as consisting of four dimensions. Consequently, we excluded three OHIP items related to denture wearers and five to the symptom status. While this concept should provide improved OHRQoL structural validity, it can limit comparability with other studies using 49 OHIP items.

The major strength of this study is that we used a highly precise statistical technique that allows modeling the variables directly by eliminating measurement errors that occur during data analysis (34, 43). Even though we provided valuable insights into the magnitude of overlap between OHRQoL and HRQoL constructs, further research of the magnitude between the two constructs' dimensions can be explored, e.g. OHRQoL dimensions-HRQoL and HRQoL dimensions-OHRQoL. A future research synthesis that would summarize and analyze the correlations of available and future studies would provide a thorough understanding of the association between the two constructs of interest.

5 CONCLUSIONS

Our study provides good evidence that OHRQoL and HRQoL constructs overlap substantially, which is informative for public health because in the OHRQoL assessment, valuable medical information is embedded and vice versa; low HRQoL can be indicative also of impaired oral health.

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CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

Reviewed and approved by the Institutional Review Board of the HealthPartners Institute, Minnesota, USA (Study Number A11-136).

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PRODUCTIVITY LOSSES DUE TO MIGRAINE IN SLOVENIA: AN ANALYSIS OF ABSENTEEISM AND PRESENTEEISM COSTS BASED ON ADMINISTRATIVE AND SELF-REPORTED DATA

STROŠKI IZGUB PRODUKTIVNOSTI ZARADI MIGRENE V SLOVENIJI: ANALIZA STROŠKOV ABSENTIZMA IN PREZENTIZMA NA PODLAGI PODATKOV IZ ADMINISTRATIVNEGA VIRA IN ANKETE

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ABSTRACT

Introduction: Migraine is associated with significant morbidity and a significantly negative impact on the quality of life. A better understanding of the economic impact of migraine is becoming increasingly important. This paper aims to shed light on absenteeism and presenteeism costs of migraine in Slovenia.

Methods: We use the administrative national-level database on sick leave due to migraine for 2016. The absenteeism cost estimate is based on the number of patients with migraine on physician-determined sick leave and average daily labour costs. We calculate productivity costs from a social perspective regardless of who incurs them. Data from the national registry on sick leave are coupled with data from a web-based self-reported survey to also include the cost of presenteeism. MIDAS and WPAI presenteeism items were used and several different scenarios were designed to assess presenteeism costs.

Results: We estimated annual absenteeism costs per absentee due to migraine at the amount of EUR 531 in 2016 using the NIPH's administrative data on sick leave. Annual absenteeism costs per absentee due to migraine based on self-reported data amounted to EUR 626. The estimated annual presenteeism costs per patient range from EUR 344 – 900.

Conclusion: Estimating the economic burden of a disease is becoming increasingly important. This paper is an insight into the absenteeism and presenteeism costs of migraine in Slovenia.

Keywords:
migraine, economic burden of illness, absenteeism, presenteeism, indirect costs

IZVLEČEK

Uvod: *Migrena spada med pogoste kronične bolezni, ki ima močno negativen učinek tako na kakovost življenja samega prizadetega posameznika in njegovih bližnjih kot tudi na družbo kot celoto. Za boljše razumevanje slednjega postaja vse pomembnejše tudi ekonomsko vrednotenje tega negativnega učinka, vključno z upoštevanjem posrednih stroškov, med katerimi velja posebej izpostaviti stroške absentizma in prezentizma. S tem prispevkom proučujemo stroške absentizma in prezentizma zaradi migrene v Sloveniji.*

Metode: *Uporabili smo podatkovno bazo NIJZ za odsotnost zaradi migrene za leto 2016. Ocena stroškov absentizma temelji na številu pacientov z migreno in številu dni bolniških odsotnosti zaradi migrene, ki jo opredeli zdravnik (v nasprotju s samooceno, pridobljeno z različnimi vprašalniki). Želeli smo ovrednotiti stroške izgub produktivnosti z družbenega vidika, zato smo v ceni dela upoštevali tako povprečno neto plačo, ki vključuje prispevke zaposlenih kot tudi prispevke delodajalcev. Poleg tega tudi nismo ločevali nadomestila za odsotnost z dela zaradi zdravstvenih razlogov, ki ga za krajše odsotnosti krije delodajalec, od nadomestila za daljše časovno obdobje, ki ga krije obvezno zavarovanje. Podatke iz nacionalne baze smo dopolnili s podatki, zbranimi s spletno anketo, na podlagi katerih smo lahko ocenili tudi stroške prezentizma. V anketi sta bila kombinirana dva različna instrumenta za ovrednotenje stroškov prezentizma, in sicer MIDAS in WPAI, zato smo stroške prezentizma ocenili ob upoštevanju različnih scenarijev.*

Rezultati: *Ocenjeni povprečni letni strošek absentizma na koristnika staleža je bil 531 evrov v letu 2016, če smo upoštevali podatke iz nacionalne baze bolniškega staleža. Povprečni letni strošek absentizma na koristnika staleža na podlagi anketnih podatkov pa je znašal 626 evrov. Ocena letnih stroškov prezentizma na pacienta se ob upoštevanju omenjenih različnih scenarijev giblje na širokem intervalu med 344 in 900 evri.*

Sklep: *Za ustrezno obvladovanje bolezni je ključnega pomena ustrezno ovrednotenje z boleznijo povezanega bremena. Če že ne moremo oceniti oviranosti, ki jo posamezniku in njegovim bližnjim predstavljajo bolečina in z njo povezane omejitve, je ekonomsko breme bolezni bolj otipljivo. Pri oceni ekonomskega bremena je bistveno, da so poleg neposrednih stroškov bolezni upoštevani tudi posredni stroški. V tem prispevku se osredotočamo na ocenjevanje stroškov absentizma in prezentizma zaradi migrene v Sloveniji.*

Ključne besede:
migrena, ekonomsko breme bolezni, absentizem, prezentizem, posredni stroški

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1 INTRODUCTION

Migraine is a very common headache disorder affecting around 12-14% of adults, with significant negative impacts on the quality of life (1, 2). There is a lack of adequately collected epidemiological data on headache and migraine in Slovenia. The 2012 study (3) of the adult working population has shown that the prevalence of headaches was 38.1%. Migraine represents a setback not only for the affected person but also for society as a whole. Researchers and policy-makers explore both the direct and indirect costs of migraine to determine its economic burden (4). Being incurred by the health system, society, family and individual patients, the direct costs consist of healthcare costs such as medical care expenditures and non-healthcare costs such as transportation, relocating and informal care (5). Indirect costs include productivity losses borne by the individual, family, society, or the employer due to absenteeism, presenteeism, premature death and economic inactivity as well as losses in education and job promotion, unwanted job changes, lost time from work for caregivers, and replacement market value for lost domestic services (5, 6).

Early research on the economic burden of migraine began in the USA (7). Increasingly more is now known about it also in Europe. While there are large differences in estimated costs between countries due to methodological differences (6), most studies show that indirect costs exceed the direct costs (6, 8-10). An influential paper by Linde et al. (10) found that indirect costs of migraine accounted for 93% of all costs, two-thirds of which were attributable to reduced productivity, i.e. presenteeism, rather than absenteeism. Other studies (6, 11-13) also support this conclusion. An average efficiency level when working with a migraine was estimated at 65% (11) and even 56% (13). A recent US study (14) that evaluated presenteeism among employees showed that migraine is among the conditions with the highest estimated daily productivity loss and annual cost per person.

Costs of migraine have also been estimated for Slovenia (15, 16). The more recent study (16) allocated a 74% share of all costs to indirect costs, thereby supporting the conclusions of studies for other countries. However, these estimates are based on extrapolated data from the European study on costs of brain disorders for 2010 (8) and exclude presenteeism costs.

The aim of this paper is to investigate both absenteeism and presenteeism costs of migraine in Slovenia. We contribute to existing research for Slovenia (15, 16) because our calculations do not build on extrapolated data based on foreign studies, but on national level sick leave data provided by the Slovenian National Institute of Public Health (NIPH) and on a small retrospective self-reported study of migraine that also incorporated the MIDAS and WPAI items on absenteeism and presenteeism. This enables us to estimate both absenteeism and presenteeism costs while previous research for Slovenia addressed lost production due to work absence and early retirement.

2 METHODS

Estimating productivity costs requires selecting both a suitable approach for assigning a monetary value to lost productivity and an appropriate measurement method for absenteeism and presenteeism.

2.1 Valuation of Lost Productivity

We adopt the human capital method that takes the earnings of an individual as a proxy for their productivity (17). To calculate productivity costs, we use the daily labour costs per worker separately for both genders in 2016, given that the studied administrative data on absenteeism refer to this year. In Slovenia, the average daily labour costs amounted to EUR 90.17 for women and EUR 95.81 for men in 2016 (18).

Average daily labour costs are calculated by dividing respective annual labour costs by the 252 working days in Slovenia in 2016. Annual labour costs per worker are calculated based on the labour cost structural statistics of the Statistical Office of Slovenia. They comprise wages and salaries, including social contributions payable by employees, social contributions paid by employers and other expenditures paid by the employers. In Slovenia, persons with compulsory insurance are entitled to a sickness cash benefit that for patients with migraine typically amounts to 80% of their earnings. The sickness cash benefit is paid either by the employer or the Health Insurance Institute of Slovenia, depending on the length of absence. By estimating absenteeism costs using daily labour costs per worker, we capture both the 20% share of the burden carried by patients and the 80% share of absenteeism costs incurred by either the employer or the social insurance fund. We thus calculate absenteeism costs from a social perspective regardless of who incurs them.

One important pitfall of the human capital approach is that differences in absenteeism costs between different diseases may be a consequence of wage differences rather than the actual length of absences and the levels of impairment (9). In such circumstances, estimates of indirect costs for illnesses affecting mostly manual uneducated labour or women may underestimate their burden of illness. This is relevant also for migraine since prevalence, incidence and remission rates vary by sex, socioeconomic status and other factors (19). This is why we use both average overall daily labour cost and average

gender-specific daily labour costs in Slovenia. In 2016, the average daily labour cost per worker for both genders combined equalled EUR 93.21 (18). Educational-level and profession-specific labour costs are not used, as available datasets do not incorporate this information about the studied migraineurs.

2.2 Estimating Absenteeism Costs

Absenteeism is estimated using the national sick-leave database, coupled with data from the self-reported study that includes the Migraine Disability Assessment Test (MIDAS) and Work Productivity and Activity Impairment (WPAI) items, measuring absenteeism and presenteeism.
We use the administrative database of the NIPH on sick leave due to migraine for 2016. Surveys reflect patients' subjective perceptions about the type of their headaches, whereas in our administrative database the diagnoses are recorded by medical professionals at the time of sick leave occurrences according to the International Classification of Diseases (Version ICD-10-AM). This database includes the entire population of employed individuals and others entitled to sickness benefits that are on formal sick leave due to migraine rather than a specific sample. Part-time employees and self-employed individuals as well as employees with flexible work schedules, who take formal sick leave less often, represent a small share. The database for 2016 consists of 2,416 records of absence from work of full-time employees due to migraine. These records refer to 1,743 patients. Besides the duration of sick leave, information on gender, age group and month of the sick leave termination are also available. Absenteeism costs based on administrative data are estimated using Equation 1.

$$\textit{Annual absenteeism cost per absentee} = \sum_{i=1}^{N=1743} (\textit{length of sick leave}_i \times \textit{average (overall) daily labour costs}) \div N \quad \text{(Eq. 1)}$$

The length of sick leave is the yearly number of days off work for an individual patient with diagnosed migraine (code G43 of ICD-10-AM). Average overall labour costs are specified in Section 2.1. Eq. 1 is modified by replacing the average overall daily labour costs with the average gender-specific daily labour costs to determine the gender-specific absenteeism costs.

Absenteeism is also studied based on the data from a wider self-reported study (20). A web survey using a recall period of 3 months was conducted between 15 November and 12 December 2017 to analyse the prevalence of headache and migraine, their impact on the working population and the treatment processes. A total of 1,207 adult employees with headaches, in addition to 102 general practitioners and 50 neurologists, were surveyed. There were 146 migraineurs out of 1,207 respondents. After excluding outliers (i.e., patients outside the range of three standard deviations from the mean number of days at work affected by migraine) 142 migraineurs were included in the analysis. The survey comprises 20 questions referring to the diagnosis, the current disease treatment and management, the use of headache diaries, migraine's adverse effects and the productivity losses. One item capturing absenteeism is from the MIDAS instrument, which is one of the most widely used questionnaires to measure the impact of headaches on work functioning and is also included in the Slovenian national guidelines for treatment of migraine (21).

This item measures the number of days lost form work or school in the last 3 months. Absenteeism costs estimated using this approach are calculated using Equation 2.

$$\textit{Absenteeism cost per absentee in a 3-month period} = \sum_{i=1}^{n=142} (\textit{no. of days out of work in the last 3 months}_i \times \textit{average (overall) daily labour costs}) \div n \quad \text{(Eq. 2)}$$

Eq. 2 is also modified by replacing the average overall daily labour costs with the average gender-specific daily labour costs from Section 2.1.

An important challenge of using self-reported data with a 3-month recall is the calculation of absenteeism costs at an annual level. The national-level data on sick leave indicate that the frequency and intensity of sick leave is not constant throughout the year. To extrapolate results from the 3-month period covered by the survey to the annual level, we introduce conversion factors estimated from the administrative data on sick leave. Conversion factors are estimated by comparing average absences from work in a corresponding 3-month period to the average absences on an annual level.

2.3 Estimating Presenteeism Costs

Presenteeism is studied using the MIDAS and WPAI instruments, each including one presenteeism item (22).

In the WPAI presenteeism item, 0 indicates no effect on work and 10 complete prevention from working. The estimated presenteeism costs based on this WPAI item are calculated using Equation 3.

$$\textit{Presenteeism cost per patient in a 3-month period} = \sum_{i=1}^{n=142} (\textit{no. of work days with reduced productivity in the last 3 months}_i \times \textit{impairment while working with migraine}_i / 10 \times \textit{average (overall) daily labour costs}) \div n \quad \text{(Eq. 3)}$$

The number of working days with reduced productivity in the last 3 months is determined as the difference between the number of migraine days and the number of days of absence from work in this same period.

MIDAS identifies the number of days at work with substantially reduced productivity (i.e. more than 50%) over a 3-month period. The estimated presenteeism costs based on this MIDAS item are calculated using Equation 4.

$$\begin{aligned} &Presenteeism\ cost\ per\ patient\ in\ a\ 3\text{-}month\ period \\ &= \sum_{i=1}^{n=142} (no.\ of\ work\ days\ with\ at\ least\ 50\%\ productivity\ loss_i \quad \text{(Eq. 4)} \\ &\times \ 0.5 \ \times \ average\ (overall)\ daily\ labour\ costs) \ \div \ n \end{aligned}$$

To enable a comparison between estimated presenteeism and absenteeism costs, the former need to be extrapolated from a 3-month period to an annual level. We do this using conversion factors from Section 2.2. We thus assume that migraine intensity within the observed 3-month period compared to the whole year had a comparable effect on both absenteeism and presenteeism.

3 RESULTS

3.1 Absenteeism Costs

Figure 1 shows the distribution of the 1,743 migraineurs on sick leave from the national database in 2016 by age and gender (85.4% women, 14.6% men). Over 80% of migraine-related absences lasted for up to five days. The average annual length of absence from work due to migraine was 5.70 days, 5.65 for women and 5.96 for men.

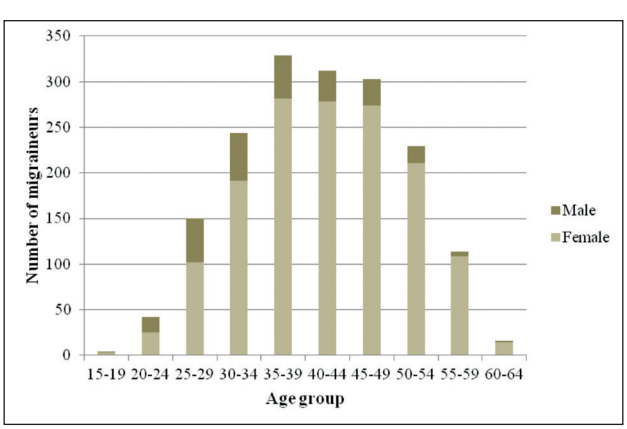

Figure 1. Distribution of migraineurs by 5-year age groups and gender, national database, 2016.

The average annual absenteeism cost per absentee estimated using Eq. 1 amounted to EUR 531. The total annual absenteeism cost for all 1,743 migraineurs on formal sick leave in 2016 is thus estimated at EUR 925,762. Table 1 shows the results for both genders combined and stratified by gender, estimated at labour costs from Section 2.1.

Table 1. Absenteeism costs for migraine in Slovenia, full-time employees, 2016, EUR.

	Gender		
	Female	**Male**	**Total**
Average length of sick leave (days)	5.65	5.96	5.70
Average annual cost per absentee[1]	527	555	531
Gender-specific average annual cost per absentee[2]	510	571	519
Total annual absenteeism cost[1]	784,735	141,027	925,762
Gender-specific total annual absenteeism cost[2]	759,141	144,961	904,102

Note:
1 – calculated with the average overall labour cost for both genders combined in 2016
2 – calculated with the average gender-specific labour cost in 2016

We also estimate absenteeism costs using the self-reported data and Eq. 2. The self-reported average length of absence from work in a 3-month period was 4.40 days (4.18 for women and 4.89 for men).

These results are not directly comparable to the results based on the national database due to differences in the covered period. To enable a comparison, we use the administrative data to determine the average absence from work only for the period from September to November 2016. This time span is observed because the autumn period is also included in the survey and this helps us control possible seasonal triggers of migraine. In the above-mentioned 3-month period, there were 594 patients recorded in the national sick leave database with approximately the same gender proportion as in the whole year of 2016. Their 3-month average absence length was 3.77 days, 3.78 and 3.75 for women and men, respectively. By comparing the average length of absences from work in the three months in autumn to the annual average absences reported in Table 1, we calculate the 1-year-to-3-month ratios equalling 1.510 for both genders combined, 1.497 for women and 1.588 for men for 2016.

The estimated self-reported absenteeism costs calculated on the annual level amount to EUR 626 per absentee for both genders combined, thus exceeding the cost estimated using administrative data by 18% (11% for women and 30% for men).

3.2 Presenteeism Costs

According to Eq. 3, we need both the number of working days with reduced productivity and the efficiency while working with a migraine to estimate the presenteeism cost per absentee in a 3-month period (Figure 2). Over 50% of migraineurs stated that their level of impairment while working with a migraine was between 5 and 7 (out of 10).

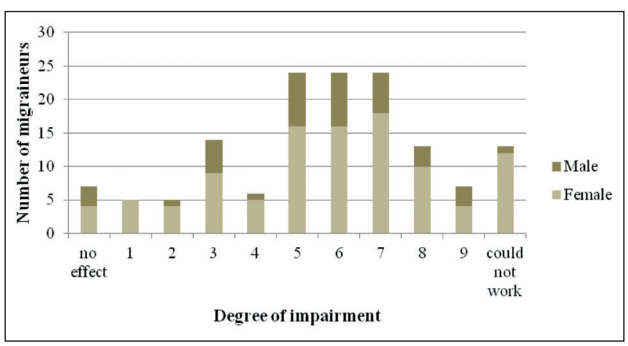

Figure 2. Distribution of self-assessed degree of impairment while working with migraine by gender.

According to the survey, most respondents, i.e. 75.4% (72.8% for women and 82.1% for men), report that the average number of migraine days per month is less than 4. One problem in the calculation of the number of working days with reduced productivity arises from the survey's design. Specifically, the question regarding the length of absence provided different pre-determined intervals. To overcome this problem, we calculate the presenteeism costs by considering several different scenarios shown in Table 2, i.e. 1) taking the lower bounds of the intervals, 2) taking the middle points of the intervals and 3) taking the upper bounds of the intervals as the relevant value for the number of migraine days per month. The upper limit of the last interval is set at the maximum number of working days within a month.

Table 2. Intervals for the average number of migraine days per month and the assigned value under different scenarios.

Average number of migraine days per month	Scenario		
	Min	Middle	Max
Less than 4 days	1	2	3
4-7 days	4	5.5	7
8-14 days	8	11	14
15 or more days	15	18.5	22

The estimated annual presenteeism costs in three different scenarios are presented in Table 3. The survey enables estimates for the observed 3-month period. To enable comparisons of presenteeism costs with absenteeism costs, we converted the 3-month values to the annual level using the conversion factors calculated in Section 3.1.

Given that both the conversion factors and the daily labour cost per worker are for 2016, the estimated presenteeism costs in Table 3 also refer to 2016 to enable comparability with estimated absenteeism costs.

Table 3. Estimated annual presenteeism cost per patient, three scenarios, Slovenia, 2016, EUR.

Scenario	Average annual cost based on overall labour cost (EUR)[1]			Average annual cost based on gender-specific labour cost (EUR)[2]		
	Female	Male	Total	Female	Male	Total
Min	401	267	364	388	275	357
Middle	668	503	623	646	517	611
Max	950	767	900	919	789	883

Notes:
1 – calculated with average overall labour cost for both genders combined in 2016
2 – calculated with average gender-specific labour cost in 2016

The results presented above refer to the WPAI presenteeism item. By using Eq. 4, we estimate presenteeism costs using the MIDAS presenteeism item as well (Table 4). A specific number of days with substantially reduced productivity was reported directly by the surveyed patients. Again, the 3-month values were extrapolated to the annual level by using the conversion factors from Section 3.1.

Table 4. Estimated annual presenteeism cost per patient based on the number of days with 50% productivity impairment, Slovenia, 2016, EUR.

	Gender		
	Female	**Male**	**Total**
Average annual number of days with substantially reduced productivity	7.27	8.10	7.50
General average annual cost per patient[1]	339	378	349
Gender-specific average annual cost per patient[2]	328	388	344

Notes:
1 – calculated with the average overall labour cost for both genders combined in 2016
2 – calculated with the average gender-specific labour cost in 2016

4 DISCUSSION

Methods such as the friction cost method (23), the willingness to pay method (24) and the human capital approach (17, 11, 10) are used to assign a monetary value to lost productivity. We use the human capital approach, which is most widely used in other studies and has also been used in previous research for Slovenia (15, 16). We use both overall and gender-specific annual labour costs per worker as a proxy for their productivity and calculate absenteeism costs from a social perspective regardless of who incurs them (the patient, the employer or the social insurance fund). We use the average overall labour costs to prevent wage differences from influencing the estimated productivity costs. Such estimates reflect differences in actual length of absences and levels of impairment without wage gap distortions (9). The estimated overall and gender-specific results are similar, as the gender labour cost gap is low (EUR 90.17 for women and EUR 95.81 for men in 2016). Given that prevalence of migraine is higher in lower income and lower educational groups (19), it would be beneficial to also estimate productivity costs using actual labour costs of the studied migraineurs. The necessary information, however, is not included in the available datasets. Educational-level-specific results would probably differ more notably from our gender-specific results. The average daily labour costs for those with primary education are 34.6% below the overall average while for those with tertiary education they are 38.4% above the overall average (18).

A wide array of approaches for measuring productivity losses is used. A top-down method based on national registries is mostly used for estimating direct costs, while a bottom-up approach is applied for indirect costs using retrospective population-based studies with different recall periods (11). Different instruments have been used to assess illness-related productivity losses. Papers addressing migraine from a relevant systematic review (25) adopted, for example, the Health and Labour Questionnaire, Work Productivity Short Inventory and the 13-item Stanford Presenteeism Scale. Another review (26) also included 7 papers on presenteeism for migraineurs using MIDAS, the Migraine Work and Productivity Loss Questionnaire – MWPLQ and the Osterhaus Technique. Another review (27) recommended two instruments for migraine, i.e. the Employer Health Coalition of Tampa Assessment Instrument and the MWPLQ. Some recent papers on migraine expand the array to the WPAI (28) and different versions of the HALT questionnaire (29). In our study, we combine both the administrative sick-leave database and the self-reported survey combining the WPAI used in some of the more recent studies (28) and the widely used MIDAS, which is also included in Slovenian national guidelines for migraine treatment (21).

We estimated the annual absenteeism costs per absentee at the amount of EUR 531 in 2016, using the NIPH's administrative data on sick leave due to migraine. Annual absenteeism costs per absentee due to migraine based on self-reported data amounted to EUR 626. Results based on the 3-month survey data were extrapolated to the annual level by taking into consideration the seasonal variation revealed by the administrative database. We thus took a different approach from most studies that collect data for a limited time period and then recalculate these figures pro-rata to obtain days lost from work over a 12-month period (e.g. 13). Results based on self-reported data exceed those based on administrative data by 18%. This could be due to underrepresentation of employees with flexible working arrangements in the administrative database. The estimated absenteeism costs also exceed the previously estimated indirect costs for Slovenia ranging from EUR PPP 181 – 191 (15, 16). These estimates cover lost production due to work absence and early retirement and are not comparable with our results because they extrapolate from foreign studies. They are also lower considering that gross wages and not total labour costs are used for the purpose of valuation.

The estimated annual presenteeism costs per patient with a migraine range from EUR 344 to 900. Lowest estimates are calculated based on the number of days with substantially

(more than 50%) reduced productivity that disregards those days when patients are impacted by migraine to a lesser degree. Results obtained with the minimum and middle scenarios for the number of days affected by migraine are EUR 364 and 623, respectively. An overview of published cost studies for migraine in Europe (11) shows a wide variation in the estimated presenteeism cost per patient between different countries (EUR 50 in Sweden, EUR 138 in the Netherlands, EUR 356 in Germany and EUR 365 in the UK). Another survey in eight countries representing 55% of the adult EU population (10) showed that the mean per-person annual presenteeism costs of migraine amount to EUR 765. Two recent studies show that absenteeism and presenteeism costs equal EUR 535 in Latvia and EUR 483 in Lithuania (30). Our larger estimates can be explained, firstly, by the fact that most respondents reported a high level of impairment while working with migraine (between 5 and 7), which is below the average efficiency levels from other studies (e.g. 56% (13) and 65% (11)). Secondly, we use total labour costs and not just wages to estimate productivity costs. Thirdly, we use overall average daily labour costs thereby disregarding the fact that migraine prevalence is higher for low income groups.

Several limitations of our study need to be addressed. Both the national-level sick leave database and the data from a web-based study have some shortcomings. The administrative database consists of formal sick leave predominantly for full-time employees and there is weak representation of employees with more flexible work arrangements. The sample in the self-reported study is small and non-random. Therefore, the results cannot be considered as statistical estimates but can, nevertheless, provide some insight into absenteeism and presenteeism due to migraine in Slovenia. While reporting bias is an issue when using administrative data, recall bias is involved in self-reported studies. Furthermore, the questionnaire only targets a 3-month period, thereby complicating the drawing of conclusions at an annual level. An additional limitation of our study is that we do not use a control group, which could allow a more specific allocation of productivity losses to migraine. The fact is, migraine has a high comorbidity rate (e.g. 31, 32) and it is not always possible to distinguish between absenteeism due to comorbidity and migraine itself. Another limitation is that we address absenteeism and presenteeism costs but fail to incorporate early retirement, work inactivity, unemployment or underemployment, fewer opportunities for promotion and education, unintended changes in occupation and the burden on informal caregivers. We also disregard impairment of social life and leisure activities and fail to include productivity losses for persons engaged exclusively in domestic production (33).

One of the key strengths of our study lies in its twofold contribution to existing research for Slovenia. Firstly, previous estimates (15, 16) were calculated from extrapolated data of studies for other countries, while our estimates are based on self-reported and administrative data for the Slovenian population. Secondly, we estimate both gender-specific and overall absenteeism and presenteeism costs.

5 CONCLUSIONS

We estimated the annual absenteeism costs per absentee due to migraine at the amount of EUR 531 in 2016 using the NIPH's administrative data on sick leave. The annual absenteeism costs per absentee due to migraine based on self-reported data amounted to EUR 626. The presenteeism costs were assessed under different scenarios based on a self-reported study including MIDAS and WPAI presenteeism items. The estimated annual presenteeism costs per patient range from EUR 344 to 900.

CONFLICTS OF INTEREST

The core data of the article is derived from a survey conducted by Ipsos and funded by Novartis. The authors of the article declare that no conflicts of interest exist in terms of this article's content.

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ETHICAL APPROVAL

Not applicable.

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LONG-TERM EFFECTIVENESS AND COST EFFECTIVENESS OF MULTIPLE MYELOMA TREATMENT STRATEGIES FOR ELDERLY TRANSPLANT-INELIGIBLE PATIENTS IN SERBIA

DOLGOROČNA USPEŠNOST IN STROŠKOVNA UČINKOVITOST STRATEGIJ ZDRAVLJENJA MULTIPLEGA MIELOMA PRI STAREJŠIH BOLNIKIH, KI NISO PRIMERNI ZA PRESADITEV, V SRBIJI

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ABSTRACT

Introduction: Evidence on long-term effectiveness and cost effectiveness of treatment sequences for multiple myeloma (MM) is sparse. We used published data and country-specific data to assess the cost effectiveness of four-line treatment sequences for elderly transplant-ineligible patients with MM in Serbia.

Method: We developed a Markov cohort model to compare long-term effectiveness and cost effectiveness of five sequential MM treatment alternatives from the perspective of the national healthcare provider. Effectiveness parameters on progression, mortality and adverse events were extracted from published clinical trials. Costs were based on price lists of the National Health Insurance Fund. We compared life expectancy, costs, and incremental cost-effectiveness ratios among alternative courses of action. The model was analyzed over a lifelong time horizon applying a 3% annual discount rate for effectiveness outcomes and costs. Robustness of the model was tested in multiple deterministic sensitivity analyses.

Results: The sequences were defined by the frontline treatment: MPT (melphalan-prednisone-thalidomide), MPV (melphalan-prednisone-bortezomib), CTD (cyclophosphamide-thalidomide-dexamethasone), VCD (bortezomib-cyclophosphamide-dexamethasone) and BP (bendamustine-prednisone). MPV sequence resulted in the highest remaining life expectancy (4.76 life years). Cost-effectiveness analysis resulted in three non-dominated strategies: MPT, VCD, and MPV sequences, with an incremental cost-effectiveness ratio of EUR 35,300 per life-year gained (LYG) for VCD and EUR 47,200/LYG for MPV relative to MPT.

Conclusion: MPV sequence was the most effective in terms of life expectancy for elderly transplant-ineligible MM patients in Serbia. Bortezomib-based strategies would be recommended for the frontline treatment of patients with MM in Serbia if the willingness-to-pay threshold is around EUR 35,000-60,000/LYG.

Keywords: multiple myeloma, sequential treatment, long-term effectiveness, cost effectiveness

IZVLEČEK

Uvod: *O dolgoročni uspešnosti in stroškovni učinkovitosti zaporedij zdravljenja multiplega mieloma (MM) ni veliko dokazov. Na podlagi objavljenih podatkov in podatkov za posamezne države smo ocenili stroškovno učinkovitost štirih zaporedij zdravljenja starejših bolnikov z MM, ki niso primerni za presaditev, v Srbiji.*

Metoda: *Za primerjanje dolgoročne uspešnosti in stroškovne učinkovitosti petih alternativ zaporednega zdravljenja MM z vidika nacionalnega izvajalca zdravstvenega varstva smo razvili kohortni model Markova. Parametre uspešnosti glede napredovanja, umrljivosti in neželenih dogodkov smo pridobili iz objavljenih kliničnih preskušanj. Stroški temeljijo na cenikih nacionalnega sklada za zdravstveno zavarovanje. Med različnimi ukrepi smo primerjali pričakovano življenjsko dobo, stroške in mejno razmerje stroškovne učinkovitosti. Model smo analizirali v vseživljenjskem časovnem okviru, pri čemer smo za rezultate uspešnosti in stroške uporabili 3-odstotno letno diskontno stopnjo. Robustnost modela smo preizkusili z več determinističnimi analizami občutljivosti.*

Rezultati: *Zaporedja so bila opredeljena z zdravljenjem v prvi liniji: MPT (melfalan-prednizon-talidomid), MPV (melfalan-prednizon-bortezomib), CTD (ciklofosfamid-talidomid-deksametazon), VCD (bortezomib-ciklofosfamid-deksametazon) in BP (bendamustin-prednizon). Pri zaporedju MPV je bila pričakovana preostala življenjska doba najdalјša (4,76 leta življenja). Pri analizi stroškovne učinkovitosti so bile ugotovljene tri neprevladujoče strategije: zaporedja MPT, VCD in MPV z mejnim razmerjem stroškovne učinkovitosti 35.300 EUR na pridobljeno leto življenja (LYG) za VCD in 47.200 EUR/LYG za MPV glede na MPT.*

Sklep: *Zaporedje MPV je bilo najuspešnejše v smislu pričakovane življenjske dobe starejših bolnikov z MM, ki niso primerni za presaditev, v Srbiji. Strategije, ki temeljijo na bortezomibu, bi bile priporočljive za zdravljenje bolnikov z MM v prvi liniji v Srbiji, če je prag pripravljenosti na plačilo približno 35.000-60.000 EUR/LYG.*

Ključne besede: *multipli mielom, zaporedno zdravljenje, dolgoročna uspešnost, stroškovna učinkovitost*

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1 INTRODUCTION

Multiple myeloma (MM) is the second most common hemato-oncological disease (1) manifested by an uncontrolled monoclonal malignant proliferation of plasma cells in the bone marrow. MM usually affects elderly people, with a median age of about 65 years at diagnosis (2). The global burden of MM is high and rising, mostly due to the increase in incident cases and mortality of MM in middle-income countries (3). In Serbia, MM is a relatively rare disease occurring in around 200 patients per year (4). The disease prognosis has been changed after the introduction of novel treatment agents, such as thalidomide, bortezomib, and lenalidomide. The improved efficacy of these drugs, in terms of progression-free survival (PFS) and overall survival (OS), was presented in several clinical trials (5-7). However, the novel treatment options are also more costly than the standard melphalan-prednisone treatment (8) and the availability and affordability of these medicines is limited in middle-income European economies (9). In Serbia, thalidomide and bortezomib are used in routine clinical practice. Lenalidomide is recommended as an option for relapsed or resistant disease and has been recently approved (3), but it is still not available in treatment centers across the country and is therefore rarely used. In the current situation of economic crisis that Serbia is going through, the healthcare budget resources directed to the treatment of uncommon diseases are limited and require careful weighing of benefits, harms, and costs of treatment alternatives (10). The novel treatment agents are tested in treatment-naive, relapsed, as well as refractory and heavily pretreated patients. However, evidence about the effectiveness of different sequential treatment combinations is sparse and not easily obtainable in prospective clinical studies, as this would require a large study population and a very long follow up. In addition, healthcare policy decision-making and resource allocation have to be based on a systematic and transparent assessment of benefits, harms, and costs, best addressed by the use of decision-analytic modeling combining different sources of evidence (11).

The aim of this study was to assess the clinical effectiveness and cost effectiveness of common sequential treatment pathways for elderly transplant-ineligible patients with MM in Serbia. Furthermore, our goal was to evaluate whether wider use of lenalidomide in everyday clinical practice would change the model-based recommendations.

2 METHODS

2.1 Model Structure

We adopted the structure of a state-transition Markov model previously developed for the Austrian context (12). To depict treatment patterns in the Serbian healthcare system, important structural changes and parameter adaptations were implemented. To transfer and adapt evidence from another healthcare system to the Serbian national context, we followed a stepwise framework developed for HTA agencies (13). We analyzed the Serbian model over a lifelong time horizon following the established recommendations (14, 15) and a national cost-effectiveness guideline (16). The target population consisted of patients with MM ineligible for stem cell transplantation who were 65 years or older. The model was analyzed from the perspective of the Serbian national healthcare provider. We assessed life expectancy (in life years, LYs), costs (in euros, EUR) and the incremental cost-effectiveness ratio (ICER; in euros per life year gained (LYG)). In the base-case analysis, we applied a 3% annual discount rate for both clinical outcomes and costs (17). The model was programmed in the software TreeAge 2016 (TreeAge Software, Inc. Williamstown, MA).

2.2 Compared Sequential Treatment Strategies

We compared five sequential treatment pathways commonly used for elderly patients with MM in the Serbian healthcare setting. The treatment pathways were based on the national guideline for the treatment of MM (18), adapted by Serbian clinical experts. As front-line treatment options, we assessed combinations of melphalan, prednisone, and thalidomide (MPT); melphalan, prednisone, and bortezomib (MPV); cyclophosphamide, thalidomide, and dexamethasone (CTD); bortezomib, cyclophosphamide, and dexamethasone (VCD); and bendamustine and prednisone (BP). After progression, patients were switched to the second-line treatment with a different mechanism of action (for example, patients on the first-line thalidomide-based protocols were switched to the bortezomib- or lenalidomide-based regimens in the second line) (Table 1).

Table 1. Evaluated treatment sequences.

Treatment sequences			
First-line Tx; Data source	**Second-line Tx; Probability of switching protocol; Data source**	**Third-line Tx Probability of switching protocol; Data source**	**Palliative Tx; Data source**
MPT (19)	1. VCD, 20% of cases (20) 2. VD, 70% (21) 3. RD, 10% (22)	1. RD, 30% (22) 2. BTP, 40% (23) 3. Chemo, 30% *	CP (24, 25)
MPV (26)	1. CTD, 90% (27) 2. RD, 10% (22)	1. RD, 30% (22) 2. BTP, 40% (23) 3. Chemo, 30% *	CP (24, 25)
CTD (28)	1. MPV, 30% (29) 2. VD, 60% (21) 3. RD, 10% (22)	1. RD, 30% (22) 2. BTP, 40% 3. Chemo, 30%*	CP (24, 25)
VCD (30)	1. MPT (31) 2. RD, 10% (22)	1. RD, 30% (22) 2. BTP, 40% (23) 3. Chemo, 30% *	CP (24, 25)
BP (32)	1. RD, 100% (22)	1. BTP, 50% (23) 2. Chemo, 50% *	CP (24, 25)

Legend: B-bendamustine; C-cyclophosphamide; Chemo-standard chemotherapy; D-dexamethasone; M-melphalan; P-prednisone; R-lenalidomide; T-thalidomide; Tx-treatment; V-bortezomib; *, Chemotherapy included the following protocols: DCEP (dexamethasone, cyclophosphamide, etoposide, cisplatin) (33, 34), DT-PACE (dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide) (35, 36). Patients switched from first-line treatment to different second- and third-line treatment options. The proportion of patients that switched to each particular protocol is presented in Table 1 (%). Data sources are referenced in parentheses.

As a third-line treatment, patients received a combination of bendamustine, thalidomide, and prednisone (BTP), lenalidomide and dexamethasone (RD) or standard chemotherapy. Palliative treatment consisted of oral administration of low-dose cyclophosphamide and dexamethasone. We assumed administration of a maintenance treatment consisting of daily thalidomide after completion of each treatment protocol, except for RD, which is maintained until progression, and BP recommended for patients with peripheral neuropathy that could deteriorate through thalidomide maintenance.

Figure 1 shows the Markov model with health states and respective state-to-state transitions.

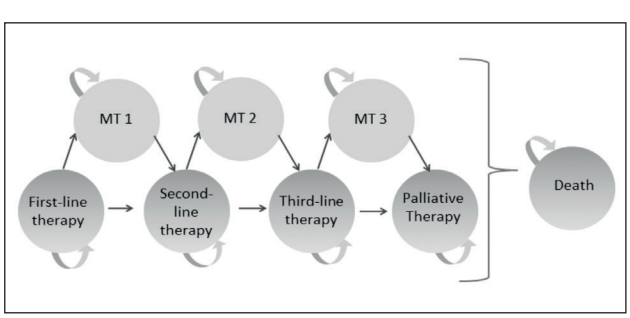

Figure 1. Markov health states and state-to-state transitions. Legend: MT, maintenance treatment; Numbers 1, 2, and 3 indicate the treatment line.

After being diagnosed with MM, all patients received first-line treatment. In the case of relapse or recurrence, patients switched to second-line treatment. If the disease did not progress during the treatment, patients transitioned to the maintenance treatment. Patients could die from MM in the second-line and all subsequent treatmnts, while death from other causes was possible in all the states.

2.3 Natural History and Effectiveness Parameters

The analyzed cohort consisted of 65-year old transplant-ineligible patients with MM. Based on clinical expert estimates, 60% of the population were males. The mortality from causes other than MM was derived from the age- and sex-specific mortality rates reported in the Serbian statistical life tables (37). Guideline-recommended treatment patterns (18) were discussed with nine clinical experts from Serbia within a Delphi panel and revised based on the real-world clinical practice in terms of exact frequency, dose, and route of drug administration. Efficacy data (PFS and OS) and safety data (frequency of grade 3 and 4 adverse events occurring in more than 5% of the study population) were extracted from randomized clinical trials. To derive the first-line treatment effectiveness, we fitted a Weibull curve to the weighted proportions of patients who survived without

progression, extracted from all randomized controlled trials comparing MPT with MP (38). Kaplan Meier curves reported in respective clinical trials (Table 1) were used for the extraction of survival and progression probabilities. Exponential survival models were assumed and excess mortality method was used to derive MM-specific mortality as a difference in overall mortality rates reported in the studies and the mortality from other causes extracted from corresponding life tables. Protocol durations (time to maintenance treatment) were implemented from the guideline recommendations. Probabilities of switching to particular second-line treatment protocols were based on estimates of the Delphi panel (Table 1).

2.4 Costs

A bottom-up micro-costing method was applied to analyze healthcare resource consumption and associated costs (39). Healthcare resource utilization during MM treatment was estimated based on the national guideline (18) and clinical experts' estimates. The unit costs of drug acquisition, diagnostic procedures, hospitalization, outpatient care, and injectable drug administration were extracted from the National Health Insurance Fund (NHIF) databases (40-42) and converted to 2018 euros based on purchasing power parities (1 euro=56.3 Serbian dinars) (43). Details on unit costs and cost calculation can be found elsewhere (39).

2.5 Analyses

In the base-case analysis, we evaluated five sequential four-line MM treatment strategies in terms of remaining life expectancy and cost effectiveness. In order to assess the robustness of the model, we tested the sensitivity of its results to parameter changes. Based on recommendations of the national cost-effectiveness guideline (16), we applied a 1.5% discount rate for clinical outcomes while keeping the 3% discount rate for economic outcomes, and also analyzed the scenario with a 5% discount rate applied to both health outcomes and costs (44).

The incremental cost-effectiveness ratios (ICERs) for the treatment sequences are strongly dependent on the underlying probabilities to switch from the initial treatment to subsequent treatment options. To assess the impact of probabilities of switching to a particular second-line treatment on the model-based recommendations, we structurally adapted the model to assess the cost effectiveness of all potential first- and second-line treatment combinations, analyzing 11 different sequences. The third-line treatment was kept the same.

As lenalidomide is still not available in institutions across Serbia, we varied second- and third-line probabilities of switching to lenalidomide-based protocols from 0 to 'increased by 100%' to account for the possibility of gradually increased administration of lenalidomide in future, once it becomes widely available.

Finally, progression and survival probabilities for third-line chemotherapy were based on observational studies, because of the lack of randomized controlled trials. Therefore, we analyzed the change in the results if we exclude these treatment options from the analysis.

2.6 Model Validation

The face validity of the model was discussed with clinical experts and other decision-analytic modelers. Internal verification of the model was assessed using a thorough examination of parameters, formulas, and codes used in TreeAge by two independent modelers. The health states were mutually exclusive and collectively exhaustive and the rule of symmetrical branching was satisfied (45).

3 RESULTS

3.1 Base-Case Analysis

The base-case analysis resulted in a remaining life expectancy ranging from 3.70 to 4.76 LYs, depending on the treatment sequence (Table 2). The most effective treatment sequence was Starting with MPV with a remaining discounted life expectancy of 4.76 LYs. For comparison, the life expectancy of the general 65-year old population in Serbia is 15.8 years based on the life-table estimates (37).

In the cost-effectiveness analysis, three strategies were identified as non-dominated: Starting with MPT, VCD, and MPV.

Table 2. Discounted base-case analysis results.

Strategy	Cost (€)	Life expectancy (LYs)	ICER (€/LYG)
Starting with MPT	116,500	3.70	-
Starting with CTD	123,400	3.41	Dom
Starting with VCD	126,700	3.99	35,300
Starting with MPV	163,300	4.76	47,200
Starting with BP	373,400	3.98	Dom

Legend: BP, bendamustine, prednisone; CTD, cyclophosphamide, thalidomide, dexamethasone; Dom, dominated, ICER, incremental cost-effectiveness ratio; LY(s), life year(s); LYG, life year gained; MPT, melphalan, prednisone, thalidomide; MPV, melphalan, prednisone, bortezomib; VCD, bortezomib, cyclophosphamide, dexamethasone; €, euro.

3.2 Scenario and Sensitivity Analyses

The results of the discount rate variations are presented in Table 3. Non-dominated strategies remained the same as in the base-case analysis, but the ICERs changed, as expected.

Table 3. Variation of annual discount rates.

Discount rate →	1.5% for effectiveness; 3% for costs			5% for effectiveness and costs		
Strategy	**Cost (€)**	**Life expectancy (LYs)**	**ICER (€/LYG)**	**Cost (€)**	**Life expectancy (LYs)**	**ICER (€/LYG)**
Starting with MPT	116,500	3.85	-	110,500	3.51	-
Starting with CTD	123,400	3.53	Dom	117,900	3.25	Dom
Starting with VCD	126,700	4.16	32,500	121,800	3.77	43,800
Starting with MPV	163,300	5.01	43,100	156,100	4.47	49,600
Starting with BP	373,400	4.15	Dom	351,800	3.77	Dom

Legend: BP, bendamustine, prednisone; CTD, cyclophosphamide, thalidomide, dexamethasone; Dom, dominated; Ext Dom, extended dominated; ICER, incremental cost-effectiveness ratio; LY(s), life year(s); LYG, life year gained; MPT, melphalan, prednisone, thalidomide; MPV, melphalan, prednisone, bortezomib; VCD, bortezomib, cyclophosphamide, dexamethasone; €, euro

When we analyzed 11 treatment sequences assuming an equal likelihood of switching to second-line treatment options, four sequences were identified as non-dominated: 1. frontline MPT and VD after treatment failure (MPT→VD), 2. MPT→VCD, 3. MPV→CTD and 4. MPV→RD (Figure 2).

When varying the probability to switch to lenalidomide protocols, non-dominated strategies remained the same (Table 4).

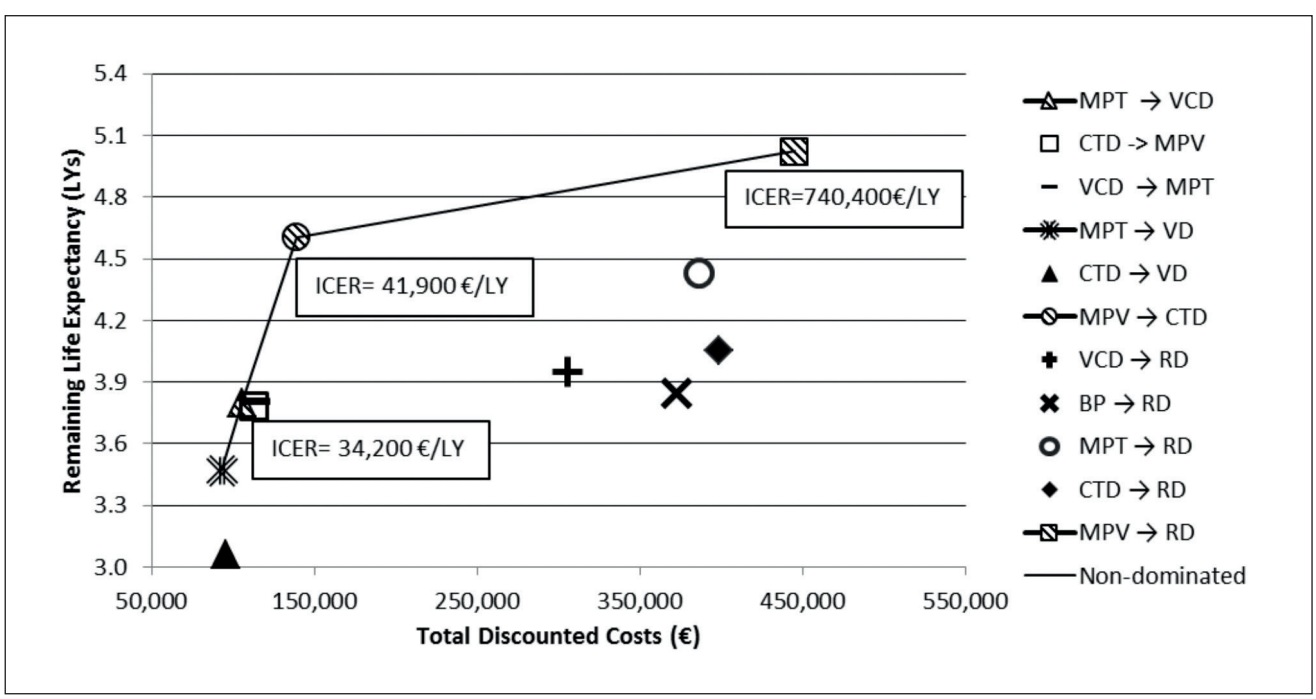

Figure 2. Sensitivity analysis - Cost-effectiveness plane. Sequences defined by the combinations of first- and second-line treatment. The thick line is the cost-effectiveness frontier.

Legend: BP, bendamustine, prednisone; CTD, cyclophosphamide, thalidomide, dexamethasone; ICER, incremental cost-effectiveness ratio; LY(s), life year(s); MPT, melphalan, prednisone, thalidomide; MPV, melphalan, prednisone, bortezomib; RD, lenalidomide, dexamethasone; VCD, bortezomib, cyclophosphamide, dexamethasone; VD, bortezomib, dexamethasone; €, euro.

Table 4. Sensitivity analysis results – varying probability of switching to the lenalidomide-based treatment options.

Strategy	Without RD options			Probability of switching to RD increased by 20%			Probability of switching to RD increased by 50%			Probability of switching to RD increased by 100% (i.e., doubled)		
	Cost (€)	Life expectancy (LYs)	ICER (€/LYG)	Cost (€)	Life expectancy (LYs)	ICER (€/LYG)	Cost (€)	Life expectancy (LYs)	ICER (€/LYG)	Cost (€)	Life expectancy (LYs)	ICER (€/LYG)
Starting with MPT	73,000	3.63	-	124,700	3.71	-	137,400	3.73	-	160,300	3.77	-
Starting with CTD	76,900	3.29	Dom	132,800	3.43	Dom	147,300	3.47	Dom	174,200	3.54	Dom
Starting with VCD	82,800	3.89	36,900	136,400	4.00	39,800	151,400	4.03	46,500	178,800	4.09	Ext Dom
Starting with MPV	112,900	4.68	38,000	174,100	4.77	48,700	190,600	4.80	51,000	220,200	4.84	55,800
Starting with BP*	373,400	3.98	Dom	373,400	3.98	Dom	373,400	3.98	Dom	373,400	3.98	Dom

Legend: BP, bendamustine, prednisone; CTD, cyclophosphamide, thalidomide, dexamethasone; Dom, dominated; ICER, incremental cost-effectiveness ratio; LY(s), life year(s); LYG, life year gained; MPT, melphalan, prednisone, thalidomide; MPV, melphalan, prednisone, bortezomib; VCD, bortezomib, cyclophosphamide, dexamethasone; €, euro
*BP had a 100% probability of switching to lenalidomide-based treatment in the base-case analysis; thus the results remained the same.

An additional analysis was performed to assess robustness of the results if we assume no use of chemotherapy as a third-line treatment option. In this case, life expectancies and costs of the strategies were notably higher (Table 5). The strategies remaining non-dominated were the MPT sequence and the MPV sequence with an ICER of EUR 55,800/LY.

Table 5. Sensitivity analysis – ranking of the sequences when excluding the third-line chemotherapy.

Strategy	Cost (€)	Life expectancy (LYs)	ICER (€/LYG)
Starting with MPT	210,200	4.40	-
Starting with CTD	223,100	4.16	Dom
Starting with VCD	251,100	4.92	Ext Dom
Starting with MPV	266,000	5.53	55,800
Starting with BP	390,200	4.92	Dom

Legend: BP, bendamustine, prednisone; CTD, cyclophosphamide, thalidomide, dexamethasone; Dom, dominated; Ext Dom, extended dominated; ICER, incremental cost-effectiveness ratio; LY(s), life year(s); MPT, melphalan, prednisone, thalidomide; MPV, melphalan, prednisone, bortezomib; VCD, bortezomib, cyclophosphamide, dexamethasone; €, euro.

4 DISCUSSION

Based on the results of our analysis, the sequence with frontline MPV provides the most beneficial outcome in terms of life expectancy. The treatment sequences starting with bortezomib-based protocols were cost effective for the treatment of transplant-ineligible elderly patients with MM in Serbia compared to thalidomide- and bendamustine-based protocols, if the willingness-to-pay (WTP) threshold is around EUR 35,000-60,000/LYG. A more detailed assessment of the compared strategies, taking into account first- and second-line treatment combinations, resulted in four non-dominated strategies: MPT→VD, MPT→VCD, MPV→CTD, MPV→RD. Our analysis shows that, if the NHIF is willing to pay around EUR 40,000/LYG, the options starting with MPV should be favored in the treatment of elderly patients with MM. Keeping in mind that the annual gross domestic product per capita (GDP) in Serbia in 2017 (the last reference year) was EUR 10,700, the implementation of the MPV→CTD sequence might be considered cost effective from the country's perspective (43). The World Health Organization considers an intervention cost effective if its cost per disability-adjusted life-year averted (DALY) is less than three times a country's annual GDP per capita (46). We were unable to calculate DALYs due to the lack of country-specific and detailed disease-specific disability weights. However, we can assume that the MPV→RD sequence, with an ICER of over EUR 700,000/LYG, would not be considered cost effective in Serbia.

A systematic literature review that assessed the cost effectiveness of bortezomib-based options for treatment of MM, reported that the bortezomib-based regimens were cost effective in most of the published reports (47).

However, the cost-effectiveness reports assessed the health-economic impact of bortezomib-based regimens considering only one treatment line, as a first-line treatment or after relapse (47). Only one study analyzed the lifelong sequential MM treatment. Based on this study, the sequence potentially providing better survival outcomes in a group of elderly patients in the Dutch setting was thalidomide → lenalidomide → bortezomib (48).

The decision-analytic model that evaluated the cost utility of different first-line MM treatments in transplant-ineligible patients from the US perspective identified the MPV treatment as cost saving in comparison to MPT and melphalan, prednisone and lenalidomide with lenalidomide maintenance (49). However, it must be noted that thalidomide is available only at a patent-protected price in the US, while in Serbia a generic drug is available at a much lower price than bortezomib (EUR 12 vs. EUR 655 per unit).

Like all decision-analytic modeling studies, our study has several limitations, since the model development required several assumptions to be made. The model was constructed based on the Serbian national guideline recommendations and Serbian clinical experts' opinions. However, the results of the Delphi panel implied that different treatment pathways might be used across different institutions and among clinical experts in Serbia. Thus the results of our analysis might not be exhaustive enough to cover all treatment-related issues in daily clinical routine. Therefore, it would be important to confirm our findings by parameterizing the model with real-world effectiveness data. Furthermore, we systematically searched for the studies that match the guideline-recommended treatment patterns used in Serbia. However, the drug dosing and frequency and route of administration were not always perfectly matched. Survival estimates extracted from trials were modified to disease-specific survival estimates, and Serbian life-tables were applied to simulate the life-expectancy of the model population. This challenging task required complex modeling and a number of assumptions; still, it allowed us to adjust the outcomes of international trials to a specific country population. After patients progressed, we assumed the effectiveness of the subsequent treatment to be independent of the type of prior treatments. This might not be the case in the real world, since drugs with a common mechanism of action may also have similar resistance pathways. However, the patients in our analysis were assigned to a treatment utilizing a different mechanism of action after failure, except for the sequence assuming switching from thalidomide-based protocols to lenalidomide, which was found to be unaffected by previous thalidomide therapy (50). Finally, our model did not consider the quality of life of patients on different treatments, because the evidence was sparse and the implementation of existing data would diminish the robustness of our results. Further research should address the gap in treatment-specific utility estimates, which will provide a solid basis for cost-utility analysis.

The comparison of benefits, harms, and costs of relevant alternatives is stressed as a necessity for healthcare policy decision making in the European Union (51) as well as in Serbia (52, 53). Our analysis provides an insight into a daily clinical routine and commonly used treatment pathways and synthesizes the data from different sources in order to assess the clinical and economic impact of lifelong MM treatment in Serbia.

5 CONCLUSION

In conclusion, sequential MM treatment with frontline MPV achieves the highest remaining life expectancy for the elderly transplant-ineligible population. This treatment sequence can be considered cost-effective from the Serbian health care perspective if the WTP threshold ranges from EUR 35,000-60,000/LYG.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

Ethical approval was not required as patients were not included in the study.

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RISK FACTORS FOR VOICE PROBLEMS IN PROFESSIONAL ACTORS AND SINGERS

DEJAVNIKI TVEGANJA ZA GLASOVNE TEŽAVE PRI POKLICNIH PEVCIH IN IGRALCIH

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ABSTRACT

Keywords:
risk factors, voice disorders, voice quality

Introduction: The purpose was to determine the incidence of voice disorders in a group of professional actors and singers, to compare the two groups, and to investigate the potential causes of their voice problems.

Methods: 65 actors and 63 singers from professional theatres and choirs were included. The data concerning voice problems, their possible causes, and factors adversely affecting voice quality were obtained through a questionnaire. The results were compared between the groups of professional singers and actors, and between the subgroups of singers and actors both with and without frequent voice problems.

Results: The incidence of frequent voice problems over the entire career in singers and actors was lower than reported in the literature. Professional actors displayed more inappropriate life and vocal habits than the singers. Significant risk factors for voice disorders in singers turned out to be loud speech (p=0.029) and the presence of allergies or asthma (p=0.048). No such significant risk factors were found in actors.

Conslusion: The study confirmed the importance of preventive examination of the vocal tract function before enrolling in studies for an elite voice user. Professional singers and especially actors demonstrated insufficient knowledge of proper voice care. The results suggest that elite voice users require additional information on voice hygiene and occasional professional help from college to the end of career. Speech and language therapists can play a crucial role in such voice care in order to effectively prevent voice problems in elite voice users.

IZVLEČEK

Ključne besede:
rizični faktorji, glasovne motnje, kakovost glasu

Uvod: *Namen raziskave je bil ugotoviti, kako pogosto se pojavljajo glasovne težave v skupini poklicnih igralcev in pevcev, raziskovali smo tudi potencialne vzroke zanje.*

Metode: *Vključili smo 65 poklicnih igralcev in 63 poklicnih pevcev iz profesionalnih gledališč oziroma pevskih zborov in od njih s pomočjo anonimnega vprašalnika dobili podatke o glasovnih težavah in morebitnih vzrokih zanje. Primerjali smo skupini pevcev in igralcev ter podskupini poklicnih pevcev oziroma igralcev s pogostimi glasovnimi težavami in brez njih.*

Rezultati: *Pojavnost pogostih glasovnih težav v celotni karieri je bila pri pevcih in igralcih nižja kot v drugih podobnih raziskavah. Izkazalo se je, da imajo poklicni igralci pomembno več neprimernih govornih navad ter negativnih dejavnikov za glas kot poklicni pevci. Kot pomembna rizična dejavnika za pogoste glasovne težave sta se pri pevcih izkazala glasen govor (p = 0,029) in prisotnost alergij (p = 0,048). Pri igralcih nismo našli nobenega pomembnega dejavnika tveganja za glasovne težave.*

Zaključek: *Rezultati raziskave so potrdili pomen preventivnega pregleda funkcije vokalnega trakta pred začetkom študija za poklic elitnega uporabnika glasu. Poklicni pevci in še posebno poklicni igralci so pokazali preslabo poznavanje skrbi za glas. Rezultati raziskave kažejo, da bi tako poklicni pevci kot igralci tudi v času študija in svoje poklicne poti potrebovali dodatne informacije o skrbi za glas ter občasne usmerjene preglede. Prav logoped bi lahko imel ključno vlogo v vseživljenjski skrbi za glas in preprečevanje glasovnih težav pri elitnih glasovnih uporabnikih.*

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1 INTRODUCTION

In modern societies, about one third of the labour force works in professions in which one's voice is the primary tool. Voice problems are common throughout the general population, but they are even more common in professions which require prolonged voice use such as talking in surroundings with background noise, situations where there is a great distance between the speaker and the listener, poor room acoustics, a lack of adequate equipment such as voice amplifiers, etc (1).

Professional actors and singers perform a profession that requires a great vocal load and good voice quality at the same time. At work, they expose their vocal tract to various risk factors, which are more likely to cause voice problems. It is to be expected that frequent voice problems can jeopardise their professional careers. Therefore, they are legitimately classified among elite voice users as proposed by Koufman and Isaacson (2).

Singers and actors are among the most frequent visitors of voice clinics. In Boston, it was established that subjects working in arts and entertainment have the greatest relative risk for voice disorders requiring special care in a tertiary laryngological centre among all the patients' occupations (3).

Only a few surveys on the incidence of voice disorders in singers and actors have been performed. A systematic review and meta-analysis was conducted in order to find the incidence of self-reported voice problems in singers. The overall prevalence of self-reported dysphonia in singers was 46.09% (95% confidence interval: 38.16-54.12), with an incidence of 40.53% in classical singers (4).

Goulart and Vilanova conducted a survey in a group of professional actors on the occurrence of voice problems during their everyday vocal load. Thirty-five percent of the included actors reported voice problems, with 16% reporting problems since the beginning of their professional careers (5).

In Slovenia, candidates for the study of classical solo singing and (drama) acting must pass a phoniatric ear, nose and throat examination in order to prove that their vocal tracts are healthy and capable of the great vocal load required for their future occupation. The future actors also have a speech therapist's assessment of both speech and articulation before being accepted into the study programme. Therefore, future professional singers and actors must prove that they have healthy vocal tracts before their enrolment in the study programmes for occupations that involve a great vocal load and demand for high voice quality (6). There have been no studies on the prevalence of voice problems in elite voice users in Slovenia. The purpose of the study was to determine how frequently professional actors and singers report their voice problems, to compare the two groups in regards to voice problems, and to identify the risk factors for their voice problems.

2 METHODS

Only professional actors and singers were included in the study. One hundred and thirty questionnaires were sent to the 5 largest professional theatres in Slovenia and 126 questionnaires to singers in the two largest professional choirs in Ljubljana.

The data on voice problems of professional actors and singers and their possible causes was obtained through this anonymous questionnaire. The questionnaire was similar to the one used for future (dramatic) acting and solo singing students during their phoniatric examinations, which are administered before they can be accepted to their selected study programmes. The questions sought information on age, gender, length of career, daily vocal load, voice rest during voice problems, vocal habits (speaking loudly, shouting frequently and fast speaking rate), factors affecting voice quality (gastroesophageal reflux, frequent throat clearing, allergies and asthma, smoking). All of the questionnaires that were returned were included in the study. In order to establish the prevalence of the voice problems of these elite voice users over different time periods, the professional singers and actors were asked about their voice problems during their studies, over the last year, and throughout their careers. Recurrent voice problems over the entire career with an impact on working ability manifesting more than three times per year were considered "frequent voice problems". They also detailed their opinion of the reasons for their voice problems.

The results of the questionnaires obtained from the professional singers were compared to the results of the professional actors. In order to identify the factors causing voice problems, data on vocal load, vocal habits and certain factors influencing voice quality in a subgroup of singers and actors with frequent voice problems over the entire career was compared to data from those with infrequent or no voice problems.

The data in the completed forms was statistically analysed using the x^2 test, the Fisher's exact test, the t-test, and the Mann-Whitney test (in the case of non-normal arrangement of the data) included in the programme package SPSS 20.0 (SPSS Inc., Chicago, USA). All the statistical tests were two-sided and a p-value of 0.05 was considered to be statistically significant.

3 RESULTS

Of the 130 questionnaires distributed to professional theatres in Slovenia, a total of 65 (50%) questionnaires were returned. Out of 126 questionnaires sent to professional choirs, we received 63 (50%). Thus, 128 subjects were included in our study: 65 professional actors (27 females, 38 males; mean age 43.03 years; SD 11.93 years) and 63 professional singers (32 females, 31 males; mean age 45.05 years; SD 11.52 years) There were no statistical differences between the singers and the actors regarding age (t-test, p=0.557) and gender (Fisher exact test, p=0.294).

All included questionnaires were at least 90% completed. Professional actors had worked in their occupation between 1 and 47 years (mean 19.66 years; SD 12.19 years) and professional singers between 1 and 39 years (mean 18.83 years; SD 10.53 years). There were no significant differences between the groups regarding length of career (Mann-Whitney test, p=0.679). Professional actors reported from 2 -16 hours of daily vocal load, while singers' daily vocal load ranged from 1 -7 hours.

The great majority of actors and singers had voice problems following the completion of vocal loading tasks while suffering from an upper respiratory tract infection. Thirteen singers and thirteen actors did not specify the cause of their voice problems. All these elite voice users did not report frequent voice problems or reported no problems. The groups did not differ in regards to the incidence of voice problems in any of the periods of their professional life or in the cause of their voice disorders (Table 1).

Table 1. Frequency and causes of voice problems in professional singers and actors during their studies, over the last year and over their entire careers. Fisher's exact test and chi-squared test were used for statistical analysis. (URI = upper respiratory tract infection).

Paramater	Professional Singers N=63	Professional Actors N=65	P
Frequent voice problems during their studies	1	1	1.000
Frequent voice problems in the last year	9	5	0.265
Frequent voice problems in their careers	13	8	0.241
Cause of voice problems			
• URI	5	7	
• vocal load	8	6	0.729
• URI + vocal load	37	39	

There were some significant differences between professional actors and professional singers regarding diseases and vocal and other habits influencing voice quality. Professional actors reported speaking loudly more frequently as well as a fast speaking rate, shouting and smoking. At least one inappropriate vocal habit (speaking loudly, fast speaking rate, frequent shouting) was reported in 31 singers and 59 actors (Fisher exact test, p=0.000). On the other hand, professional singers more frequently reported typical symptoms of gastroesophageal reflux (heartburn and/or regurgitation) (Table 2).

Table 2. Parameters affecting voice quality in professional singers and in professional actors. Fisher's exact test and Mann-Whitney test were used for statistical analysis.

Paramater	Professional Singers N=63	Professional Actors N=65	P
Smoking	11	33	0.000
Symptoms of gastroesophageal reflux	26	15	0.037
Frequent throat clearing	27	33	0.376
Allergies, asthma	19	10	0.058
Speaking loudly	26	57	0.000
Shouting frequently	4	29	0.000
Fast speaking rate	16	44	0.000
Voice rest during voice problems	34	3	0.254
Vocal load / hours per day (mean/standard deviation)	6.25 / 2.44	4.23 / 1.20	0.000
Vocal load during spare time	21	19	0.704

Comparing professional singers with frequent voice problems during their career to those without frequent voice problems revealed significant differences in two parameters. The professional singers with frequent voice problems reported more often loud speech and allergy problems than the singers without frequent voice problems (Table 3).

Table 3. Parameters affecting voice quality in professional singers with frequent voice problems in their careers and in professional singers without frequent voice problems. Fisher's exact test, t-test, and Mann-Whitney test were used for statistical analysis.

Paramater	Professional Singers With Frequent Voice Problems N=13	Professional Singers Without Frequent Voice Problems N=50	P
Age in years (mean / standard deviation)	44.38 / 9.13	45.22 / 12.14	0.818
Length of career in years (mean / standard deviation)	20.00 / 8.82	18.52 / 10.99	0.655
Vocal load in h/day (mean / standard deviation)	4.46 / 1.18	4.16 / 1.21	0.430
Smoking	4	7	0.216
Symptoms of gastroesophageal reflux	8	18	0.216
Frequent throat clearing	7	20	0.531
Allergies, asthma	7	12	0.048
Speaking loudly	9	17	0.029
Shouting frequently	1	3	1.000
Fast speaking rate	6	10	0.075
Vocal load during spare time	6	15	0.329

Comparing the group of professional actors with frequent voice problems (n=8) to the group of professional actors without frequent voice problems (n=56) did not offer up any particular differences (Table 4). One of the actors did not provide an answer about frequent voice problems.

Table 4. Parameters affecting voice quality in professional actors with frequent voice problems in their careers and in professional actors without frequent voice problems. Fisher's exact test, t-test, and Mann-Whitney test were used for statistical analysis.

Paramater	Professional Actors With Frequent Voice Problems N=8	Professional Actors Without Frequent Voice Problems N=56	P
Age in years (mean / standard deviation)	44.38 / 9.13	45.22 / 12.14	0.818
Length of career in years (mean / standard deviation)	20.00 / 8.82	18.52 / 10.99	0.655
Vocal load in h/day (mean / standard deviation)	4.46 / 1.18	4.16 / 1.21	0.430
Smoking	6	27	0.259
Symptoms of gastroesophageal reflux	2	12	1.000
Frequent throat clearing	5	27	0.708
Allergies, asthma	0	10	0.337
Speaking loudly	7	49	1.000
Shouting frequently	4	25	1.000
Fast speaking rate	4	40	0.244
Vocal load during spare time	2	17	1.000

4 DISCUSSION

Professional actors and singers depend on their voices to pursue their profession. They need healthy vocal tracts with great endurance to manage the great vocal load at work. In Slovenia, only such candidates are enrolled in study programmes as elite vocal users. In the phoniatric examination performed prior to their acceptance (solo singing or drama acting), they must demonstrate both normal anatomy and function in their vocal tract (6). In the event that they report vocal and life style habits that may jeopardize their voice quality over the course of their careers, they receive information on proper voice care. They are also informed of the fact that maintaining harmful habits and an improper life style during their careers can lead to serious voice problems and can even endanger their career in the long run.

Our study did not reveal frequent voice problems in a considerable section of the included professional singers and actors. Only 12.3% of actors and 20.6% of singers admitted having recurrent voice problems that prevent their performance more than three times per year in their career. The data from the literature shows voice problems occurring more often than in our research, although the study design was not exactly the same in other studies. Goulart and Vilanova reported 35% of the actors included in their study with voice problems in the daily voice load. In 16% of actors, the problems started even at the beginning of their careers (5). In classical choir singers or professional opera choristers, self-reported voice problems were detected in 38% - 43.59% (7, 8). We suppose that one of the important reasons behind the small percentage of professional actors and singers with voice problems in our study is the preventive phoniatric examination and, in the case of future actors, also the speech therapist's assessment before enrolment in the study of drama acting or solo singing in Slovenia. Consequently, only one actor and one singer from our study had frequent voice problems during their study period and also later in his/her career. On the other hand, at the time of their study, the vocal load was not as extensive as later on in their careers, therefore voice problems become more evident after one starts working in an occupation with great vocal load. It is possible that other studies included singers and actors who did not conclude a proper professional study programme, and did not have to demonstrate having a healthy and well-functioning vocal tract. The data for this assumption are lacking in the literature.

Another piece of evidence for the correct selection of candidates as future actors is the fact that only 12.5% of actors had frequent voice problems in their careers in spite of the fact that half of them were smokers, and almost all of them had improper voice habits. There were no significant differences between the singers and the actors regarding frequent voice problems in their educational period, in the last year, and over their entire career. On the contrary, the actors' daily vocal load was significantly greater than the vocal load of the singers.

Another reason for the small percentage of singers with frequent recurrent voice problems in our study could be their style of singing, and proper education. In a group of 100 healthy singers, Koufman et al tried to find out whether factors such as gender, professional or amateur singing, and style of singing influence vocal muscles' tension. The lowest incidence of excessive muscle tension was observed in professional singers, singers with formal singing education, and in singers of classical opera or choir singing (9). The singers in our study were members of two professional choirs with a classical singing repertoire. A formal education in singing training is a necessity for employment in a professional choir. Pestana et al. reported in his meta-analysis that the overall prevalence of self-reported dysphonia in singers was 46.09%, with an incidence of 40.53% in classical singers. In their systematic review and meta-analysis, the authors stressed a considerable heterogeneity of the reviewed studies including lacking data on the professional education of the participants of the study (4).

The unhealthy vocal and other behaviour noticed among elite voice users in our study is worrying because it can result in benign vocal fold lesions (10). The presence of inappropriate speech habits in almost all included actors (90.8%) is understandable, since their work often requires loud speech, fast talking, crying, shouting, singing and dancing at the same time (11). The nature of the work of professional choir singers does not demand other harmful speech habits but voice overload is possible. Nevertheless, professional singers expressed inappropriate speaking habits at a rate of almost 50%. Speaking loudly was also one of the risk factors for frequent voice disorders during their career of professional singer. On the other hand, other studies do not report such a high incidence of voice abuse as ours. One of the published voice profile analyses of 16 solo singers revealed voice abuse only in 6% (12). It is possible that one of the reasons for our unfavourable results about considering proper voice care is a lack of information on vocal hygiene during the career. Candidates for elite vocal performers receive information on possible improper vocal and lifestyle habits that can influence their voice quality and their careers only at the time of phoniatric examination before being accepted into the academy. Later on, during their studies, they have courses on singing techniques, rhetoric issues and performing, but no lectures on the physiology of phonation, voice disorders, voice care and vocal hygiene. We suppose that supplementing a curriculum for solo singers and actors with such information would be beneficial for the voice health of these elite vocal performers.

The professional singers in our study reported typical symptoms of gastroesophageal reflux more often than the actors. We can find the results of frequent gastroesophageal reflux in singers in the literature (13-15). Even in recent papers, opera singers and solo singers reported heartburn, regurgitation, coughing and hoarseness more often than the controls (16). The reason is probably the increased intraabdominal pressure during singing which causes the retrograde flow of gastric content up the oesophagus to the level of the larynx and pharynx (17). The occupation of a professional singer or actor combines a lifestyle with working late, inappropriate nutritional habits, late meals in the evening or even at night and a lot of stress. All these are risk factors that influence acid reflux. It is also possible that professional singers report LPR more often because of their need for a high voice quality and are more watchful in terms of voice changes (18). In any event, allergy and asthma, but not gastroesophageal reflux, were found to be risk factors for frequent voice problems in singers. Professional singers should be aware of a possible negative influence of these diseases on their voice quality, and should seek early medical help when having such health problems.

In the group of professional actors, we need to highlight the problem of smoking, as almost half of them reported smoking. Other studies also proved smoking to be a problem in the majority of actors (19, 20). Another research study showed that the percentage of improper habits (smoking, late meals in the evening, vocal abuse), regardless of voice education and getting information about voice hygiene, remains high (21). Smoking is not as frequent among singers as among actors, as was also shown in our study (17% of singers are smokers). Among Broadway musical theatre performers, tobacco use was reported by only 10.4% of them (22). The low percentage of smokers among singers was found also in a study of Timmerman (12).

Professional singers more often considered voice rest during voice problems (54%) than professional actors (46%). It is possible that they are more sensitive to the quality of their voices because, in singing, even a slight alteration of the voice can influence one's performance capabilities. On the other hand, there are some reports of more abusive voice use during hoarseness in singers as well. A study by Boominathan showed that only 22% of singers considered voice rest during voice problems (23).

A person having a voice problem or getting over an acute respiratory infection, should reduce voice load to avoid the development of a functional voice disorder (24). Even though professional singers and actors are aware of the necessity for voice rest during voice problems, they cannot always fully consider it due to the nature of their work. The results of our study showed that a great majority of the participants had voice problems following the completion of vocal loading tasks while suffering from a respiratory infection.

In order to further reduce inappropriate lifestyle issues, improper habits and speech abuse, the managers of theatres and professional choirs should organize occasional workshops for their employees, where they will be able to renew their knowledge of the anatomy and functioning of the vocal tract, the causes of voice problems and methods of preventing problems. Such knowledge can help them to avoid the occurrence of voice disorders. In this area of lifelong education for elite voice users, the speech therapist can play a very important role, not only with information on the influence of harmful factors on the voice, but also with practical instructions for the most rational voice use and the correct method of phonation and modulation of phonation when performing and talking.

5 LIMITATIONS OF THE STUDY

One of the limitations of the study is the subjective perception of voice problems reported in the questionnaire. In the case of additional phoniatric and speech pathologist examination of the included professional singers and actors, a better insight would be given into the actual state of the voice apparatus of elite voice users in Slovenia.

On the basis of the questionnaire used we did not obtain information about the exact time of appearance of voice problems. Therefore we cannot exclude the possibility that ageing of the voice or hormonal problems influenced voice quality in the participants.

Another limitation of the study is the small number of participants. In the evaluation of this factor, it should be noted that there are only a few professional choirs and only eleven professional theatres in Slovenia.

6 CONCLUSION

The present study among elite voice users in Slovenia confirmed the importance of preventive examinations before enrolment in the study of drama acting and solo singing. According to the results, professional actors and singers have insufficient knowledge or disrespect of proper voice care. Worse voice behaviour was demonstrated by actors, whose percentage of inappropriate speech and smoking habits was far too high for a representative of elite voice users. Speaking loudly and having an allergy or asthma proved to be risk factors for frequent voice problems in professional singers. Professional singers and actors should have additional information on the risk factors that impair their voice quality as well as occasional phoniatric or speech and language therapist examinations.

Speech and language therapists can play a crucial role in lifelong learning and monitoring elite voice users, thereby effectively preventing voice problems that might render them unable to pursue their profession.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

This study was approved by the Republic of Slovenia

National Medical Ethics Committee (document No. 0120-334/2015-2).

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PHYSICIANS' ATTITUDES TOWARD ADOLESCENT CONFIDENTIALITY SERVICES: SCALE DEVELOPMENT AND VALIDATION

ODNOS ZDRAVNIKOV DO ZAUPNOSTI STORITEV PRI MLADOSTNIKIH: OBLIKOVANJE LESTVICE IN PREVERJANJE

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ABSTRACT

Introduction: Confidentiality is one of the oldest ethical principles in healthcare. However, confidentiality in adolescent healthcare is not a universally-accepted doctrine among scholars. The ethical acceptability of confidential services in adolescents' healthcare is based on perceptions of adolescent maturity and an appreciation of its importance to adolescents' access and utilization of healthcare services. Despite legal policies that promote adolescents' rights, physicians' attitudes toward adolescent confidentiality can be a determining factor in their ultimate decision to protect adolescents' confidentiality.

Method: A new Attitude towards Adolescent Confidentiality Scale was developed based on the results of a qualitative interview study. This new instrument was administered to a sample of 152 physicians working at school pediatric and gynecology departments in 13 primary healthcare institutions in Belgrade. Principal component analysis was applied to determine the main components of the scale. Reliability was assessed by calculating Cronbach alpha and mean inter-item correlations.

Results: Psychometric analysis of the final 19-item version of the scale showed a high level of reliability (Cronbach alpha of 0.83). Principal component analysis showed four components, which present subscales of the instrument: Confidentiality in clinical situation, Iimportance of confidentiality, Adolescent maturity, and Communication with parents.

Conclusions: The instrument showed satisfactory levels of reliability and validity. The results of the scale dissemination may be a valuable tool for needs assessment for future educational interventions and training programs that will raise physicians' awareness of the importance of adolescent confidentiality.

Keywords:
adolescent, confidentiality, attitude of health personnel, psychometrics, primary healthcare, surveys and questionnaires

IZVLEČEK

Uvod: *Zaupnost je eno najstarejših etičnih načel v zdravstvenem varstvu. Vendar zaupnost pri zdravstvenem varstvu mladostnikov med strokovnjaki ni splošno sprejeta doktrina. Etična sprejemljivost zaupnih storitev pri zdravstvenem varstvu mladostnikov temelji na dojemanju zrelosti mladostnikov in priznavanju njene pomembnosti za dostop mladostnikov do storitev zdravstvenega varstva in njihovo uporabo. Kljub pravnim politikam, ki spodbujajo pravice mladostnikov, je lahko odnos zdravnikov do zaupnosti mladostnikov odločilni dejavnik pri končni odločitvi za zaščito zaupnosti mladostnikov.*

Metoda: *Na podlagi rezultatov kvalitativne raziskave z intervjuji smo oblikovali novo lestvico odnosa do zaupnosti mladostnikov. Novi instrument smo izvedli v vzorcu 152 zdravnikov, zaposlenih v pediatričnih in ginekoloških oddelkih v 13 ustanovah primarnega zdravstvenega varstva v Beogradu. Za določitev glavnih komponent lestvice smo opravili analizo glavnih komponent. Zanesljivost smo ocenili z izračunom koeficienta Cronbach alfa in povprečnih korelacij med postavkami.*

Rezultati: *Rezultati psihometrične analize končne različice lestvice z 19 spremenljivkami so pokazali visoko raven zanesljivosti (koeficient Cronbach alfa 0,83). Analiza glavnih komponent je pokazala štiri komponente, ki predstavljajo pomožne lestvice instrumenta: zaupnost v posebnih kliničnih stanjih, pomembnost zaupnosti pri zdravstvenem varstvu mladostnikov, zrelost mladostnikov in starševska odgovornost ter komunikacija in skrivnosti med mladostniki in starši.*

Sklepi: *Instrument je pokazal zadovoljive ravni zanesljivosti in veljavnosti. Rezultati razširjanja lestvice so lahko dragoceno orodje za oceno potreb pri prihodnjih izobraževalnih intervencijah in programih usposabljanja, ki bodo zdravnike ozaveščali o pomembnosti zaupnosti mladostnikov.*

Ključne besede:
mladostnik, zaupnost, odnos zdravstvenega osebja, psihometrija, primarno zdravstveno varstvo, ankete in vprašalniki

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1 INTRODUCTION

Confidentiality – the obligation of a healthcare professional not to disclose the information obtained within a confidential relationship to anyone without the patient's permission – is one of the oldest ethical principles in healthcare (1). However, confidentiality in adolescent healthcare is not a universally-accepted doctrine among physicians (2). The acceptability of providing confidential services in adolescent healthcare depends on physicians' perception of adolescent maturity and apprehension of the importance of confidentiality with respect to adolescents' access and utilization of healthcare services. A widely accepted psychological study from 1982 demonstrated that most adolescents reach the formal operational stage of cognitive development by mid-adolescence, and these studies concluded that adolescents' decision-making capacity is much like that of adults (3). However, more recent psychology and neuroscience findings suggest that the social and emotional competences of adolescents (such as impulse control and ability to appreciate long-term consequences) are still developing, rendering adolescents' judgments immature and susceptible to risky behavior (4). These findings led some to conclude that adolescents' immature judgments impede them from making adequate healthcare decisions, and decisional authority should be shifted back to parents (5, 6). This negative assessment of the maturity of adolescent judgment represents the main argument against confidentiality policies (5, 6). However, empirical data suggest that adolescents would forgo healthcare when confidentiality is not guaranteed, implying that confidentiality is a key factor in adolescents' utilization of healthcare (7, 8). These findings can be explained by psychoanalytic theories which emphasize separation from parents as a key step to accomplish individuation processes (9, 10). The need to keep secrets from parents is associated with the process of separation, and this is very common in older adolescents on the path to emotional autonomy and independence (11).

Despite contradictory views on the issue of adolescents' rights (12), many European countries have implemented legal regulations that allow confidential services for minors of a certain age, or minors who possess adequate decision-making capacity (13). European countries lack evidence regarding physicians' practice of respect for confidentiality in adolescent healthcare. Studies from Lithuania, Belgium and Spain show that many physicians are reluctant to spend time alone with adolescents, and that they usually tend to inform parents without asking adolescents for permission (14-16). Physicians' attitudes can be a determining factor in their final decision to protect adolescents' confidentiality, despite legal policy that promotes adolescents' rights (14-16). Understanding the attitudes and beliefs of physicians who provide healthcare to adolescents may help tailor policies for specific socio-cultural milieus. Although several studies aimed to explore physicians' attitudes toward the adolescent right to confidentiality in healthcare (14-19), to our knowledge no psychometrically validated instrument was developed and implemented.

The aim of this study was to develop and validate a comprehensive instrument for measuring physicians' attitudes related to the issue of adolescent confidentiality with an emphasis on reproductive healthcare. A psychometrically valid instrument could be used to evaluate the physician's sensitivity and readiness to promote adolescent healthcare by respecting adolescents' confidentiality rights. The results of such evaluations would represent valuable information for enhancing the education and training of physicians.

2 METHODS

2.1 Study Design and Sampling

A cross-sectional survey was conducted in the period from November 2017 to August 2018. Data were collected from a sample of physicians working at school pediatric departments and gynecology departments (from the age of 15 adolescent girls are referred to the gynecology department at the primary care level) in 13 primary healthcare institutions in the territory of Belgrade, Serbia. There are 16 primary healthcare institutions in Belgrade, but 3 institutions declined to participate in the study. We chose to conduct our study at the primary healthcare level because it has the main role in health prevention and promotion. Primary care physicians are in a position to establish relationships of trust with adolescent patients, and to influence them to seek advice and care for sensitive health issues such as sexuality and reproductive care. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, University of Belgrade (approval number: 29/ VI-1).

2.2 Data Collection

Participants were approached at their work offices by the principal researcher after receiving approval from the heads of the departments. Questionnaires were self-administered and anonymous. The survey took approximately 10 minutes to complete. All participants signed informed consent sheets prior to the survey.

2.3 Instrument Development

The items developed for the scale were based on a qualitative interview study exploring primary care physicians' knowledge, beliefs, attitudes and experiences regarding their legal obligation to protect adolescents' confidentiality in healthcare (20). The qualitative study included 12 interviews with primary care pediatricians

and gynecologists. Some of the categories obtained by inductive qualitative content analysis were the basis for the key constructs in the study of confidentiality attitudes and main domains in this survey's questionnaire. Categories that served as a basis for questionnaire development were: respect for the person, condition for trust, clinical situations where confidentiality is most important, parent-adolescent sexuality communication, decision-making capacity of adolescents, and parental responsibility. In accordance with the relevant literature on adolescent confidentiality, it was expected that appreciation of the main reasons for confidentiality (respect for autonomy and establishing doctor-patient trust), a positive attitude toward confidentiality in specific clinical situations, positive views on the maturity of adolescent judgment, and recognition of the adolescent's need to keep their reproductive and sexual health problems private from parents, would contribute to an overall positive attitude toward respecting adolescents' right to confidentiality in reproductive healthcare (21, 22). Items of the questionnaire were partially formulated employing phraseology from physicians interviewed to generate a richer understanding of target respondents.

Content validity of the instrument was established in the following steps. First, the main concepts were defined based on a literature review and the results of the qualitative study. Second, a panel of 5 experts in a content domain (one expert from each of the fields of psychology and public health) were sent a questionnaire and were invited to evaluate the items. Experts were presented with constructs and asked to match items with a corresponding construct. They confirmed that the instrument items were relevant, accurate, and adequately represented the theoretical constructs that the questionnaire was designed to measure. Third, the questionnaire was piloted in a group of 10 primary healthcare physicians to assess the intelligibility of the questions. The instrument was suitable for all participants, so no adjustments were necessary.

The final version of The Attitudes toward Adolescent Confidentiality Scale consisted of 20 statements (items of the scale) which represent various constructs related to the right to confidentiality in adolescent healthcare, evaluated on a 5-point agreement scale (from 1 "Strongly disagree" to 5 "Strongly agree") (Table 1). Reverse coding was applied for negatively connoted statements (A8, A9, A10 and A20 in the Table 1.). The attitude score was calculated by summation of points for each item.

2.4 Psychometric Evaluation of the Instrument

Principal component analysis with varimax rotation was applied to determine the main components (factors) representing constructs that the scale is supposed to investigate, and items with factor loadings less than 0.3 were removed. Because no validated scales of similar constructs were found, construct validity was assessed by calculating the correlation coefficients between each pair of subscale scores. The Kaiser-Meer-Olkin measure of sampling adequacy and Bartlett test of sphericity were calculated.

The reliability of the scale was assessed by calculating the Cronbach alpha coefficients and mean inter-item correlations. Cronbach alpha was calculated for each factor, too. Test-retest reliability analysis was impractical because Serbian primary healthcare physicians were reluctant to complete the survey again due to the ongoing significant work overload in Serbia. Furthermore, a split-half reliability test was performed and Spearman-Brown coefficient calculated.

Descriptive statistics were applied to determine the sample characteristics. Mean scores for the total scale and sub-scales were calculated. Mean scores for individual items of the scale were calculated to assess the importance our respondents attach to particular constructs related to adolescent confidentiality (23). In all analyses $p < 0.05$ was considered statistically significant. All analyses were performed using the statistical program IBM SPSS Statistics 20 (SPSS).

3 RESULTS

The total number of physicians who completed the survey was 152 (78 from the school pediatric department and 74 from the gynecology department), reflecting a response rate of 80.0% (the total number of physicians working at the school pediatrics and gynecology departments during the survey period was 190). The majority of participants were female (83.6%), with the average age in the sample being 50.8±9 years.

The Kaiser–Meyer–Olkin measure value (KMO=0.77) and the Bartlett's test of sphericity result ($x2=1320.80$, $p<0.001$) indicated the adequacy of the data for factor analysis. Principal component analysis with varimax rotation of all factors that achieved eigenvalues greater than 1 was performed for the 20-item scale. This resulted in 6 factors with eigenvalues ranging from 5.19 to 1.08, accounting for 66.63% of the item variance. However, the scree plot suggested a four-factor solution (Figure 1), so additional principal component analysis was performed with four fixed factors, accounting for 54.87% of the item variance. Of the 20 total items, one did not show significant factor loading (24), and was excluded from the scale (A20 in Table 1-The family should be involved in making important decisions regarding health of all its members). Factor loadings for 20 items after varimax rotation are presented in Table 1.

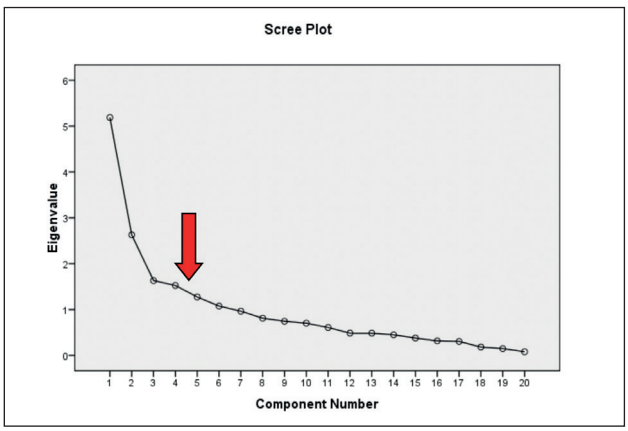

Figure 1. Inflection on the scree plot justifying the 4-factor solution.

Table 1. Factor loadings after varimax rotation and Kronbach alphas for the final 19-item scale.

Scale items	Factor I	Factor II	Factor III	Factor IV	Kronbach alpha if item was deleted
A1- Adolescent won't share sensitive information regarding sexual and reproductive health with physician if they fear that parents might find out.				0.692	0.836
A2- With confidentiality guaranteed adolescent patients will more likely seek medical help, speak openly about risky behaviors and continue with the treatment of reproductive health issues.		0.616			0.838
A3- Confidentiality is important for establishing a relationship of trust between the physician and the adolescent patient.		0.843			0.833
A4- By respecting confidentiality a physician shows respect for the adolescent patient's person.		0.904			0.831
A5-Confidentiality is the ethical duty of every physician.		0.822			0.833
A6- A 15-year-old adolescent is capable of independent decision-making.			0.729		0.826
A7- A 15-year-old adolescent is capable of independently consenting to a medical procedure.			0.722		0.828
A8- Adolescents are not able to adequately predict the long-term consequences of their decisions.			0.461		0.842
A9- Adolescents don't possess adequate competence for decision-making.			0.531		0.843
A10- Parents are legally responsible for their children until the age of majority, therefore they have a right to be informed about all facts regarding their child's health.			0.546		0.839
A11- Adolescents communicate poorly with their parents about sexuality and reproductive health problems.				0.682	0.839
A12- Parents have difficulty accepting their adolescent children's emerging sexuality.				0.673	0.841
A13- Adolescents should be provided confidential counseling on sexual and reproductive health.	0.344				0.836
A14- Adolescents should be provided confidential contraceptive pill prescriptions.	0.560				0.825
A15-Adolescents should be provided confidential diagnostics of STDs.	0.882				0.819
A16-Adolescents should be provided confidential treatment of STDs.	0.909				0.816
A17-Adolescents should be provided confidential pregnancy testing and prenatal care.	0.819				0.814
A18- Adolescents should be provided confidential abortion service.	0.745				0.818
A19- Adolescents should be provided confidential treatment of ovarian cysts.	0.649				0.830
A20- The family should be involved in making important decisions regarding the health of all its members.*	0.002	0.228	0.288	0.287	

*The item did not show significant factor loadings greater than 0.3 and was excluded from the final scale.
Factor I – Confidentiality in specific situations, Factor II – Importance of confidentiality,
Factor III – Adolescent maturity, Factor IV – Communication with parents

The items that cluster around the same factors suggest that factor 1 represents Confidentiality in specific situations, factor 2 represents the Importance of confidentiality, factor 3 represents Adolescent maturity, and factor 4 represents Communication with parents. Table 2 shows the correlations among the four subscale scores.

Because subscales measure different constructs related to the issue of adolescent confidentiality, correlations between subscales were mostly significant but moderate, as expected (Pearson correlation coefficients ranging from 0.07 to 0.42), implying that subscales are related but not redundant. Confidentiality in specific situations and the Importance of confidentiality were significantly associated with all other subscales. The only non-significant correlation was between the third (Adolescent maturity) and the fourth (Communication with parents) scales.

Table 2. Correlations among 4 subscale scores.

	1	2	3
2	.24**		
3	.42**	.17*	
4	.20*	.35**	.07

*Correlation is significant at the 0.05 level
**Correlation is significant at the 0.01 level
1 – Confidentiality in clinical situations
2 – Importance of confidentiality
3 – Adolescent maturity
4 – Communication with parents

Reliability for the final 19-item version of the scale was assessed. Cronbach alpha for the overall scale was 0.84. The mean inter-item correlation for 19 items was 0.20, which falls within the acceptable range of 0.15-0.50 (25). The Spearman-Brown coefficient associated with the items was 0.895, which is acceptable, confirming the scale's reliability.

Table 3 lists four subscales with their labels, number of items, average scores and Cronbach alphas. The first two factors had Cronbach alphas that exceeded 0.80. The third factor (Adolescent maturity) had a Cronbach alpha of 0.64, which is considered satisfactory in exploratory research (26), while the fourth factor had an alpha of 0.58 (Communication with parents). Since the fourth factor had only three items, its reliability was additionally tested by calculating mean inter-item correlation, which was within the acceptable range (0.33).

The average total score on the attitude scale in the sample was 71.18±10.742, belonging to the middle tertile of the score range; this can be interpreted as a moderate attitude toward confidentiality in adolescent healthcare. The average scores for subscales are presented in Table 3. For the first and fourth subscale the average scores also belong to the middle tertile, reflecting a moderate attitude, while for the third subscale (Adolescent maturity) the average score belongs to the lower tertile, reflecting a negative attitude. For the second subscale (Importance of confidentiality) the average score belongs to the higher tertile, reflecting a highly positive attitude.

Mean scores for individual items of the scale are presented in Table 4. The highest scores were observed for all items in the Importance of confidentiality subscale, implying the respondents perceived the importance of their ethical duty. Moreover, confidentiality in counseling on sexual and reproductive health was perceived as highly important, too. However, the lowest scores were observed for items from the Adolescent maturity subscale (A6, A7, A8 and A10 at the Table 4.).

Table 3. Characteristics of 4 subscales.

Subscale	Number of items	Mean ±SD (Range)	Tertile	Cronbach alpha
1. Confidentiality in specific situations	7	23.51±6.725 (7-35)	Middle	0.863
2. Importance of confidentiality	4	18.26±2.664 (4-20)	Third	0.830
3. Adolescent maturity	5	11.59±2.993 (5-25)	First	0.639
4. Communication with parents	3	10.74±2.038 (3-15)	Middle	0.584

Table 4. Respondents' evaluations of the The Attitudes toward Adolescent Confidentiality Scale items.

Item	Mean score ± Standard deviation	Min-Max	Skewness	Kurtosis
A1- Adolescent won't share sensitive information regarding sexual and reproductive health with physician if they fear that parents might find out.	3.65±1.07	1-5	-0.594	-0.244
A2- With confidentiality guaranteed adolescent patients will more likely seek medical help, speak openly about risky behaviors and continue with the treatment of reproductive health issues.	4.24±0.97	1-5	-1.666	2.693
A3- Confidentiality is important for establishing a relationship of trust between the physician and the adolescent patient.	4.65±0.76	1-5	-2.941	10.091
A4- By respecting confidentiality a physician shows respect for the adolescent patient's person.	4.63±0.79	1-5	-3.008	10.275
A5-Confidentiality is the ethical duty of every physician.	4.74±0.72	1-5	-3.612	14.267
A6- A 15-year-old adolescent is capable of independent decision-making.	2.47±098	1-5	0.202	-0.226
A7- A 15-year-old adolescent is capable of independently consenting to a medical procedure.	2.31±1.01	1-5	0.319	-0.650
A8- Adolescents are not able to adequately predict the long-term consequences of their decisions.	1.93±0.82	1-5	0.782	0.737
A9- Adolescents don't possess adequate competence for decision-making.	3.05±0.89	1-5	0.025	0.119
A10- Parents are legally responsible for their children until the age of majority, therefore they have a right to be informed about all facts regarding their child's health.	1.84±0.97	1-5	0.905	0.090
A11- Adolescents communicate poorly with their parents about sexuality and reproductive health problems.	3.64±0.79	1-5	-0.384	0.212
A12- Parents have difficulty accepting their adolescent children's emerging sexuality.	3.45±0.87	1-5	-0.391	0.126
A13- Adolescents should be provided confidential counseling on sexual and reproductive health.	4.47±0.80	1-5	-1.862	4.241
A14- Adolescents should be provided confidential contraceptive pill prescriptions.	3.80±1.22	1-5	-0.795	-0.368
A15-Adolescents should be provided confidential diagnostics of STDs.	3.74±1.29	1-5	-0.677	-0.823
A16-Adolescents should be provided confidential treatment of STDs.	3.59±1.33	1-5	-0.555	-0.962
A17-Adolescents should be provided confidential pregnancy testing and prenatal care.	2.78±1.50	1-5	0.245	-1.315
A18- Adolescents should be provided confidential abortion service.	2.33±1.36	1-5	0.679	-0.733
A19- Adolescents should be provided confidential treatment of ovarian cysts.	2.80±1.46	1-5	0.244	-1.297

3.1 Summary of Factors

The first factor included items related to the attitude of respect for confidentiality in specific clinical situations. Its reliability was very good (Table 3). The mean score on this subscale was moderate, with higher scores for items related to preventive health measures (counseling and contraception) (Table 3). Lower scores were observed on items related to abortion and pregnancy.

The second factor covered items related to the perception of the importance of confidentiality in adolescent healthcare (ethical duty, respect for persons, condition for trust and condition for healthcare service access). This subscale also had very good reliability (Table 3). Respondents' scores on this subscale were the highest scores, indicating they had a positive attitude towards the reasons that support confidentiality policies (Table 3).
The third subscale included items related to the maturity of adolescents and parental responsibility. This subscale had satisfying reliability (Table 3). A negative average attitude was found on this subscale (Table 3).

The fourth factor covered items related to the issues of communication and secrecy between adolescents and parents regarding sexuality and reproductive health. Communication with parents subscale had a Cronbach alpha below the acceptable level (Table 3), but its mean inter-item correlation was sufficient to keep this subscale in the instrument. Further work with developing the

concept of secrecy in the adolescent-parent relationship and adding more items to this subscale are needed to improve this domain of the scale, and only the total score should be used for the time being. Respondents' scores on this subscale were moderate (Table 3).

4 DISCUSSION

4.1 Summary of Main Findings

In this article we describe the development and validation of a research instrument aimed at measuring physicians' attitudes towards adolescent confidentiality in healthcare. This study used a systematic approach to develop the instrument, and thoroughly analyzed the instrument's reliability and validity. The overall reliability of the 19-item Attitudes towards Adolescent Confidentiality Scale was acceptable, showing high consistency of the total scale (Cronbach alpha of 0.83). Principal component analysis showed four components, which present subscales of the instrument: Confidentiality in a specific situation, the Importance of confidentiality, Adolescent maturity, and Communication with parents (Table 3).

The developed scale also showed a satisfying level of construct validity, given that the subscales correlated in expected ways (Table 2). Physicians' higher acceptance of confidentiality in specific medical situations was associated with stronger beliefs that confidentiality is important, as well as with more positive assessments of adolescent maturity and decision-making capacity. Also, higher acceptance of the importance of confidentiality was associated with stronger belief that adolescents keep secrets from parents and do not want parents to find out. As expected, the attitude toward adolescent maturity and parental responsibility was not significantly correlated to recognition of adolescents' need to keep their sexual and reproductive health secret from parents, since those subscales present significantly different constructs. A negative attitude toward the maturity of adolescents' judgment and a positive attitude toward parental authority in healthcare decision-making underlie the strongest arguments against adolescent confidentiality policies in the literature (5, 6). Appreciation of the fact that adolescents would rather forgo needed sensitive healthcare because of the fear that parents might find out led to the formulation of confidentiality policies which aim to increase adolescents' access to healthcare services (27-29).

The surveyed physicians demonstrated a moderate overall attitude toward the adolescent's right to confidentiality in healthcare, which was expected in Serbian physicians, given that the general attitude toward children's rights in the general Serbian population is predominantly negative (30). The moderate attitude reflects physicians' doubts and confusion and suggest that confidentiality protection in adolescent healthcare may not be consistently implemented. This result is in line with the empirical evidence showing that the socio-cultural context strongly influences the implementation of minors' rights (31). In societies with dominant patriarchal cultures, physicians are less inclined to promote children's autonomy in healthcare (32). An inter-cultural comparison of results would be important in future explorations of socio-cultural influences on the implementation of minors' participation rights in healthcare. Empirical evidence from the U.S. shows that despite recommendations and legal requirements, less than half of adolescents aged 15-17 spent some time alone with a physician during a visit (33, 34), implying that the importance of adolescent confidentiality is not universally accepted.

As expected, scores on the subscale Confidentiality in specific situations were higher for items related to preventive health measures (counseling and contraception) (Table 3). Lower scores were observed on items related to abortion and pregnancy, which was expected and consistent with the results of other studies that suggest that a significant number of physicians believe that adolescent pregnancy and abortion should never be kept confidential and parents should be included in making decisions in these situations (18, 35). Respondents' scores on the Importance of confidentiality were the highest scores (Table 3), which is in line with the results of other studies where a majority of physicians agreed with the importance of adolescents' right to confidentiality (18, 35). Despite recognizing its importance, the physicians surveyed inconsistently maintained confidentiality in their practice (18, 35). A negative average attitude was found on the Adolescent maturity subscale, which implies that many physicians disagree with legal regulations that allow 15-year-old patients to independently consent to medical procedures (Table 3). Similar findings were found in a survey by Riley et al., where respondents, although they agreed that confidentiality should be an adolescent's right, were less confident that adolescents possess adequate maturity to independently consent to care for sensitive medical issues (18). Healthcare practitioners often have a patronizing view of adolescent patients, believing they are immature and in need of protection (36). These findings reflect the main dilemma surrounding the issue of confidentiality in adolescent healthcare: Are adolescents mature enough to make sound autonomous decision in healthcare? We argue that this question should be put aside in the field of reproductive health, and the emphasis be put on public health justification that is based on the health benefits of adolescents getting needed medical help. Physicians' negative attitude toward adolescent maturity jeopardizes adolescents' access to healthcare, especially in areas of reproductive and mental health. Thus it is important to address physicians' beliefs and prejudices in order to tailor educational interventions.

Respondents' scores on the Communication with parents subscale were moderate, which indicates a lack of consensus on this issue among the population of surveyed physicians (Table 3). However, the results of numerous studies with adolescents showed that many adolescents value confidentiality highly in healthcare and prefer that parents not be informed about their reproductive health issues (contraception, sexually transmitted diseases) (7, 33, 37, 38). Insisting on parental notification would only discourage adolescents from seeking necessary medical care.

4.2 Limitations of the Study

There are important limitations to this study. First of all, our sample of primary care physicians was small, although sufficient for running principal component analysis (39). For the purpose of exploratory research, we decided to include only physicians working in Belgrade, and their number was not large. Still, data collection took several months. Excess workload and continued health professional emigration that is going on in Serbia were the main obstacles to instrument administration, and this also precluded test-retest analysis. The scale should be validated on a larger sample of physicians, since skewness and kurtosis suggest that distribution in our sample was not normal (Table 4). Physicians from both urban and rural areas should be included to examine the influence of geographic and socio-cultural factors on physicians' acceptance of minors' rights in healthcare. Furthermore, it would be useful to validate translated versions of the instrument in different countries and cultures. We invite the broader professional community to adapt and validate the scale for their populations. Secondly, the majority of participants in our sample were females (83.6%). According to the report of The Statistical Office of the Republic of Serbia, gender ratio in the total sample of Serbian medical doctors is 2:1 (for female and male doctors, respectively) (40). According to the World Health Organization's evaluation of primary healthcare in Serbia, primary care is dominantly provided by women (41). In this evaluation 89% of respondents were women. So the sample in our study adequately represents the gender ratio of primary healthcare in Serbia.

Thirdly, we did not include private healthcare institutions. Future studies are needed to explore differences in attitudes and approaches in adolescent healthcare between public and private clinics. Fourthly, our sample was sufficient for the principal component analysis as an initial exploration of the instrument's factor structure. Confirmatory factor analysis in a different sample is needed to evaluate the factor structure.

5 CONCLUSIONS

The Attitudes toward Adolescent Confidentiality Scale includes four sub-scales to assess physicians' general attitudes toward confidentiality in adolescent healthcare services and to discern their beliefs and opinions regarding confidentiality as an ethical principle in general, confidentiality in specific medical situations, maturity and competence of adolescents and the issue of communication and secrecy between adolescents and parents. This instrument can be used as a tool for assessing physician's acceptance of legal requirements for minors' confidentiality rights in national samples. Moreover, dissemination of results of the scale may contribute to needs assessments for future educational interventions and training programs, and possibly enhance physicians' appreciation of the importance of adolescent confidentiality and their preparedness to protect adolescents' rights in healthcare. Finally, respondents may have reflected on their own understandings and attitudes while responding to the scale questions, which is itself a benefit and may increase receptiveness to additional education.

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CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICAL APPROVAL

The study was approved by the Ethics Committee of the Faculty of Medicine, University of Belgrade (approval number: 29/VI-1).

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THE ROLE OF TELECARDIOLOGY IN DEALING WITH PATIENTS WITH CARDIAC RHYTHM DISORDERS IN FAMILY MEDICINE – SYSTEMATIC REVIEW

VLOGA TELEKARDIOLOGIJE PRI OBRAVNAVI BOLNIKOV Z MOTNJAMI SRČNEGA RITMA V DRUŽINSKI MEDICINI – PREGLED LITERATURE

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ABSTRACT

Keywords:
telecardiology, primary healthcare, cardiac rhythm disorders, cost effectiveness

Purpose: Heart rhythm disorders (HRD) are often present in patients visiting their family physician (FP). Dealing with their problems is not always simple, efficient and cost effective. The aim of this paper is to review the existing literature about the use and experience of telecardiology in patients experiencing HRD.

Methods: We conducted a review of literature in PubMed biographical databases (MeSH thesaurus), Web of Science and Cochrane, between 1995 and 2019. We included original articles in English that describe the use of telecardiology at primary and secondary healthcare levels. Exclusion criteria are those publications that discuss heart failure or observation of the activity of pacemakers or defibrillators and the age of patients under 18 years. A total of 19 papers met the inclusion criteria, thirteen of them were original scientific articles and we included them in the analysis.

Results: Use of telemedicine can shorten the time from diagnosis to the necessary treatment (2/13), telemedicine can reduce mortality in patients with acute myocardial infarction (4/13), it can shorten the time to diagnose atrial fibrillations (4/13), it can help determine the diagnosis for patients complaining about heart rhythm disorders which were not detected on the standard ECG recording (2/13) and can also help identify cardiac causes for syncope or collapse (2/13). All studies have confirmed that the use of telecardiology significantly reduces the number of unnecessary referrals to a cardiologist or hospitalization, and shortens the time needed to treat patients with life-threatening conditions.

Conclusion: The use of telecardiological techniques increases the quality and safety of work in managing patients with cardiovascular disease in FP practice. Usage of telecardiologic devices can also save money and bridge the gap between the primary and secondary healthcare levels.

IZVLEČEK

Ključne besede:
telekardiologija, primarna zdravstvena oskrba, motnje srčnega ritma, stroškovna učinkovitost

Namen: *Bolezni srčnega ritma (BSR) so pogoste težave posameznikov, ki obiščejo svojega družinskega zdravnika (DZ). Obvladovanje njihovih težav ni vedno preprosto, pričakovano in stroškovno učinkovito. Namen tega prispevka je pregledati obstoječo literaturo o uporabi telekardiologije in izkušnjah bolnikov z motnjami srčnega ritma z njo.*

Metode: *Pregledali smo literaturo v biografskih bazah PubMed (MeSH tezaver), Web of Science in Cochrane, objavljeno med leti 1995 in 2019. Kriterijem vključitve je ustrezalo skupno 19 prispevkov. Vključitveni kriteriji so obsegali originalne znanstvene članke, ki opisujejo uporabo telekardiologije na primarni in sekundarni zdravstveni ravni. Izključitveni kriteriji so bili obravnava bolnikov s srčnim popuščanjem, delovanje pacemakerjev in vgrajenih defibrilatorjev ter starost bolnikov, nižja od 18 let. Trinajst prispevkov je bilo originalnih znanstvenih člankov in smo jih vključili v analizo.*

Rezultati: *Uporaba telemedicine lahko skrajša čas od diagnoze do potrebnega zdravljenja (2/13), telemedicina lahko zmanjša smrtnost pri bolnikih z akutnim miokardnim infarktom (4/13), lahko skrajša čas za diagnozo atrijskih fibrilacij (4/13), lahko pomaga postaviti diagnozo bolnikom, ki tožijo zaradi motenj srčnega ritma, ki niso bili odkriti na standardnem posnetku EKG (2/13), in lahko pomaga pri iskanju kardialnih vzrokov sinkope oziroma omedlevice (2/13). Vse študije so potrdile, da uporaba telekardiologije znatno zmanjša število nepotrebnih napotitev h kardiologu, zmanjša število hospitalizacij in skrajša čas zdravljenja bolnikov z življenjsko nevarnimi stanji.*

Zaključek: *Uporaba telekardioloških tehnik povečuje kakovost in varnost dela pri obravnavi bolnikov s kardiovaskularnimi težavami v praksi DZ. Uporaba telekardioloških pripomočkov lahko tudi prihrani denar in odpravi vrzel med primarno in sekundarno ravnijo zdravstvene oskrbe.*

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1 INTRODUCTION

In Europe, 50% of all deaths occur due to cardiovascular diseases (1). In 2016, cardiovascular diseases were a cause of 40% of all deaths in Slovenia, 47% of women's deaths and 32% of men. When talking about cardiac diseases there are three main causes of death: acute myocardial infarction, arrhythmia and heart failure. The age-standardized mortality rate in Slovenia had surpassed the European average in the eighties and nineties of the previous century. However, this difference has been decreasing since 2000 and is getting closer and closer to the European average (2). In terms of the causes of primary care visits, cardiac diseases represent 5.60% of the total number of visits, i.e. 283,143 medical check-ups. Cardiac diseases are the seventh most common cause for visits to the family medicine physician (FP) (3). This data shows that medical service expenses related to cardiovascular diseases are high. Arrhythmia affects millions of people each year. Some types of arrhythmia are hard to diagnose as they occur sporadically, whereas others do not present any danger for health (e.g. supraventricular extrasystole (SVES) or paroxysmal supraventricular tachycardia (PSVT), but they can still cause symptoms and discomfort to patients. On other hand, there are still some life-threatening arrhythmias, such as ventricular tachycardia (VT), which can significantly affect patient's health (4, 5). In everyday practice doctors are still using the common methods, such as referring patients to a cardiologist and/or recording an ECG, when treating patients without having the opportunity to access the modern technology in this field of medicine. The other methods, e.g. an ultrasound, an MRI/CT scan or a scintigraphy require a specialist's time, are very expensive and the waiting time is long. Considering the dimension and the severity of the problem, the need for cheaper yet reliable continuous monitoring of the cardiovascular system has arisen. Telemedicine is a concept that describes telecommunication and information technology with the purpose of providing medical help remotely. With the help of information and communications technology, it enables medical service when the healthcare provider and patients are not in the same place geographically. It helps to minimize the distance and improves access to medical service that is not always available in remote rural areas. The early form of telemedicine included the telephone and the radio, while in modern times video calls and more progressive diagnostic methods are available in various mobile apps, and telemedical devices have become more and more popular (6). The use of what is called eHealth, which could be considered a part of telehealth, lies in its ability to access medical data while not being limited to a specific location (7). The use of eHealth has been increasing in recent years, especially low-cost sensors that trace various physiological parameters, such as body temperature, heartbeat and blood pressure (8). Within digital health, mHealth (mobile Health) involves all applications of telecommunications and multimedia technologies for the delivery of healthcare information. mHealth refers to the practice of medicine supported by mobile devices such as mobile phones, tablets, personal digital assistants and the wireless infrastructure (9).

Digital technology is becoming an increasingly important tool for a family physician, especially in communication with patients and colleagues, with the presumption that connections in the telecommunications network are secure enough for the exchange of sensitive data in the form of text, sound, image or other information transmission (10). With the help of these transferred data, a physician can treat or control the course of treatment, advise certain diagnostic methods and prevent deterioration in the patient's condition (11).

Telecardiology is a specialized version of telemedicine, which is a newer method of managing patients with suspected or known cardiac problems (12); it allows FP's direct access to consultant specialists by forwarding the ECG records via telephone or wireless connection (13). Through its use, the quality, speed and cost-effectiveness of treating patients with cardiovascular problems on the primary level can be improved.

The purpose of this article is to evaluate the state of activity in telemedicine on the primary level in Slovenia and around the world and to review the existing literature about the use and experience of telecardiology at the primary healthcare level, to see where and if there is an opportunity of improvement and further research.

2 METHODOLOGY

2.1 Database

We performed a literature search using PubMed (1995-2019; thesaurus MeSH), Web of Science (1995-2019) and Cochrane (1995-2019). We used the following terms: Telemedicine AND Primary Healthcare OR Healthcare AND Cardiac rhythm disorders AND Cost effectiveness. The search was limited to English-language articles. We searched within the title, abstract and keywords.

Original articles and systematic reviews which describe the use of digital techniques in cardiology (telecardiology), especially with adults that suffer from cardiovascular diseases such as heart rhythm disorders or chest pain, were included in the review.

2.2 The Course of Choosing Academic Publications

Out of all the publications, there were only six that discussed the use of telecardiology in primary healthcare, and for this reason we also included the secondary healthcare level. Publications that discuss heart failure or

observation of the activity of pacemakers or defibrillators were not included. Another exclusion criterion was the age of patient under 18 years. The search strategy consisted of five steps. In the first step, we performed a search in the databases according to search terms. In the second step, we reviewed the titles and excluded those appearing not to correspond to our search terms. Removing of duplicates was the third step. The abstracts of the remaining articles were reviewed in the fourth step. The abstracts that did not meet the inclusion criteria were excluded. In the fifth step, we reviewed the full text of the remaining articles and excluded those that again did not correspond to the type of study eligible for our review under our inclusion and exclusion criteria. Nineteen articles were included, from which thirteen were original articles and six of them were systematic reviews. The results of the thirteen original articles were analyzed and the findings were summarized (Figure 1).

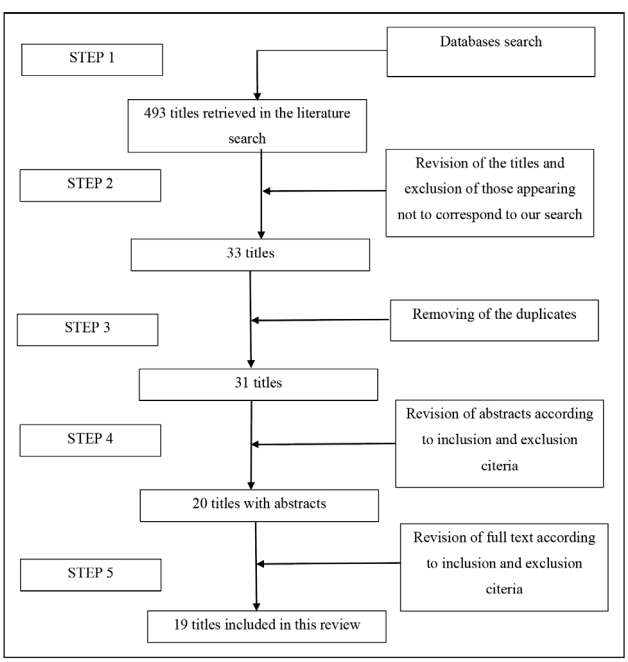

Figure 1. The course of choosing academic publications that were included in the research and analysis.

3 RESULTS

A total of nineteen articles were included in this review after applying the search strategy (Figure 1). Six of the articles were systematic reviews dealing with telecardiology and its cost-effectiveness only on the primary as well as on other levels of healthcare (Table 1).

Table 1. Number of academic publications considering the search term from the database of publications.

Search term	Number of results			Number of publications included in the analysis
	PM	Coch	WS	
Telemedicine AND Primary Healthcare AND Cardiac rhythm disorders AND Cost effectiveness	5	0	8	6
Telemedicine AND Healthcare AND Cardiac rhythm disorders AND Cost effectiveness	29	32	419	13
TOTAL	34	32	427	19

Legend: PM - PubMed; Coch - Cochrane; WS - Web of Science

The authors of included articles (Table 2) used different ECG accessories to establish the heart's activity. Its values provided us with information about coronary circulation (14-16, 18) and hearth rhythm (17, 19-26). With the help of telemedicine, i.e. telecardiology, the collected data and information were forwarded to a person in another location, who was more competent in this field and could provide quicker and more effective treatment for the patient.

Table 2. Authors, number of participants, study type, use of accessories and research fields in analyzed original articles.

First author	Year	Country	Number of participants	Study type	Accessory	Research field			Reference
						HRD	STEMI	Syncope	
Scalvini	2002	Italy	952	Prospective, randomized study	Portable ECG		*		(14)
Lieberman	2006	United Kingdom	3.259	Prospective, case control study	Stationary ECG		*		(15)
Sorensen	2007	Denmark	759	Prospective, randomized study	Stationary ECG		*		(16)
Leijdekkers	2009	Australia	200	Prospective, case control study	Wireless ECG sensor	*			(17)
Chan	2012	Canada	594	Prospective, randomized study	Stationary ECG		*		(18)
Orchard	2014	Australia	88	Quantitative study	Wireless ECG sensor	*			(19)
Brunetti	2014	Italy	109.750	Cost analysis study	ECG record	*			(20)
Klein-Wiele	2016	Germany	184	Retrospective, cross-sectional study	Stationary ECG	*			(21)
Halcox	2017	United Kingdom	1001	Retrospective, randomised controlled trial	Wireless ECG sensor	*			(22)
Rozena	2018	United States of America	98	Prospective, single-center study	Wireless ECG sensor	*			(23)
Bumgarner	2018	United States of America	100	Prospective, non-randomized, adjudicator-blinded study	Stationary ECG vs Wireless ECG sensor	*			(24)
Sutton	2018	United Kingdom, Germany	177 physicians	Quantitative study, comparative assessment	Stationary ECG vs insertable cardiac monitoring			*	(25)
Benditt	2019	United States of America	199 physicians	Quantitative survey	Stationary ECG vs insertable cardiac monitoring			*	(26)

The effect of telemedicine on the time span from diagnosis of myocardial infarction to the necessary treatment was explored by Scalvini. He divided the time from the moment of experiencing chest pain until reperfusion of the myocardium with the help of PCI (percutaneous coronary intervention) in three groups: from the beginning of the pain to the decision to seek medical help; from the moment of this decision to actually visiting a physician and finally from the visit to the PCI (14). A total of 200 emergency physicians, who were sending their ECG records via telecommunication networks to 22 cardiologists, participated in this research. They found out that the time from the actual visit at the physician's office to the PCI can be significantly reduced with the help of this technology. The same study indicated that also the number of referrals was reduced, with 74% of patients not needing any further treatment. Lieberman came to similar findings. His research was carried out on 3259 patients, who were divided into an intervention and a control group (15). He found that 58% of the participants in the intervention group were referred to a cardiologist right after the emergency physician carried out the ECG recording. In the control group they were able to have a teleconsultation with a cardiologist and that gave them the opportunity to treat 90% of patients by themselves without having to refer them to specialists. In this study it was pointed out that the costs can be significantly reduced if teleconsultation is used, because fewer patients would be referred to a specialist.

With the help of telecardiology, Sorensen also tried to reduce the time taken from the patient's home to the hospital with a Cath Lab (16). He included 13 ambulances and their patients with a suspicion of acute myocardial infarction. These ambulances were equipped with an ECG recording device that was sending the records directly to a cardiologist via telephone lines. In the first six months of use they treated 11% of patients with STEMI (ST-Elevation Myocardial Infarction) and after that the numbers went up to 73%. In other words, patients were directly referred to the PCI without being treated in the hospital. The study has proven that even patients that live far away from the hospital can be treated appropriately and with the same quality as those living near the hospital.

All the described studies included patients with chest pain and suspicion of acute myocardial infarction (14-16),

whereas Chan tried to find out whether telecardiology can reduce the mortality of patients after STEMI (18). He was interested in the one-year survival in patients with STEMI after PCI; the research included 594 patients. After calling the emergency service, the patients were divided into two groups. One group followed the common protocol of treating a patient with STEMI, whereas the other 167 patients were treated with the help of an ECG algorithm to establish the diagnosis of acute myocardial infarction. All patients were sent to the Cath Lab and were treated there. After one year, they found out that patients who were treated with the help of the ECG algorithm, got treatment sooner and that their mortality was reduced by 62% in comparison to the control group. Klein-Wiele carried out a study with the purpose of establishing the actual number of patients presenting with palpitations that actually have heart rhythm disorders. In his study, he included patients that were complaining about chest pain and those with palpitations. Twelve FP participated in this study, which was carried out in Germany (21). Patients had to be in the sinus rhythm during the treatment and had to have complains about palpitations in their medical history. The study established that 61.4% of the patients did not have any HRDs. In 14.7% of cases it was paroxysmal atrial fibrillation and in 6.5% ventricular tachycardia. In 88.7% of all patients, their FP changed their pharmacotherapy, whereas 26.8% were referred to a psychotherapist. 2.8% of the patients were treated with cardioversion and one patient had a Cardioverter Defibrillator (ICD) implanted.

Some studies were also carried out to assess the satisfaction of physicians as well as patients with the use of telemedical equipment (15-17, 13). Leijdekkers conducted a similar study. He compared the usefulness of the ECG sensor in comparison to the standard Holter monitor (17). Cardiologists included in the study patients with a low risk of heart rhythm disorder. Patients had to carry the sensor for one day and after that they only had to use it in case of a strange feeling in their chest. They had to return the device after two to four weeks. Additionally, they had to answer a questionnaire about how they would rate the usefulness of the sensor and simplicity of handling it. A total of 21 out of 47 patients had already carried a Holter monitor in their past and they answered that (89.3%) the sensor is handier, and its use is simpler (90.5%). In the rest of the studies, physicians had to fill out a questionnaire about satisfaction with different methods of telecardiology (15, 16, 19). Mostly they were satisfied, because the treatment was quicker and more effective.

In assessing atrial fibrillation (AF) 4 studies used a wireless ECG sensor. Orchard used an innovative iPhone ECG – an iECG sensor which operates with Apple iPhones and aims to diagnose atrial fibrillation in seemingly healthy persons older than 65 years (19). She included three ambulances, in which nurses made screening tests with patients older than 65 years before the actual check-up at the doctor. This test lasted for about 30 seconds and the recording was sent via wireless network to a validated algorithm, which showed whether the atrial fibrillation is present or not. Before the patient visited the physician, they already had received this information. During the screening test, 19% of the 88 participants had atrial fibrillation.

Halcox (22) conducted a trial of AF screening using an AliveCor Kardio monitor attached to a Wi-Fi-enabled iPod in 1001 patients divided into two groups; 19 patients were diagnosed with AF versus 5 in the control group. He concluded that screening twice weekly with this method is more likely to identify incident AF. Similarly, Rozena (23) used Cardiio Rhythm Mobile Application for AF detection. The application correctly identified 93.1% of AF and showed promising potential in accurate detection of AF. Bumbarner compared Kardia Band with Apple Watch to a 12-lead ECG (24). His reports were similar to Rozena's, the device showed 93% sensitivity and 84% specific in accurately differentiated AF from sinus rhythm.

All studies emphasized that the use of telemedicine is beneficial, but Brunetti was interested in the costs surrounding telemedicine (20). The cost-analysis was carried out with patients who had called the emergency service at a certain time. Paramedics had a 12-lead ECG that they used for the diagnostic approach. This ECG report would be sent via mobile phone connection with a telemedical centre; therefore, the cardiologist could see the record. If the patient had STEMI, he was immediately transferred to PCI. At the time of this research, they recorded 109,750 ECGs. They compared the costs of the teleconsultation with those of receiving the patient at the hospital and then transferring them to PCI. They found out that the final price for treating one patient can vary from EUR 8.10 to EUR 38.4 for one treatment. The treatment provided with telemedicine was cheaper.

Sutton (25) and Benditt (26) were interested in cardiac rhythm disorders in patients experiencing syncope or collapse. The guidelines recommend the use of Holter monitoring when syncope or collapse recurrence is daily and wearable monitors for those recurring monthly (27). Sutton took a survey of 177 participants, emergency doctors (ED) and cardiologists form Germany and the United Kingdom (25). Among ED, 20% from the UK and 31% from Germany chose diagnostic ambulatory electrocardiogram monitoring rather than Holter monitoring when dealing with patients having daily symptoms; but when treating patients for infrequent events (less then 1 per month) 15-30% of them chose Holter monitoring and only 50% selected an insertable cardiac monitor. For cardiologists, 6% from the UK and 10% from Germany did not choose Holter for daily symptoms but for infrequent symptoms, and 80% would select an insertable cardiac monitor. He concluded that in evaluating syncope or collapse, most

physicians use diagnostic ambulatory electrocardiogram monitoring according to the guidelines. Benditt conducted similar research in the United States of America and he interviewed 199 doctors of different specializations (26). Responders reported that 17-23% syncopes have cardiac cause and 25% chose ambulatory electrocardiogram monitoring rather than Holter for daily events, but for less frequent events 12-18% would choose a Holter, 20-34% a conventional or a mobile cardiac telemetry system and 53-65% an insertable cardiac monitor.

Table 3. Principal findings.

Reference	Topic, study question	Sample size	Methods	Main results	Level of healthcare		
					Primary	Secondary	Both
(14)	Can telemedicine shorten the time from diagnosis of acute myocardial infarction to the necessary treatment?	200 emergency physicians, who were sending their ECG records via telecommunication networks to 22 cardiologists	They divided the time from the moment of experiencing chest pain until reperfusion of the myocardium with the help of PCI in three groups: from the beginning of the pain to the decision to seek medical help; from the moment of this decision to actually visiting a physician and finally from the visit to the PCI	The time from the actual visit at physician's office to the PCI can be significantly reduced with the help of this technology and 74% of patients were not in need of further treatment.			*
(15)	Can telemedicine shorten the time needed from visit to FP to cardiologist in the case of acute myocardial infarction?	3259 patients, who were divided into an intervention and a control group	Participants in the intervention group were referred to a cardiologist right after the emergency physician carried out the ECG recording. In the control group they had a chance of teleconsultation with a cardiologist	58% in the intervention group were referred to a cardiologist, in the control group they treated 90% of patients by themselves without having to refer them to specialists.	*		
(16)	Can telecardiology reduce the effect of the patient being distant from the hospital with a Cath Lab?	13 ambulances and their patients with suspicion of acute myocardial infarction.	Ambulances were equipped with an ECG recording device that was sending the records directly to a cardiologist via telephone lines.	At first, they treated 11% of patients with STEMI and after a period of time, the number went up to 73%.		*	
(17)	Is the ECG sensor more user friendly in comparison to the standard Holter monitor?	47 patients	Personal Health Monitor sensor versus Holter monitoring	21 of 47 patients already had carried a Holter monitor in their past and they answered that (89.3%) the sensor is handier, and its use is simpler (90.5%).		*	
(18)	Can telecardiology reduce the mortality of patients with acute myocardial infarction?	594 patients with STEMI after PCI	After calling the emergency service, the patients were divided into two groups. One group followed the common protocol of treating a patient with STEMI, while the other 167 patients were treated using the ECG algorithm to establish acute myocardial infarction.	The patients who were treated with the help of ECG algorithm, got treatment earlier and this reduced their mortality by 62% in comparison to the control group.		*	
(19)	Can iphone ECG screening by nurses help find more incident AF?	88 patients (age 74.8±8.8 years)	AliveCor Kardio monitor attached to a WiFi-enabled iPhone used for routine scanning for AF	19% had AF		*	

Reference	Topic, study question	Sample size	Methods	Main results	Level of healthcare		
					Primary	Secondary	Both
(20)	Is telemedicine cost effective?	109,750 ECG records	Paramedics had a 12-lead ECG, this ECG report would be sent via mobile phone to a telemedical center, where the cardiologist could see the record.	They compared the costs of the teleconsultation with those of receiving the patient at the hospital and then transferring them to PCI. They found out that the final price for treating one patient can vary from EUR 8.10 to EUR 38.4 for one treatment. The treatment provided with telemedicine was cheaper.	*		
(21)	Can telemedicine detect arrhythmia in patients with palpitation?	12 FP and cardiologists, 184 patients (age 57.5±14.4 years)	FP sent ECGs twice per day in case of palpitations	61.4% of the patients did not have any HRDs. In 14.7% it was paroxysmal AF and in 6.5% ventricular tachycardia. In 88.7% their FP changed their pharmacotherapy, while 26.8% were referred to a psychotherapist.	*		
(22)	Is screening using an AliveCor Kardio monitor attached to a Wi-Fi-enabled iPod more likely to identify incident AF?	1001 patients divided into two groups (age 72.6±5.4 years)	AliveCor Kardio monitor attached to a Wi-Fi-enabled iPod versus 12-lead ECG in patients with AF	19 patients were diagnosed with AF versus 5 in the control group		*	
(23)	Is Cardiio Rhythm Mobile Application accurate for AF detection?	98 patients (age 67±10 years)	Cardiio Rhythm Mobile Application versus 12-lead ECG in patients with AF	The application correctly identified 93.1% of AF		*	
(24)	Can Kardia Band accurately differentiate sinus rhythm from AF compared to a standard ECG report?	100 patients (age 69±11 years), 169 simultaneous ECG and Kardia band reports	Kardia band with Apple Watch versus 12-lead ECG in patients with AF	The device showed 93% sensitivity and 84% specific in accurately differentiate AF from sinus rhythm		*	
(25)	By following guidelines for treating syncope or collapse, what kind of monitoring would doctors use?	177 physicians, ED: 33 UK, 40 Germany; cardiology: 54 UK, 50 Germany;	A qualitative survey	20% ED from the UK and 31% from Germany choose a diagnostic ambulatory ECG monitoring rather than Holter monitoring when dealing with patients having daily symptoms; but when treating patients for infrequent events (less then 1 per month) 15- 30% of them chose Holter monitoring and only 50% selected an insertable cardiac monitor. For cardiologists 6% from the UK and 10% from Germany did not choose Holter for daily symptoms but for infrequent symptoms and 80% would select an insertable cardiac monitor			*

Reference	Topic, study question	Sample size	Methods	Main results	Level of healthcare		
					Primary	Secondary	Both
(26)	By following guidelines for treating syncope or collapse, what kind of monitoring would doctors use?	199 physicians: 35 emergency doctors, 35 primary care, 30 hospitalists, 30 neurologists, 69 cardiologists	A qualitative survey	25% chose an ambulatory electrocardiogram monitoring rather than Holter for daily events, but for less frequent events 12-18% would choose a Holter, 20-34% a conventional or a mobile cardiac telemetry system and 53-65% an insertable cardiac monitor			*

4 DISCUSSION

Use of telemedicine can reduce the time and cost from diagnosis to the necessary treatment. It can reduce mortality in patients with acute myocardial infarction. In addition to this, it can reduce the time to diagnose atrial fibrillation and help in diagnosing patients with heart rhythm disorders (HRD) which could not be seen, i.e. diagnosed, in the standard ECG record.

The studies have shown that the use of telemedicine can improve patient treatment on different levels of healthcare. Even though only 19 studies were found in this research, medical improvement in this field is visible. The outcomes of these studies have a great impact on the further development of digital medical techniques and algorithms for more qualitative treatments. Moreover, a cost evaluation study has also shown that telemedicine is cheaper in comparison to other, common treatments (20). All studies have proven that telemedicine is crucial for reducing unnecessary referrals to cardiologists or hospitals and essential for quicker treatment of patients that suffer from a life-threatening disease.

The fact is that there is great technological progress even in Slovenia and many sophisticated devices are available, especially in the field of treating diabetes mellitus type 2, where a similar study was conducted using the eDiabetes application for better self-management of DM type 2 patients not using insulin (28). Despite that, there is only one study running in Slovenia which includes an ambulatory ECG recording device, although old studies have shown great advantages for the use of telecardiology in the family doctor's office (29). The study uses a small body sensor measuring ECG on patients visiting their FP's and complaining about cardiac rhythm disorders. The telecardiology devices are small, portable and can normally be activated by simply pressing the button. They can to be transported from one room to the other, which means that they can be taken on home visits. They are user friendly for the physician as well as for the patient. They can be daunting due to their completeness, but users must accept and trust them. In this study there is also a part for FP's to learn how to use the ECG recording device and how to interpret the results; if in doubt, they can send the report to a consulting colleague or cardiologist. By doing so, they become more competent in interpreting the results and they can improve their quality of care. The big advantage in body sensor usage is that it is patient-controlled, and even though it can record and measure long time intervals, its benefits are short measurements sent from patients to their doctors when they feel discomfort.

The price is also an important factor when talking about telecardiology devices, because the initial input in the device can be a great obstacle for many physician's offices that operate within the public health network. Although the software is normally included in the price of the device, its management requires training and some knowledge of computer and law policies. This can be a big challenge for people who do not trust modern and proven technology.

4. 1 Limitations of the Studies

A low number of well-planned intervention studies, especially on the primary level, and only a few patients included in them, were the main limitations that influenced the conclusion of this research. In our review of the literature, we find only three studies on the primary care level dealing with telecardiology (15, 20, 21). Although many patients were included, they all were treated with the help of a standard ECG, which means that there were no studies on primary care with the use of a standard ambulatory ECG. A drawback of three studies (14, 17, 19) out of thirteen included studies is the absence of control groups, which prevent an actual evaluation of cost-effectiveness of the use of telecardiology.

5 CONCLUSION

Telecardiology techniques can revolutionize the treatment of patients with cardiovascular diseases in FD´ offices. They can also save money and surpass the gap between primary and secondary healthcare levels. Even though the telecardiology devices are user friendly, their management requires some training and knowledge about computer and law policies. That could be a challenge for future physicians. Further research is needed to assess the effectiveness and usefulness of telecardiology at the primary healthcare level.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

ETHICAL APPROVAL

The research carried no risk of violating ethical principles.

FUNDING

There is no financial interest or risk.

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Prevolnik Rupel V, Srakar A, Rand K. Valuation of EQ-5D-3L health states in Slovenia: VAS based and TTO based value sets.
Zdr Varst. 2020;59(1):8-17. doi: 10.2478/sjph-2020-0002.

VALUATION OF EQ-5D-3L HEALTH STATES IN SLOVENIA: VAS BASED AND TTO BASED VALUE SETS

VREDNOTENJE ZDRAVSTVENIH STANJ EQ-5D-3L V SLOVENIJI: VREDNOSTI ZDRAVSTVENIH STANJ, PRIDOBLJENE Z METODAMA VAS IN TTO

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ERRATUM

With the publication of the article Prevolnik Rupel V, Srakar A, Rand K. Valuation of EQ-5D-3L health states in Slovenia: VAS based and TTO based value sets. Zdr Varst. 2020;59(1):8-17 the annexes of the article Prevolnik Rupel V, Ogorevc M. The EQ-5D health states value set for Slovenia. Zdr Varst. 2012;51:121-40 are annulled.

Annex 2. Slovenian EQ-5D-3L TTO value set.

11111	1	23131	0.110331	32222	-0.04587	12313	0.339647
21111	0.691926	33131	-0.31072	13222	0.435866	22313	0.253041
31111	0.031683	11231	0.337698	23222	0.338903	32313	-0.21037
12111	0.854207	21231	0.251278	33222	-0.1541	13313	0.189377
22111	0.650513	31231	-0.21156	11322	0.496714	23313	0.114978
32111	0.014633	12231	0.314623	21322	0.391737	33313	-0.30733
13111	0.541753	22231	0.23034	31322	-0.12126	11123	0.489698
23111	0.429896	32231	-0.2258	12322	0.468105	21123	0.385714
33111	-0.09848	13231	0.168104	22322	0.367061	31123	-0.12493
11211	0.868331	23231	0.095144	32322	-0.13642	12123	0.461394
21211	0.657217	33231	-0.32183	13322	0.294999	22123	0.361229
31211	0.017495	11331	0.211402	23322	0.212447	32123	-0.14004
12211	0.796531	21331	0.135448	33322	-0.23811	13123	0.289654
22211	0.618923	31331	-0.29251	11132	0.334117	23123	0.207561
32211	0.000642	12331	0.191311	21132	0.248036	33123	-0.2415
13211	0.516078	22331	0.116779	31132	-0.21376	11223	0.466087
23211	0.408253	32331	-0.30602	12132	0.31114	21223	0.365309
33211	-0.1113	13331	0.060763	22132	0.22717	31223	-0.1375
11311	0.586148	23331	-0.00576	32132	-0.22797	12223	0.438761
21311	0.466541	33331	-0.39751	13132	0.165128	22223	0.341445
31311	-0.07741	11112	0.855456	23132	0.092364	32223	-0.15248
12311	0.552902	21112	0.651123	33132	-0.32387	13223	0.271472
22311	0.439197	31112	0.014895	11232	0.314975	23223	0.190898
32311	-0.09306	12112	0.787311	21232	0.230661	33223	-0.25311
13311	0.360469	22112	0.613326	31232	-0.22558	11323	0.320011
23311	0.271824	32112	-0.00192	12232	0.292508	21323	0.235239
33311	-0.19778	13112	0.511461	22232	0.21017	31323	-0.22245
11121	0.79555	23112	0.40433	32232	-0.23969	12323	0.297411
21121	0.618334	33112	-0.11365	13232	0.149146	22323	0.214651
31121	0.000374	11212	0.797481	23232	0.077419	32323	-0.23659
12121	0.740509	21212	0.619492	33232	-0.3349	13323	0.153362
22121	0.58299	31212	0.000902	11332	0.191619	23323	0.081364
32121	-0.01625	12212	0.742097	21332	0.117065	33323	-0.33198
13121	0.486125	22212	0.584067	31332	-0.30581	11133	0.186835
23121	0.38264	32212	-0.01573	12332	0.171921	21133	0.112611
33121	-0.12681	13212	0.487033	22332	0.098707	31133	-0.30905
11221	0.749104	23212	0.383422	32332	-0.31922	12133	0.167229
21221	0.588784	33212	-0.12633	13332	0.043559	22133	0.094327
31221	-0.01346	11312	0.553401	23332	-0.02205	32133	-0.32243
12221	0.701178	21312	0.439612	33332	-0.41	13133	0.039385
22221	0.555376	31312	-0.09282	11113	0.545678	23133	-0.026
32221	-0.02989	12312	0.522032	21113	0.433178	33133	-0.41305
13221	0.462642	22312	0.413299	31113	-0.09657	11233	0.170513
23221	0.362315	32312	-0.10829	12113	0.514718	21233	0.097393
33221	-0.13937	13312	0.33711	22113	0.407098	31233	-0.32018
11321	0.526239	23312	0.250746	32113	-0.11199	12233	0.151215
21321	0.416854	33312	-0.21192	13113	0.331492	22233	0.079355
31321	-0.10618	11122	0.741288	23113	0.245658	32233	-0.33346
12321	0.496261	21122	0.583519	33113	-0.21537	13233	0.025106
22321	0.391348	31122	-0.01599	11213	0.519831	23233	-0.03955
32321	-0.1215	12122	0.694377	21213	0.411435	33233	-0.42351
13321	0.31718	22122	0.550433	31213	-0.1094	11333	0.062944
23321	0.232666	32122	-0.0324	12213	0.490162	21333	-0.0037
33321	-0.22421	13122	0.458401	22213	0.386114	31333	-0.39593
11131	0.357387	23122	0.358623	32213	-0.12469	12333	0.04544
21131	0.269051	33122	-0.14167	13213	0.31241	22333	-0.02027
31131	-0.19963	11222	0.701872	23213	0.228326	32333	-0.40863
12131	0.333756	21222	0.555878	33213	-0.22718	13333	-0.07035
22131	0.24771	31222	-0.02964	11313	0.363456	23333	-0.13051
32131	-0.21398	12222	0.659462	21313	0.27451	33333	-0.49495
13131	0.184387	22222	0.524374	31313	-0.19599		

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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, povezanih 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)

PLAGIATI

Kadar uredništvo ugotovi, da je rokopis plagiat, se rokopis takoj izloči iz uredniškega postopka. Plagiatorstvo ugotavljamo s programom za odkrivanje plagiatov CrossCheck plagiarism detection system.

ELEKTRONSKA ODDAJA PRISPEVKA

Priporočamo uporabo videoposnetka z navodili za avtorje. Prispevke oddajte v elektronski obliki s pomočjo spletne aplikacije Editorial Manager, ki se nahaja na spletnem naslovu http://www.editorialmanager.com/sjph/. V uredništvo sprejemamo po pošti le še Izjave o avtorstvu in avtorskih pravicah, ki zahtevajo lastnoročni podpis. Prosimo, da jih pošljete hkrati z elektronsko oddajo prispevka na naslov: Nacionalni inštitut za javno zdravje, za revijo Zdravstveno varstvo, Trubarjeva 2, 1000 Ljubljana.

V spletno uredniško aplikacijo se prijavite kot ‘avtor’. Prva prijava zahteva vnos podatkov o avtorju, vse naslednje prijave pa le še vnos podatkov za prijavo, ki jih na svoj elektronski naslov prejmete po prvi prijavi v sistem.

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.

Avtorji, ki v objavo pošiljate raziskovalno delo, opravljeno s pomočjo nekega podjetja, to navedite na koncu rokopisa v izjavi o financiranju. Navedete lahko tudi do dva neželena recenzenta.

Polje 'Comments' je namenjeno obveznemu predlogu treh recenzentov z imeni, nazivi, e-naslovi in zaposlitvijo. Navedete lahko tudi do dva neželena recenzenta.

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).

Po vnosu strukturiranih podatkov oddajte še priponko - rokopis (od 1 Uvod naprej), ki ne sme zajemati podatkov, ki ste jih vnesli že pred tem v strukturirana polja, zlasti ne podatkov o avtorjih. Ime datoteke ne sme vključevati avtorjevih osebnih podatkov, prav tako ne imen ustanov, vključenih v pripravo rokopisa. Grafično in slikovno gradivo je kot ves rokopis v angleškem jeziku. Vključite ga v besedilo na mesto, kamor le-to sodi in ga opremite z naslovom. Oddate torej le en sam dokument, eno priponko. V Wordu uporabite možnost Postavitev strani/Številke vrstic (tako bo na robu vsake vrstice dokumenta dodana številka vrstice).

Pri oddaji sledite napotkom, ki vam jih ponuja sistem, pomagate pa si lahko tudi z 'Editorial Manager's Tutorial for Autors'.

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.).

DOLŽINA PRISPEVKOV

Zahtevana dolžina prispevka je za vabljen uvodnik od 250 do 1000 besed, za znanstveni članek (originalni, metodološki ali sistematični pregledni) pa od 2000 do 4500 besed s slikovnim gradivom in literaturo vred. Revizija sme obsegati 5000 besed.

NASLOV IN AVTORSTVO

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.

KATEGORIJA PRISPEVKA

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

Avtorjem priporočamo, da pregledajo objavljene članke na temo svojega rokopisa v predhodnih številkah naše revije (za obdobje zadnjih pet let).

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.

Če ima članek/knjiga DOI številko, jo mora avtor navesti na koncu reference.

PRIMERI ZA CITIRANJE LITERATURE

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12. EQ-5D, an instrument to describe and value health. Accessed January 24th, 2017 at: https://euroqol.org/eq-5d-instruments/.

TABELE

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);
- v linijskih grafih naj se posamezne linije prav tako ločijo med samo z različnim črtkanjem ali različnim označevanjem (s trikotniki, z zvezdicami...), ne pa z barvo;
- v grafih naj bo ozadje belo (tj. brez ozadja).

Črke, številke ali simboli na sliki morajo biti jasni, enotni in dovolj veliki, da so berljivi tudi na pomanjšani sliki.

Ročno ali na pisalni stroj izpisano besedilo v sliki je nedopustno.

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.

Fotografijam, na katerih se lahko prepozna identiteta bolnika, priložite pisno dovoljenje bolnika.

MERSKE ENOTE

Naj bodo v skladu z mednarodnim sistemom enot (SI).

KRATICE IN OKRAJŠAVE

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.

UREDNIŠKO DELO

Prispelo gradivo z javnozdravstveno tematiko mednarodnega pomena posreduje uredništvo po tehnični brezhibnosti v strokovno recenzijo trem mednarodno priznanim strokovnjakom. Recenzijski postopek je dvojno slep. Po končanem uredniškem delu vrnemo prispevek korespondenčnemu avtorju, da popravke odobri in upošteva. Popravljen čistopis vrne v uredništvo po spletni aplikaciji Editorial Manager. Uredništvo dopušča obravnavo največ treh revizij. Če tretja revizija rokopisa ne upošteva vseh pripomb recenzentov, se rokopis umakne iz uredniškega postopka. Sledi jezikovna lektura, katere stroške krije založnik. Med redakcijskim postopkom je zagotovljena tajnost vsebine prispevka. Avtor dobi v pogled tudi prve, t. i. krtačne odtise, vendar na tej stopnji upoštevamo samo še popravke tiskarskih napak. Krtačne odtise je treba vrniti v treh dneh, sicer menimo, da avtor nima pripomb.

V uredništvu se trudimo za čim hitrejši uredniški postopek. Avtorji se morajo držati rokov, ki jih dobijo v dopisih, sicer se lahko zgodi, da bo članek odstranjen iz postopka.

Morebitne pritožbe avtorjev obravnava uredniški odbor revije.

Za objavo članka prenese avtor avtorske pravice na Nacionalni inštitut za javno zdravje kot založnika revije (podpiše Pogodbo o avtorstvu in avtorskih pravicah). Kršenje avtorskih in drugih sorodnih pravic je kaznivo.

Prispevkov ne honoriramo in tudi ne zaračunavamo stroškov uredniškega postopka.

Avtor dobi izvod tiskane revije, v kateri je objavljen njegov članek.