

# Pretilost i kronična bubrežna bolest: javnozdravstvena važnost

## Obesity and chronic kidney disease: a public health issue

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Debljina (pretilost) jedan je od vodećih javnozdravstvenih problema današnjega svijeta koji je poprimio razmjere globalne epidemije. Prekomjerna tjelesna težina i debljina jedan su od najvažnijih promjenjivih čimbenika rizika za kronične nezarazne bolesti, među kojima su najvažnije kardiovaskularne bolesti, dijabetes, određene vrste zloćudnih bolesti te kronična bubrežna bolest (KBB). Zadnjih godina sve se više shvaća važnost debljine kao čimbenika rizika za KBB te javnozdravstvena važnost KBB-a zbog sve veće učestalosti i opterećenja koje donosi na razini svijeta, kako u ekonomski razvijenim zemljama, tako i u onima slabije ekonomske razvijenosti.

### Epidemiologija pretilosti

Diljem razvijenoga svijeta, a sve više i u zemljama u razvoju, bilježimo porast broja pretilih osoba. Prema najnovijim podacima za 2015. godinu, u svijetu je pretilo više od 603 milijuna odraslih osoba te više od 107 milijuna djece, što su vrijednosti gotovo dvostruko veće od onih u 80-im godinama prošloga stoljeća<sup>1</sup>.

Kao mjera za definiranje pretilosti rabi se indeks tjelesne mase (ITM) ( $\text{kg}/\text{m}^2$ ), pri čemu vrijednost veća od  $25 \text{ kg}/\text{m}^2$  označuje prekomjernu tjelesnu težinu, a vrijednost indeksa viša od  $30 \text{ kg}/\text{m}^2$  označuje pretilost. Uporaba ITM-a za definiciju i istraživanje prevalencije pretilosti praktična je i jednostavna za primjenu, međutim, pokazalo se kako je raspodjela tjelesne masti, točnije, količina visceralne masnoće, bolji indikator za procjenu povezanosti debljine s negativnim zdravstvenim ishodima. Razlikujemo visceralnu i potkožnu tjelesnu masnoću, a najjednostavniji indikator količine visceralne masnoće jest omjer opsega struka i bokova.

Currently, obesity is one of the leading public health problems worldwide, which has grown to a global epidemic. Overweight and obesity are among the most important modifiable risk factors for chronic non-communicable diseases, notably cardiovascular diseases, diabetes mellitus, certain malignant diseases, and chronic kidney disease (CKD). The role of obesity as a risk factor for CKD, as well as the public health relevance of CKD due to its ever growing prevalence and associated burden recorded at the international level in both industrialized and developing countries, has been increasingly recognized in recent years.

### Epidemiology of obesity

An increase in the number of obese individuals has been recorded all over the industrialized world, while showing a progressive pattern also in developing countries. According to the latest data from 2015, there were more than 603 million obese adults and more than 107 million obese children in the world, the figures almost double those recorded in the 1980s<sup>1</sup>.

Body mass index (BMI,  $\text{kg}/\text{m}^2$ ) has been used as a measure to define obesity, whereby a BMI greater than  $25 \text{ kg}/\text{m}^2$  denotes overweight and BMI greater than  $30 \text{ kg}/\text{m}^2$  denotes obesity. Using BMI to define and study the prevalence of obesity is convenient and simple; however, the distribution of body fat, i.e. the amount of visceral fat, has been found to be a better indicator for assessment of the association of obesity and unfavorable health outcomes. There is visceral and subcutaneous body fat, and the waist to hip circumference ratio is the simplest indicator of visceral fat.

Current research into the prevalence of obesity in European countries suffers from some

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Postojeća istraživanja raširenosti pretilosti u europskim zemljama imaju određene metodološke probleme, kao što su korištenje nereprezentativnim uzorcima, provedba u samo nekoliko europskih zemalja te primjena nestandardnih antropometrijskih mjera koje je teško interpretirati. U studiji provedenoj u 16 europskih zemalja<sup>2</sup> 2010. godine, ukupan broj sudionika bio je 14 685, starijih od 18 godina. Prema podacima 34,8% odraslih osoba prekomjerne je tjelesne težine, a 12,8% ih je pretilo. Dakle, gotovo je polovica ispitanih osoba (47,6%) prekomjerne tjelesne težine i pretila. Hrvatska je, iza Mađarske, zemlja s najvećom prevalencijom osoba prekomjerne tjelesne težine i pretilih, s 58,2%. Po pretilosti Hrvatska je vodeća zemlja te je procijenjena prevalencija pretilosti na temelju uzorka 21,5%. Prevalencija pretilosti niža je u zemljama zapadne i južne Europe nego u zemljama srednje, istočne i sjeverne Europe (Slika 1). Prevalencija raste s dobi, a pada s višim stupnjem obrazovanja.

U usporedbi sa Sjedinjenim Američkim Državama prevalencija pretilosti u Europi je više nego dvostruko manja (14,0 prema 35,5% u muškaraca i 11,5 prema 35,8% u žena).

Važno je napomenuti kako je ovdje bila riječ o anketi u kojoj su se sudionici sami izjašnjavali o svojoj visini i težini, i nisu provedena mjerenja. Međutim, možebitne pristranosti i davanje socijalno poželjnih odgovora vjerojatno se ne razlikuju mnogo od zemlje do zemlje te čak i ako su apsolutni podaci o prevalenciji debljine neprecizni, možemo vidjeti da je pretilost u Hrvatskoj u usporedbi s ostalim europskim zemljama važan javnozdravstveni problem.

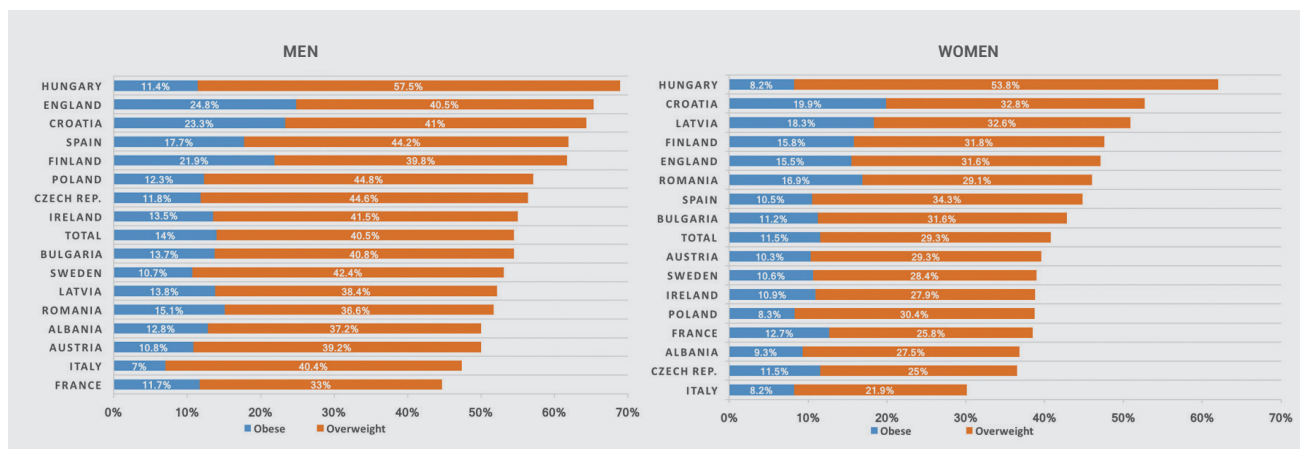
Prema nedavno objavljenim rezultatima Europske zdravstvene ankete (EHIS)<sup>3</sup>, rađenoj od 2014. do 2015. godine, na populaciji stanovnika Europske unije u dobi od 15 godina, a u kojoj je sudjelovala i Hrvatska, pretilo je 15,7% stanovnika EU-a, dok njih 34,5% ima prekomjernu tjelesnu težinu. Podatci za Hrvatsku nešto su lošiji od tog prosjeka, 18,0% stanovnika Hrvatske je pretilo, 37,7% ima prekomjernu tjelesnu težinu, a 41,9% stanovnika ima normalnu tjelesnu težinu. Prekomjerna tjelesna težina i pretilost zastupljenije su u muškaraca nego u žena, što je prikazano na Slici 2<sup>4</sup>. Pri tome treba napomenuti

methodological problems such as using non-representative samples, being conducted in only a few European countries, and employing non-standardized anthropometric measures that are difficult to interpret. A study carried out in 2010 in 16 European countries<sup>2</sup> was designed as a cross-sectional survey and included 14,685 subjects older than 18. The results obtained showed that 34.8% of adults were overweight and 12.8% were obese; accordingly, nearly half of the study subjects (47.6%) were overweight or obese. Croatia is a country with a very high prevalence of overweight and obese subjects (58.2%), second only to Hungary. Croatia is the leading country in the prevalence of obesity of 21.5%, as assessed on a study sample. The prevalence of obesity is lower in western and south Europe countries as compared with the central, eastern and north Europe countries (Figure 1). The prevalence of overweight and obesity increases with age and decreases with higher level of education.

In comparison with the United States of America (USA), the prevalence of obesity in Europe is less than half the prevalence recorded in the USA (14.0% vs. 35.5% in males and 11.5% vs. 35.8% in females).

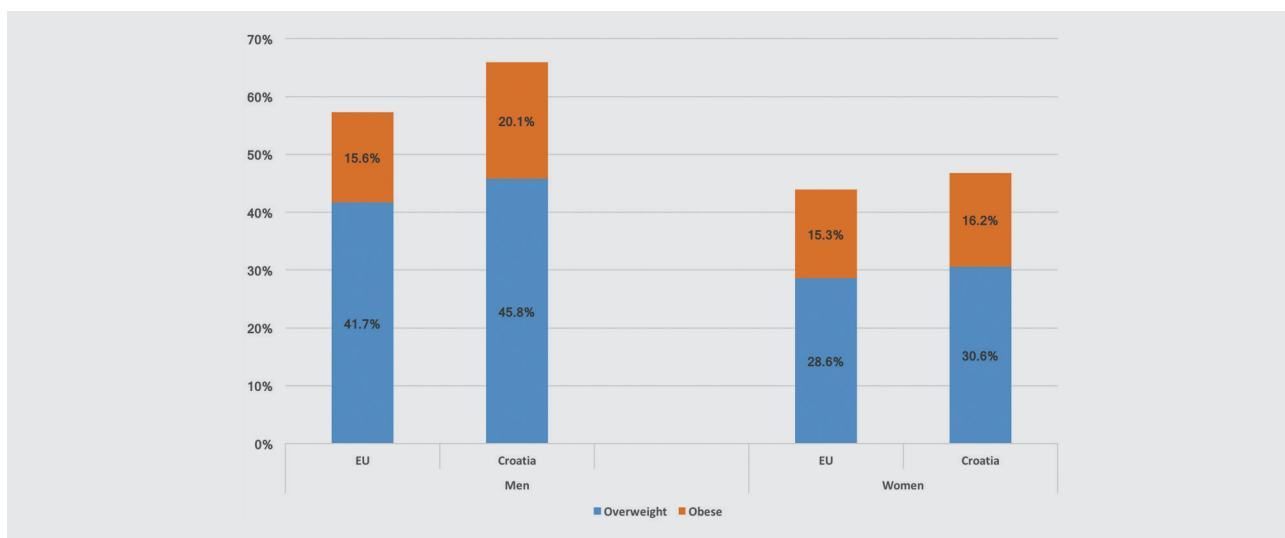
It should be noted that this was a survey in which the participants self-reported their body weight and height, and no measurements were performed. However, the potential biases and socially desirable answers probably did not differ considerably among various countries; even if absolute data on the prevalence of obesity are not precise enough, obesity in Croatia as compared with other European countries obviously poses a major public health problem.

According to the recently published results of the European Health Interview Survey (EHIS)<sup>3</sup> conducted in 2014-2015 on the European Union (EU) population older than 15, in which Croatia also took part, 15.7% and 34.5% of the EU population are obese and overweight, respectively. Data on Croatia are even worse than this mean prevalence, i.e. 18.0% of the Croatian population are obese and 37.7% overweight, while 41.9% have normal body weight. Overweight and obesity are more prevalent in males than in females (Figure 2)<sup>4</sup>. It should be



**FIGURE 1. Percent prevalence of obesity (BMI  $\geq 30\text{kg/m}^2$ ) and overweight/obesity (BMI  $\geq 25\text{kg/m}^2$ ), overall and by country, in male and female adults from 16 European countries. Prevalence estimates for the overall population were computed weighing each country in proportion to the country specific adult population.**

Source: Adapted from: Gallus S, Lugo A, Murisic B, Bosetti C, Boffetta P, La Vecchia C. Overweight and obesity in 16 European countries. European Journal of Nutrition. 2015 Aug 1;54(5):679-89.



**Figure 2. Percent prevalence of obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) and overweight/obesity (BMI  $\geq 25$  kg/m<sup>2</sup>), by gender, in Croatia and in EU. Prevalence estimates were computed by weighing using population weights.**

Source: Adapted from: Release of first EHIS wave 2 (2014) results. [Internet]. 2016. [preuzeto 19.6.2017]. Available: <http://ec.europa.eu/eurostat/web/health/health-status-determinants/data/database>

da je stupanj uhranjenosti izračunan prema antropometrijskim podacima koje su ispitanici sami naveli.

Prema istraživanju provedenom u Hrvatskoj 2003. godine (Hrvatska zdravstvena anketa) na reprezentativnom uzorku populacije starije od 18 godina, nešto više od polovice žena i 2/3 odraslih muškaraca imaju tjelesnu težinu veću od normalne (ITM  $>25$  kg/m<sup>2</sup>; žene: 54,3 %, muškarci: 63,2 %). Svaki je peti odrasli stanovnik pretio (ITM  $>30$  kg/m<sup>2</sup>; žene: 20,6 %, muškarci: 20,2 %), a trećina žena i gotovo polovica muškaraca imaju prekomjernu tjelesnu težinu (ITM: 25–30 kg/m<sup>2</sup>; žene: 33,7 %, muškarci: 43 %) <sup>5</sup>.

Prema uzorku od 3229 osoba koje su sudjelovale u Hrvatskoj zdravstvenoj anketi u 2003., a zatim i u CroHort studiji 2008., u petogodišnjem razdoblju između ovih dvaju istraživanja prosječno godišnje povećanje prevalencije pretilosti u muškaraca je bilo 10,6 %, a u žena 11,08 %. Kumulativna incidencija pretilosti u promatranome petogodišnjem razdoblju veća je u žena i iznosila je 20,5 %, a u muškaraca 8,7 % <sup>6</sup>.

Pretilost u djece također je u porastu diljem svijeta. U 2014. godini čak je 41 milijun djece mlađe od 5 godina bilo pretio ili imalo prekomjernu tjelesnu težinu <sup>7</sup>. Djeca s prekomjernom tjelesnom težinom pod povećanim su rizikom od nastanka kardiovaskularnih bolesti, dijabetesa tipa 2, teškoća sa spavanjem i astme, a često imaju probleme s tjelesnom težinom i u odrasloj dobi. U najnovije međunarodno istraživanje o zdravstvenom ponašanju učenika (*Health Behaviour in School-aged Children 2013/2014*) <sup>8</sup>, provedenom i u Hrvatskoj <sup>9</sup>, bile su uključene 42 zemlje i prikupljeni su podatci za djecu u dobi od 11, 13 i 15 godina. Udio učenika u Hrvatskoj s ITM-om većim od vrijednosti aritmetičke sredine uvećane za 1 standardnu devijaciju pada s dobi, od 33 % u jedanaestogodišnjaka, 27 % u trinaestogodišnjaka na 24 % u petnaestogodišnjaka, dok je u učenika taj pad znatnije izražen, s 20 % u dobi od 11 godina, preko 14 % u dobi od 13 godina na 9 % u dobi od 15 godina (**Slika 3**).

Što se tiče djece u dobi od 11 godina, Hrvatska se nalazi na 11. mjestu po udjelu učenika čiji je indeks tjelesne mase veći

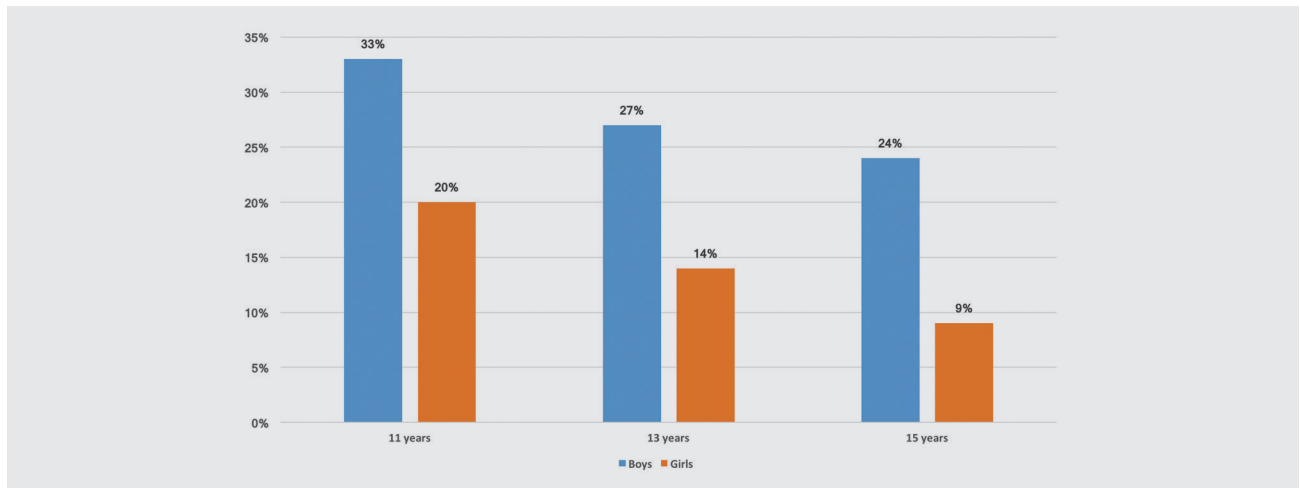
noted that the nutritional status was calculated according to anthropometric data reported by the participants.

Based on the Croatian Health Survey conducted in 2003 on a representative sample of the population older than 18, more than half of women and two-thirds of men are overweight (BMI  $>25$  kg/m<sup>2</sup>; 54.3 % of women and 63.2 % of men). Every fifth adult is obese (BMI  $>30$  kg/m<sup>2</sup>; 20.6 % of women and 20.0 % of men); and one-third of women and nearly half of men are overweight (BMI 25–30 kg/m<sup>2</sup>; 33.7 % of women and 43.0 % of men) <sup>5</sup>.

Data derived from a sample of 3229 subjects included in the Croatian Health Survey 2003 and then in the CroHort study 2008 yielded the mean annual increase in the prevalence of obesity of 10.6 % in men and 11.08 % in women during the 5-year period between the 2 surveys. The cumulative incidence of obesity in this 5-year period was higher in women (20.5 %), whereas in men it was 8.7 % <sup>6</sup>.

Obesity in children is also increasing all over the world. In 2014, 41 million children younger than 5 years were obese or overweight <sup>7</sup>. Overweight children are at an increased risk of developing cardiovascular disease, type 2 diabetes mellitus, sleep disorders and asthma, and they frequently have problems associated with being overweight in adulthood. The latest international survey of health behavior in schoolchildren (*Health Behavior in School-aged Children 2013–2014*) <sup>8</sup>, also carried out in Croatia <sup>9</sup>, included 42 countries and collected data on children aged 11, 13 and 15 years. In Croatia, the proportion of male schoolchildren with BMI exceeding the arithmetic mean value amplified by 1 standard deviation decreased with age, from 33 % in 11-year-old through 27 % in 13-year-old to 24 % in 15-year-old children, and this decrease was even more pronounced in female schoolchildren, with the respective figures of 20 %, 14 % and 9 % (**Figure 3**).

Concerning the group of 11-year-old children, Croatia ranks 11<sup>th</sup> country by the proportion of schoolchildren with BMI exceeding the arithmetic mean by 1 standard deviation. In case



**Figure 3. Percentage of overweight (bodyweight at least one standard deviation above average) school children aged 11, 13 and 15, Croatia, 2013-2014.**

Source: Hrvatski zavod za javno zdravstvo. Istraživanje o zdravstvenom ponašanju učenika. Osnovni pokazatelji zdravlja i dobrobiti učenika i učenica u Hrvatskoj, 2013/2014. Zagreb, 2016.

od aritmetičke sredine za jednu standardnu devijaciju. Glede 13-godišnjaka, nalazimo se na 14. mjestu, a, kad je riječ o 15-godišnjacima, na 20. mjestu. Na **Slici 4** prikazana je situacija po spolovima, za 11-godišnjake, u odabranim zemljama uključenima u istraživanje.

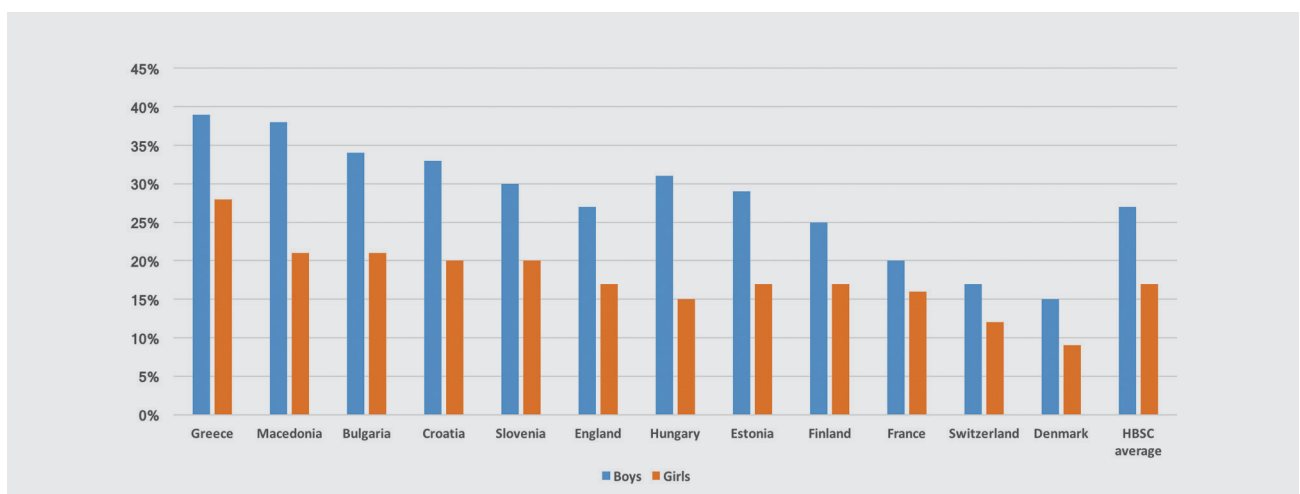
### Utjecaj pretilosti na kroničnu bubrežnu bolest

Prema nedavnom istraživanju utjecaja pretilosti na globalni teret bolesti, u 2015. godini je 4 milijuna smrti diljem svijeta barem djelomično uzrokovano visokim ITM-om, što čini 7,1 % smrti od svih uzroka. Debljina je također pridonijela tomu kao uzrok kod 120 milijuna godina života prilagođenih dizabilitetu (*Disability-Adjusted Life-Year, DALY*), što je još jedna od mjera globalnog tereta bolesti. Čak 39 % smrti povezanih s

of the 13-year-old and 15-year-old children, Croatia ranks 14<sup>th</sup> and 20<sup>th</sup> country, respectively. Results recorded on the 11-year-old children according to gender in the selected countries included in the study are shown in **Figure 4**.

### Effect of obesity on chronic kidney disease

According to the abovementioned study of the impact of obesity on the global disease burden, in 2015 there were 4 million deaths worldwide that were at least in part caused by high BMI, accounting for 7.1 % of all-cause deaths. In addition, obesity contributed as a causative agent to 120 million disability-adjusted life-years (DALY), another measure of the global disease burden. As many as 39 % of deaths associated with high BMI and 37 % of DALYs occurred in individuals with BMI lower than 30<sup>1</sup>.



**Figure 4. Proportion of overweight or obese 11-year-olds, by gender, in European countries.**

Source: Adapted from: Inchley J et al. eds. Adolescent obesity and related behaviours: trends and inequalities in the WHO European Region, 2002–2014. Observations from the Health Behaviour in School-aged Children (HBSC) WHO collaborative cross-national study. Copenhagen, WHO Regional Office for Europe, 2017.



visokim ITM-om i 37% DALY-ja dogodilo se u osoba čiji je ITM niži od 30<sup>1</sup>.

Kardiovaskularne su bolesti na prvome mjestu među uzrocima smrti i uzrocima godina života prilagođenih dizabilitetu koji su povezani s visokim ITM-om (52,4 %), a KBB se nalazi na 2. mjestu glede godina života prilagođenih dizabilitetu čiji je uzrok povišeni ITM (24,4 %)<sup>1</sup>.

Pretilost je jedan od glavnih čimbenika rizika za razvoj KBB-a. Osim posredno, kao uzročnik dijabetesa i arterijske hipertenzije koji zatim djeluju na razvoj KBB-a, pokazalo se kako je debljina i neovisan čimbenik rizika. U osoba s prekomjernom težinom pojavljuje se kompenzatorna hiperfiltracija kako bi se organizam mogao nositi s povećanim metaboličkim zahtjevima. Posljedica je i povećanje intraglomerularnoga tlaka, što može uzrokovati oštećenje bubrega te dugoročno razvoja KBB-a. Količina visceralne masnoće u tijelu pokazala se kao rizični čimbenik za razvoj i lošiji ishod KBB-a neovisno o ITM-u<sup>10</sup>. Pretilost udvostručuje rizik za razvoj KBB-a u usporedbi s normalnom uhranjenošću. Prekomjerna tjelesna težina povezana je s povećanim rizikom od bubrežnih kame-naca i karcinoma bubrega<sup>11</sup>.

## Epidemiologija kronične bubrežne bolesti

Kronična bubrežna bolest danas je važan javnozdravstveni problem zbog sve veće učestalosti, a posljedično i zbog rastuće potrebe za nadomještanjem bubrežne funkcije dijalizom i transplantacijom. Procjenjuje se da u Europi od KBB-a boluje oko 10 % populacije<sup>12</sup>. Liječenje nadomještanjem bubrežne funkcije gubitak je kvalitete života i očekivanog trajanja života oboljelih osoba, a, s druge strane, veliko financijsko opterećenje za društvo. Za ekonomski razvijena društva dijaliza i transplantacija postaju golem financijski teret, a, s obzirom na porast broja liječenih, taj će financijski teret biti neodrživ za svako društvo. Uzrok porasta KBB-a jest svakako starenje populacije, porast šećerne bolesti, ali i neregulirana arterijska hipertenzija, pretilost, prekomjerno i nekontrolirano trošenje nesteroidnih protuupalnih lijekova i izloženost raznim toksinima iz okoliša.

Kroničnu bubrežnu bolest možemo podijeliti prema stadijima, koje je definirala Inicijativa za procjenu kvalitete ishoda bolesti bubrega (engl. *Kidney Disease Outcomes Quality Initiative*, KDOQI). Razlikujemo pet stadija, koji su određeni procijenjenom glomerularnom filtracijom (engl. *estimated Glomerular Filtration Rate*, eGFR) i indikatorima strukturnih promjena na bubrežima (npr. proteinurija)<sup>13</sup>. Samim mjerenjem eGFR-a možemo detektirati CKB u stadijima 3., 4. i 5., a da bismo otkrili bolest u ranijim stadijima, 1. i 2., potrebno je provesti i mjerenje albumina u mokraći. KBB uzrokuje metaboličke, endokrine, neurološke, kognitivne poremećaje i zatajenje bubrega te je čimbenik kardiovaskularnog rizika, a komplikacije KBB-a zahvaćaju sve organske sustave.

Zadnjih godina sve se više shvaća važnost povezanosti KBB-a i kardiovaskularnog pobola i smrtnosti. Nekoliko je velikih studija opazilo kako je uz KBB zapravo veći rizik od nastanka infarkta miokarda ili moždanog udara nego od započinjanja bubrežnoga nadomjesnog liječenja. Nažalost, KBB je često bez tegoba, biva prepoznata tek u uznapredovalim stadijima, kada je kardiovaskularni rizik još veći. Prema nekim procjenama, nakon kontrole ostalih rizika za razvoj KVB-a, KBB povećava rizik od KVB-a za čak 2–4 puta<sup>14</sup>. Također,

Cardiovascular diseases are the leading cause of deaths and DALYs associated with elevated BMI (52.4 %), while CKD ranks second as a cause of DALYs due to increased BMI (24.4 %)<sup>1</sup>.

Obesity is one of the major risk factors for development of CKD. Besides its indirect effects as the cause of diabetes mellitus and arterial hypertension that subsequently influence development of CKD, obesity has been demonstrated to act also as an independent risk factor for CKD. In overweight individuals, compensatory hyperfiltration occurs to enable the body to cope with the increased metabolic requirements. This in turn results in increased intraglomerular pressure, which may lead to kidney damage and at long term to the development of CKD. The amount of visceral fat in the body has been shown to be a risk factor for development and poorer outcome of CKD independently of BMI<sup>10</sup>. Obesity doubles the risk of CKD relative to the normal nutritional status. Overweight is associated with an increased risk of renal calculi and kidney carcinoma<sup>11</sup>.

## Epidemiology of chronic kidney disease

Chronic kidney disease currently is a major public health problem due to its ever-growing prevalence, and consequentially for the increasing need of renal replacement therapy (RRT) with dialysis and transplantation. It is estimated that about 10 % of the European population suffer from CKD<sup>12</sup>. Treatment by RRT is associated with lower quality of life and life expectancy in these patients, as well as great financial burden upon the society. In industrialized countries, dialysis and transplantation impose huge financial burden, which will become unsustainable considering the steady increase in the number of these patients. The increase in the prevalence of CKD certainly is caused by the population aging, increase in the prevalence of diabetes mellitus, as well as uncontrolled arterial hypertension, obesity, excessive and unreasonable use of nonsteroidal anti-inflammatory drugs, and exposure to various environmental toxins.

Chronic kidney disease can be classified according to stages defined by the Kidney Disease Outcomes Quality Initiative (KDOQI). There are 5 stages as determined by the estimated glomerular filtration rate (eGFR) and indicators of the kidney structural changes (e.g., proteinuria)<sup>13</sup>. CKD stages 3, 4 and 5 can be detected solely by eGFR determination, whereas detection of earlier CKD stages 1 and 2 also requires determination of urine albumin. CKD causes metabolic, endocrine, neurologic and cognitive disorders, as well as renal failure, and is a cardiovascular risk factor, whereas CKD complications involve all the organ systems in the body.

In recent years, the association of CKD with cardiovascular morbidity and mortality has been ever better understood. Several large studies have shown that the risk of myocardial infarction or stroke in association with CKD outweighs the risk of initiating RRT. Unfortunately, the presence of CKD is frequently asymptomatic, and it is only recognized in advanced stages when the cardiovascular risk is even higher. According to some estimates, after control of other cardiovascular risk factors has been achieved, CKD increases this risk twofold to even fourfold<sup>14</sup>. In addition, in CKD stages 1 and 2 the cardiovascular risk is identical to the risk associated with CKD stage 3, emphasizing the importance of early detection

rizik od KVB-a u stadijima 1. i 2. jednak je riziku u stadiju 3., što ističe važnost ranog otkrivanja bolesti te povećava financijsku isplativost probirnih programa za KBB<sup>12</sup>.

KBB u ranim stadijima ne uzrokuje simptome, zbog čega je često neprepoznata, te je teško dobiti pouzdane podatke o njezinoj prevalenciji. Nedavno provedena metaanaliza za procjenu globalne prevalencije analizirala je podatke iz stotinu istraživanja, koja su uključila 112 različitih populacija. Procijenjena globalna prevalencija KBB-a u svim je stadijima 13,5 % (prema podacima za 44 populacije), dok je procijenjena prevalencija bolesti u stadijima 3.–5. iznosila 10,6 % (prema podacima za 68 populacija). Analizirani su i podatci o prevalenciji po stadijima, iz svih uključenih istraživanja te je dobivena prevalencija od 3,5 % za stadij 1., 3,9 % za stadij 2., 7,6 % za stadij 3., 0,4 % za stadij 4. te 0,1 % za stadij 5.<sup>13</sup>

Provedena regresijska analiza povezanosti prevalencije KBB-a s dobi, prevalencijom arterijske hipertenzije, dijabetesa, pretilosti, prosječnog ITM-a i pušenja pokazala je kako su starija dob te prevalencija hipertenzije i dijabetesa u većini populacija bili pozitivno povezani s prevalencijom KBB-a. Pretilost i prosječan ITM nisu bili znatno povezani s prevalencijom KBB-a, a pušenje je pokazalo negativnu povezanost (međutim, ovakva je povezanost poništena isključivanjem outlier istraživanja, u kojemu je zbog niske odsječne vrijednosti za definiranje pušača u uzorku bilo čak 69,1 % pušača)<sup>13</sup>.

Spolna raspodjela pokazuje kako je prevalencija nešto viša u žena. U istraživanjima koja su se koristila svim stadijima KBB-a prevalencija u muškaraca iznosila je 12,8 %, a prevalencija u žena 14,6 %. U studijima s podacima za stadije 3.–5. prevalencija u muškaraca iznosila je 8,1 %, a prevalencija u žena 12,1 %<sup>13</sup>.

## Kronična bubrežna bolest u Hrvatskoj

Podatci o prevalenciji KBB-a u Hrvatskoj ne postoje, a veličinu problema možemo prikazati pokazateljima izrađenima iz rutinske zdravstvene i mortalitetne statistike. Po broju umrlih, skupina bolesti sustava mokraćnih i spolnih organa na devetom je mjestu s 1072 umrle osobe u 2015. godini, od toga 494 osobe umrle su zbog bubrežnog zatajenja (**Tablica 1**). Prema broju hospitalizacija, bolesti sustava mokraćnih i spolnih organa na sedmom su mjestu s 36 542 hospitalizacije, od toga 6 605 hospitalizacija zbog bubrežnog zatajenja (**Tablica 2**). Prema broju utvrđenih bolesti i stanja zabilježenih u djelatnosti obiteljske medicine, nalaze se na četvrtome mjestu s 597 997 slučajem ili udjelom od 5,3 % u ukupnome broju utvrđenih stanja na razini primarne zdravstvene zaštite te 13 859 zabilježenom dijagnozom bubrežnog zatajenja (**Tablica 3**). Treba napomenuti kako podatci o bolestima i stanjima u primarnoj zdravstvenoj zaštiti ne mogu poslužiti za određivanje preva-

of the disease and increasing cost-effectiveness of the CKD screening programs<sup>12</sup>.

Chronic kidney disease in early stages is free from symptoms and therefore frequently unrecognized; that is why it is quite difficult to collect reliable data on its true prevalence.

A recent meta-analysis aiming at assessment of the global prevalence of CKD included data from 100 studies conducted in 112 different populations. The estimated global prevalence of CKD in all studies was 13.5 % (based on data on 44 populations), whereas the estimated prevalence of CKD stages 3-5 was 10.6 % (based on data on 68 populations). Data on the CKD prevalence according to stages in all the studies involved in the analysis yielded a prevalence of 3.5 % for stage 1, 3.9 % for stage 2, 7.6 % for stage 3, 0.4 % for stage 4, and 0.1 % for stage 5<sup>13</sup>.

Regression analysis of the correlation of CKD prevalence with age, arterial hypertension, diabetes mellitus, obesity, mean BMI and smoking habit showed positive correlation of CKD with older age, hypertension and diabetes mellitus in most of the study populations. Obesity and mean BMI were not significantly associated with CKD prevalence, whereas smoking habit showed negative correlation (however, the latter was annulled by excluding an outlier study where the low cut-off for defining smokers resulted in as many as 69.1 % of smokers in the sample)<sup>13</sup>.

Gender distribution shows the prevalence of CKD to be higher in women. In the studies involving all CKD stages, the prevalence was 12.8 % and 14.6 % in men and women, respectively. In the studies on CKD stages 3-5, the respective figures were 8.1 % and 12.1 %<sup>13</sup>.

## Chronic kidney disease in Croatia

There are no data on the prevalence of CKD in Croatia but the magnitude of the problem can be illustrated by use of indicators derived from routine healthcare and mortality statistics. Diseases of the urinary and sexual systems rank ninth by the number of deaths with 1072 dead patients in 2015, of which 494 patients died from renal failure (**Table 1**). The same group of diseases ranks seventh by the number of hospitalizations with 36,542 hospitalizations, of which 6605 hospitalizations were due to renal failure (**Table 2**). This group of diseases ranks fourth by the number of diseases and conditions recorded in family medicine offices with 597,997 cases, accounting for 5.3 % of the diseases and conditions established at primary healthcare level, of which 13,859 cases were diagnosed with renal failure (**Table 3**). It should be noted that data on diseases and conditions recorded at primary healthcare level cannot be used for determination of particular disease prevalence but only for providing an insight into the frequen-

**TABLE 1. Diseases of the genitourinary systems mortality of in Croatia, 2015.**

Diseases and related health problems, ICD-10	Code	Number	Ratio (%)
Renal failure	N17-N19	494	0.91%
Diseases of the genitourinary systems	N00-N99	1072	1.98%
Total, diseases and conditions	A00-Z99	54205	100%

Source: Croatian Institute of Public Health, Croatian Central Bureau of Statistics.

**TABLE 2. Diseases of the genitourinary systems hospitalizations in Croatia, 2015.**

Diseases and related health problems, ICD-10	Code	Number	Ratio (%)
Renal failure	N17-N19	6605	1.1%
Diseases of the genitourinary systems	N00-N99	36542	6.2%
<i>Total, diseases and conditions</i>	<i>A00-Z99</i>	<i>589215</i>	<i>100%</i>

Source: Croatian Institute of Public Health.

lencije pojedinih bolesti, nego samo kao uvid u kretanje učestalosti korištenja zdravstvenom zaštitom u djelatnostima primarne zdravstvene zaštite zbog pojedinih bolesti i stanja.

Prema rezultatima Europske zdravstvene ankete (EHIS)<sup>4</sup>, rađenoj 2014.–2015. godine u Hrvatskoj, na populaciji stanovnika starijih od 15 godina, probleme s bubrežima navodi 3,2 % muškaraca i 5,6 % žena. Podatci o bolestima prikupljeni su prema izjavama samih ispitanika o tome jesu li u zadnjih 12 mjeseci imali neku od bolesti.

cy of healthcare utilization at the primary healthcare level for a particular disease or condition.

According to the results of EHIS<sup>4</sup> conducted in Croatia in 2014-2015 on a population older than 15, kidney problems were reported by 3.2 % of male and 5.6 % of female subjects. Data on renal diseases were collected from participant reports on having suffered from some of these diseases in the past 12 months.

**TABLE 3. Diseases of the genitourinary systems diagnosed by the primary health care, Croatia, 2015.**

Diseases and related health problems, ICD-10	Code	0-6	7-19	20-64	65 and older	Total
Glomerular diseases	N00-N08	104	318	2693	1525	4640
Renal tubulo-interstitial diseases	N10-N16	2112	1172	7055	4813	15152
Renal failure	N17-N19	21	86	4123	9629	13859
Urolithiasis	N20-N23	16	678	26486	9621	36801
Cystitis	N30	8131	14894	126291	72835	222151
Other disorders of kidney and ureter (excluding N30)	N25-N39	5424	5778	48501	30189	89892
Hyperplasia of prostate	N40	0	0	25223	53415	78638
Other disorders of male genital organs	N41-N51	7655	4515	26190	10170	48530
Menopausal and other perimenopausal disorders	N95	0	0	1515	337	1852
Other disorders of female genital organs		1753	8109	60682	15938	86482
Diseases of the genitourinary systems	N00-N99	25216	35550	328759	208472	597997
<i>Total, diseases and conditions</i>	<i>A00-Z99</i>	<i>1129098</i>	<i>1315526</i>	<i>5613549</i>	<i>3209196</i>	<i>11267369</i>

Source: Croatian Institute of Public Health.

Prema podacima Hrvatskog registra za nadomještanje bubrežne funkcije na kraju 2014. godine u Hrvatskoj su 4102 osobe živjele uz pomoć nadomještanja bubrežne funkcije (NBF), što je 4,3 % manje nego prethodne godine. Udio bolesnika s presađenim bubrega narastao je za 5,2 % u odnosu prema prethodnoj godini, dok se postotak hemodijaliziranih smanjuje od 2007. godine. Populacija na NBF raste upravo zbog povećavanja broja bolesnika s transplantacijom, a usprkos smanjenju broja bolesnika liječenih hemodijalizom i peritonejskom dijalizom<sup>15</sup>.

## Mogućnosti prevencije

Alternativa epidemiji KBB-a, uznapređovanim oblicima renalne insuficijencije i povećanom mortalitetu jest rano otkrivanje KBB-a i primjena preventivnih i terapijskih mjera za usporavanje ili zaustavljanje progresije bolesti. Otkrivanje bolesti u ranijim stadijima omogućuje njezinu pravodobnu kontrolu i

According to data from the Croatian Register of Renal Replacement Therapy, at the end of 2014 there were 4102 persons in Croatia on RRT, which was by 4.3 % less than the year before. The share of patients with kidney transplant has increased by 5.2 % as compared with previous year, whereas the percentage of hemodialysis patients has been on a decrease since 2007. The population on RRT is on increase because of the growing number of transplanted patients, despite reduction in the number of patients treated with hemodialysis and peritoneal dialysis<sup>15</sup>.

## The possibilities of CKD prevention

An alternative to the epidemic of CKD, advanced forms of renal insufficiency and increased mortality is early detection of CKD and use of preventive and therapeutic measures to slow down or halt progression of the disease. Detecting the disease in its early stages allows for its timely control while reducing

smanjuje šanse da će nastupiti kronično zatajenje bubrega te potreba za dijalizom i presađivanjem tog organa<sup>12</sup>.

U nekim od europskih zemalja postoje programi ranog otkrivanja KBB-a, međutim, razlikuju se po dijagnostičkim metodama kojima se koriste, graničnim vrijednostima eGFR-a te uključenoj populaciji. Najčešće ciljne skupine u tim programima jesu oboljeli od dijabetesa, starije osobe te osobe s hipertenzijom. Problem s ovakvim pristupom jest u tome što, prema nekim procjenama, na svakog pojedinca s dijagnostičiranom hipertenzijom ili dijabetesom dolazi još jedna osoba kojoj navedene bolesti nisu dijagnosticirane, ali su već uzrokovale oštećenja organa<sup>12</sup>. Također, uporaba eGFR-a kao jedine dijagnostičke metode ne pomaže nam otkriti pojedince u ranijim stadijima bolesti, kada je intervencija od velike važnosti u smislu sprečavanja daljnjeg razvoja bolesti. Naime, prevalencija KBB-a najviša je u prvim trima stadijima, a procjena eGFR-a otkriva bolest od 3. stadija i dalje. Stoga bi u programe probira trebalo uključiti i kontrolu albuminurije. Prema istraživanju rezultata programa probira za KBB u Norveškoj, Nizozemskoj i Španjolskoj, prevalencija iznosi od 5,1 do 7 % za stadije 1 i 2 promatrane zajedno, od 4,5 do 5,3 % za stadij 3. te od 0,1 do 0,4 % za stadij 4.<sup>12</sup> Isto tako, nužno je provoditi edukaciju i podizanje svjesnosti populacije o problemu KBB-a, osobito rizičnih skupina, o čimbenicima rizika i mogućnostima prevencije. Poseban naglasak treba staviti na edukaciju o zdravim životnim navikama, kao primarnoj prevenciji, kako se bolest ne bi niti razvila.

Prekomjerna tjelesna težina i pretilost, kao i bolesti koje uzrokuju u velikoj su mjeri preventabilne, međutim, bez obzira na znanja i mogućnosti koja danas postoje, u suzbijanju epidemije pretilosti rezultati se teško postižu. Naime, problem pretilosti nije moguće riješiti na razini pojedinca i zdravstvenog sustava, nego društva u cjelini, a osobito prehrambene industrije, te okoliša koji podržava zdravi način života. Zemlje koje duži niz godina provode sveobuhvatne i sustavne programe prevencije debljine i drugih čimbenika rizika imaju manji pobol i smrtnost od najčešćih kroničnih bolesti.

Kako bi se preventivni programi mogli sustavno provoditi, potrebni su prvo zakonski i strateški dokumenti zdravstvene politike. Što se tiče pretilosti, Hrvatska je donijela niz strateških dokumenata, no još uvijek neki bitni dokumenti nisu doneseni. Akcijski plan za prevenciju i smanjenje prekomjerne tjelesne težine donesen je za razdoblje od 2010. do 2012. te u ovome trenutku ne postoji plan prevencije i kontrole debljine u Republici Hrvatskoj. Nacionalne smjernice za prehranu učenika u osnovnim školama donesene su 2013., međutim, nadzor nad primjenom izostaje, a planirane Nacionalne smjernice za prehranu radno aktivne populacije za sada su još u pripremljenoj fazi. Tijekom 2014. pokrenut je Nacionalni program „Živjeti zdravo“ koji se sastoji od komponenti zdravstvenog obrazovanja, zdravstvenog turizma, zdravlja i prehrane, zdravlja i radnoga mjesta, zdravlja i okoliša te mreže centara za promicanje zdravlja „Živjeti zdravo“, uključujući i ona za pravilnu prehranu i tjelesnu aktivnost. Izrađen je prilog Akcijskoga plana za prevenciju i nadzor nad kroničnim nezaraznim bolestima, koji uključuje suzbijanje, odnosno prevenciju čimbenika rizika, uključujući nepravilnu prehranu i debljinu, ali još uvijek nije donesen.

Dosadašnja provedena istraživanja o učestalosti tjelesne (ne)aktivnosti u Hrvatskoj upućuju da oko 60 % odrasle populacije ne sudjeluje ni u kakvom obliku tjelesnoga vježbanja. Unatoč velikomu javnozdravstvenom problemu kakav tje-

the likelihood of chronic renal failure and the need for dialysis and kidney transplantation<sup>12</sup>.

Some European countries have developed programs of early CKD detection, but they vary in the diagnostic methods used, borderline eGFR values employed, and populations involved. In these programs, the most common target groups are diabetic patients, elderly, and those with hypertension. However, a pitfall of this approach is that, according to some estimates, *per* each individual diagnosed with hypertension or diabetes mellitus there is another one in whom hypertension or diabetes mellitus has not yet been diagnosed but has already caused damage to the organs<sup>12</sup>. Employing eGFR as the only diagnostic method is of no use in detecting individuals in early stages of the disease when timely intervention is of crucial importance to prevent progression of the disease. In fact, the prevalence of CKD is highest in the first three stages of the disease, whereas eGFR determination can only detect  $\geq$ stage 3 CKD. Therefore, follow up determination of albuminuria should also be included in the CKD screening programs. According to the study that assessed the results of CKD screening programs in Norway, The Netherlands and Spain, the prevalence of pooled CKD stages 1 and 2 ranges from 5.1 % to 7 %, of stage 3 it is 4.5 %–5.3 %, and of stage 4 it is 0.1 %–0.4 %<sup>12</sup>. It is also necessary to perform education and to increase population awareness of the CKD problem, as well as of the risk factors and possibilities of prevention, in particular among the groups at risk. Special emphasis should be put on education about healthy lifestyles as primary prevention, so that the disease would not develop at all.

Overweight and obesity, as well as the disease they cause, are preventable to a great extent; however, favorable results in halting the epidemic of obesity are hard to achieve irrespective of the ever better knowledge and options currently available. The problem of obesity cannot be solved at the level of the individual and healthcare system but at the level of society as a whole, in particular food industry and environment sustaining healthy lifestyle. The countries where comprehensive and systematic programs of prevention of obesity and other risk factors have been implemented for years have lower morbidity and mortality rates of the most common chronic diseases.

Systematic performance of the programs of prevention firstly requires legal and strategic healthcare policy documents. Concerning obesity, Croatia has passed a series of strategic documents; however, some crucial documents have not yet been enacted. Action plan for the prevention and reduction of overweight was passed for the 2010-2012 period, so currently there is no plan of prevention and control of obesity in Croatia. National guidelines for the nutrition of elementary school children were enacted in 2013, however, there is no surveillance of its implementation, whereas the planned national guidelines for the nutrition of working population are still in the preliminary phase. In 2014, the *Živjeti zdravo* (Living Healthy) national program was launched, consisting of the following components: health education; health tourism; health and diet; health and work place; health and environment; and a network of the *Živjeti zdravo* (Living Healthy) centers for health promotion, including those on appropriate diet and physical activity. A proposal of the action plan for prevention and surveillance of chronic non-communicable diseases has been designed, including control and prevention of the risk factors such as unfavorable dietary habits and obesity; however, this action plan has not yet been enacted.



lesna neaktivnost znači u Hrvatskoj, do sada nisu doneseni strateški dokumenti koji bi osigurali preduvjete za učinkovitu borbu i unapređenje u navedenom području.

Stoga možemo zaključiti, kako u nas nedostaju neki bitni strateški dokumenti na razini države koji bi omogućili sustavnu provedbu programa prevencije kroničnih bolesti, kao i rano otkrivanje, uz odgovarajuće ljudske i financijske resurse, odnosno kapacitete za provedbu.

Studies of the prevalence of physical (in)activity conducted in Croatia indicate that about 60 % of the adult population are not involved in any form of physical activity. In spite of the great public health problem posed by physical inactivity in Croatia, no strategic documents to provide preconditions for efficient efforts and promotion in the area have been enacted so far.

Accordingly, it is concluded that some relevant strategic documents to enable systematic implementation of the program of prevention and early detection of chronic diseases are lacking at the national level, and so are the respective human and financial resources to ensure necessary capacities for its implementation.

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