VPLYV NADVÁHY A OBEZITY NA RIZIKO VZNIKU RAKOVINY V ČESKEJ POPULÁCII

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THE IMPACT OF OVERWEIGHT AND OBESITY ON THE RISK OF DEATH FROM CANCER IN THE CZECH POPULATION

Abstract

The article analyses the population's attributable mortality risk on selected malignant neoplasms in 2016 that could be attributed to excessive BMI in the Czech population, taking into account the eight-year gap between exposure and cancer mortality by gender. In Czechia there were 1,902 deaths in 2016 (7% of all malignant neoplasm cases) diagnosed as due to one of the selected types of neoplasms as a result of a long-term high BMI.

Keywords: Czechia, Body Mass Index, cancer, mortality

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ÚVOD

Zvýšený index telesnej hmotnosti jedinca, inými slovami nadváha (BMI ≥ 25kg/m^2) a obezita (BMI ≥ 30kg/m^2) majú medzi faktormi ovplyvňujúcimi zdravie populácie špecifické postavenie. Ide o nadmerné akumulovanie tuku v tele jedinca, ktorého hromadenie ovplyvňuje napríklad životný štýl, nutričné zvyklosti ale aj dedičnosť alebo sociálno-ekonomický status.

Nadváha a obezita predstavujú v súčasnosti závažný problém verejného zdravia a to práve z dôvodu ich neustále zvyšujúcej sa prevalencie (*WHO, 2018*). Nakoľko existujú veľké rozdiely v prevalencii, nadváha a obezita vo väčšine populácií neustále narastá (*Stevens a kol., 2012*). Od roku 1980 do 2016 sa prevalencia nadváhy a obezity celosvetovo takmer strojnásobila, pričom v roku 2016 nadváhou trpelo 39 % dospelej populácie (39 % mužov; 40 % žien), čo predstavovalo viac ako 1,9 miliárd ľudí. Celkovo môžeme konštatovať, že približné 13 % svetovej populácie (11 % mužov; 15 % žien) bolo v roku 2016 obéznych (*Kaidar-Person a kol., 2011; WHO, 2018*).

Zvýšená prevalencia nadváhy a obezity je znateľná aj vo väčšine európskych krajinách. Medzi štáty s najvyššou prevalenciou obezity patrí napríklad aj Maďarsko (21 %), Slovinsko (19 %), Poľsko (17 %) alebo Slovensko (16 %). Ku krajinám s najvyššou prevalenciou radíme však aj Česko (19 %) (*Eurostat, 2014*). Do roku 2030 sa dokonca predpokladá, že prevalencia obezity vzrastie až na 37 % u českých žien a na 36 % u mužov (*WHO, 2013*).

Nadváha a obezita sú modifikovateľné rizikové faktory ovplyvňujúce množstvo chronických ochorení, vrátane diabetu 2. typu a kardiovaskulárnych chorôb. Nadváha a obezita sú tiež spojené s výskytom rakoviny (*WHO, 2018*). Existuje dokonca niekoľko dôkazov, ktoré vysvetľujú vzťah medzi vysokým indexom telesnej hmotnosti a rizikom vzniku rakoviny. Napríklad vieme, že tukové bunky uvoľňujú hormóny ako je

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estrogén. Vysoká hladina estrogénu môže zvýšiť riziko vzniku rakoviny prsníka alebo maternice[3]. Zároveň, príliš vysoké percento telesného tuku spôsobuje inzulínovú rezistenciu, čo povzbudzuje telo k produkcii rastových hormónov. Vysoké hladiny týchto hormónov následne môžu podporiť vznik nádorových ochorení ako napríklad zhubný novotvar hrubého čreva, obličiek alebo endometria (*WCRF, 2016*). Nadmerný telesný tuk tiež stimuluje zápalové procesy. Predovšetkým chronický zápal môže v priebehu času spôsobiť poškodenie DNA, ktoré môže následne viesť k zvýšenému riziku vzniku rakoviny. Napríklad chronický lokálny zápal vyvolaný gastroezofageálnym refluxom alebo Barrettovým pažerákom je pravdepodobnou príčinou adenokarcinómu pažeráka (*Arnold a kol., 2015*). Obezita je tiež rizikovým faktorom vzniku žlčových kameňov, ktoré sú silným rizikovým faktorom zhubného novotvaru žlčníka (*Renehan a kol., 2010*).

To, že BMI je dôležitým prediktorom pre vznik chronických ochorení, vrátanie rôznych typov rakoviny, potvrdzujú viaceré výskumy (*Calle, 2003; Marmot a kol., 2007*). V roku 2002 dokonca „Medzinárodná agentúra pre výskum rakoviny" (IARC) dospela k záveru, že zamedzenie nadváhy a obezity znižuje riziko vzniku zhubného novotvaru hrubého čreva, obličiek[4], pažeráka[5] alebo postmenopauzálnej rakoviny prsníka (*IARC, 2002*). V roku 2007 IARC výsledky o príčinnom vzťahu medzi zvýšeným BMI a vznikom daných typov zhubných novotvarov len potvrdila (*WCRF, 2013*). Táto asociácia bola potvrdená taktiež metaanalýzou observačných štúdií (*Rehenan a kol., 2008*), u ktorých bola pozitívna súvislosť aj s inými typmi rakoviny (rakovina štítnej žľazy a pečene[6]). U prítomnosti obezity sa dokonca uvádza 1,5 až 3,5krát vyššie riziko vzniku rakoviny ako u osôb s normálnymi hodnotami BMI (*Anderson a kol., 2015*).

Podľa nedávnych odhadov z projektu „Global burden of disease" sa 3,9 % úmrtí na rakovinu v roku 2010 môže pripísať práve zvýšenému BMI (*Lim a kol., 2012*). Tento odhad však nezohľadnil dobu expozície nadmerného BMI, ktorá by mohla viesť k vývoju nových prípadov rakoviny (*Parkin a kol., 2014*). V podobnej štúdii, kde však autori dobu expozície už zohľadnili, celosvetovo odhadovali, že 3,6 % všetkých nových prípadov rakoviny u dospelých (vo veku 30 rokov a starších po 10ročnom období oneskorenia) v roku 2012 bolo možné pripísať práve vysokému BMI. Populačná atributívna frakcia (PAF) bola dokonca vyššia u žien (5 %) ako u mužov (2 %) (*Arnold a kol., 2015*).

Autorka Howardová *(2016)* uvádza, že obezita u populácie pretrvávajúca po dobu desiatich rokov zvyšuje riziko zhubného novotvaru prsníka o 5 % a tela maternice, konkrétne endometria o 17 %. Obdobie desiatich rokov sa vo väčšine prípadov uvádza ako „priemerná" doba oneskorenia vzniku rakoviny súvisiacej s obezitou. Toto obdobie však môže byť aj kratšie (*Renehan a kol., 2010*). Celkovo, ale len niekoľko štúdií skúmalo súvislosť medzi trvaním nadváhy, obezity a následným vznikom rakoviny. Nie je teda jasné, aká dlhá expozícia nadváhe a obezite je spojená so vznikom rakoviny (*Abdullah a kol., 2011; Stolzenberg-Solomon a kol., 2013; Bjørge a kol., 2008; Arnold a kol., 2015*).

Viacero výskumov uvádza taktiež rozdielne pôsobenie zvýšenej hladiny BMI na intenzitu úmrtnosti podľa pohlavia. Dôkazy ukazujú skôr nekonzistentné výsledky. Jedna štúdia napríklad ukázala významnú závislosť medzi BMI a zvýšeným rizikom kolorektálneho zhubného novotvaru u mužov i žien (*Alexandrova a kol., 2014*), zatiaľ čo u inej štúdie bolo zistené zvýšené riziko len u mužov (*Kitahara a kol., 2013*). Ako dôvod sa uvádzal predpoklad, že rozdiely medzi pohlavím sú spôsobené odlišnou distribúciou tuku v tele a rôznym hormonálnym systémom u mužov a žien (*Calle a kol., 2003*).

My sme sa preto snažili odhadnúť počet a podiel úmrtí na konkrétne typy zhubných novotvarov (ZN) v roku 2016, ktoré by sa mohli pripísať nadmerným hodnotám BMI u českej populácie a to s prihliadnutím na 8ročné rozpätie medzi expozíciou (nadmerným BMI) a úmrtnosťou na rakoviny podľa pohlavia. Pričom, odhad počtu a podielu úmrtí bol realizovaný na základe dostupne publikovaných záverov resp. metaanalýzy Bergström a kol. (*2001*).

3) Maternica v češtine znamená děloha.

4) Oblička v češtine znamená ledvina.

5) Pažerák v češtine znamená jícen.

6) Pečeň v češtine znamená játra.

METODIKA A DATA

Predkladajúci výskum odhaduje vplyv nadváhy (BMI ≥ 25kg/m^2) a obezity (BMI ≥ 30kg/m^2) na intenzitu úmrtnosti zhubných novotvarov v Česku v roku 2016 podľa pohlavia. Analyzovali sme ho pomocou populačnej atributívnej frakcie (PAF), ktorú sme vypočítali pomocou nasledujúceho vzorca:

$$\text{PAF} = \frac{\sum_i p_i(RR_i - 1)}{\sum_i p_i RR_i} \quad .$$

Kde p_i je rozloženie populácie podľa kategórií BMI (i) a *RRi* je relatívne riziko úmrtí na rakovinu súvisiacu s kategóriou BMI (i) prevzaté zo štúdie Bergström a kol. (2001). Špecifická PAF pre pohlavie bola vypočítaná pre jednotlivé typy zhubných novotvarov súvisiacich s obezitou. Následné vynásobenie PAF skutočnými počty zomrelých na sledované typy zhubných novotvarov nám umožňuje odhadnúť počty zomrelých na rakovinu v dôsledku zvýšeného BMI. Ide o hypoteticky pomerné zníženie počtu úmrtí, ku ktorým by došlo, keby sa expozícia rizikovému faktoru znížila na alternatívne ideálny expozičný scenár (*WHO, 2018*), v našom prípade neexistencie nadváhy a obezity v populácii.

Vychádzali sme z troch dátových zdrojov, pričom medzi prvý zdroj patrili údaje z výberového šetrenia o zdraví EHIS 2008, o BMI konkrétne o nadváhe a obezite v českej populácii (*UZIS ČR, 2011*). Ako druhý zdroj sme použili počty o úmrtí na vybrané ZN podľa pohlavia z demografickej ročenky 2016 (*ČSÚ, 2017*), čím sme predpokladali 8ročné obdobie latencie medzi expozíciou a úmrtnosťou na vybrané ZN. Obdobie latencie sme si zvolili predovšetkým na základe dostupných dát. Aj napriek tomu, že „priemerná" doba oneskorenia vzniku rakoviny súvisiacej s obezitou je vo väčšine prípadov uvádzaná ako 10ročné obdobie, toto obdobie môže byť aj kratšie (*Renehan a kol., 2010*). Medzi posledný zdroj sme zaradili odhad relatívneho rizika (RR), kde sme použili údaje z metaanalýzy od autorov *Bergström a kol. (2001)*, ktoré je možné aplikovať ako pre mužov, tak ženy. Relatívne riziká pre jednotlivé ZN používané v našich odhadoch sú uvedené v Tabuľke 1 a sú rovnaké naprieč vekovými kategóriami. Relatívne riziko uvádza o koľko je vyššie riziko porovnaní s osobami s hodnotou BMI v norme. Kódy uvedené u jednotlivých diagnóz odpovedajú 10. revízii Medzinárodnej klasifikácie nemocí (MKCH10).

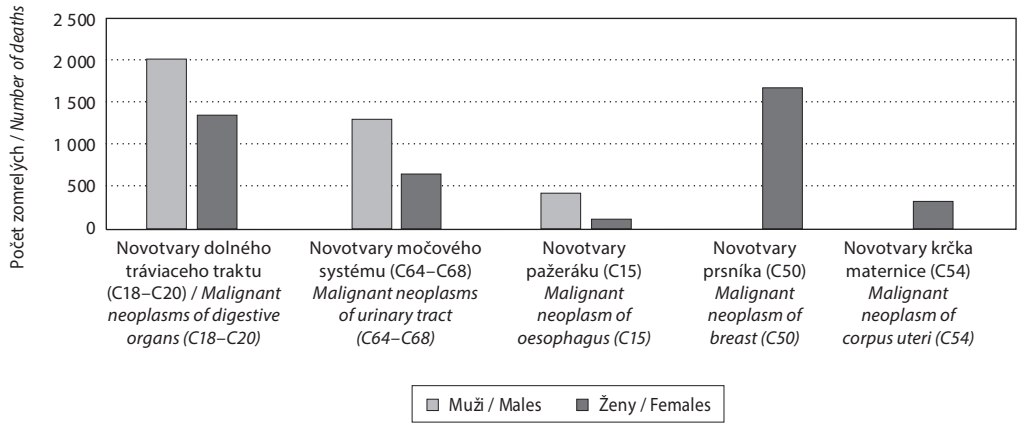
Zhubné novotvary, medzi ktorými sme analyzovali väzbu k zvýšenému BMI boli: ZN pažeráka (C15), hrubého čreva (C18), rektosigmoidového spojenia (C19), konečníka (C20) (ďalej iba ZN dolného tráviaceho traktu C18–C20), obličiek okrem obličkovej panvičky (C64), obličkovej panvičky (C65), močovodu (C66), močového mechúra (C67), iných bližšie nešpecifikovaných močových orgánov (C68) (ďalej iba ZN močového systému C64–C68), tela maternice (C54) a prsníka (C50) v postmenopauze[7]. Vzťah medzi nami vybranými ZN a zvýšeným BMI zároveň potvrdzuje aj World Cancer Research Fund International (*WCRF, 2012*).

Tab. 1: Relatívne riziko (RR) vzniku zhubných novotvarov v dôsledku nadváhy a obezity
Relative risk (RR) of malignant neoplasms associated with overweight and obesity

Typy zhubných novotvarov ***Selected malignant neoplasms***	**RR / Nadváha** ***RR / Overweight***	**RR / Obezita** *RR / Obesity*
Zhubné novotvary dolného tráviaceho traktu (C18–C20) *Malignant neoplasms of the digestive organs (C18–C20)*	1,15	1,33
Zhubné novotvary močového systému (C64–C68) *Malignant neoplasms of the urinary tract (C64–C68)*	1,36	1,84
Zhubný novotvar pažeráka (C15) *Malignant neoplasm of the oesophagus (C15)*	2,00	2,00
Zhubný novotvar prsníka (C50) *Malignant neoplasm of the breast (C50)*	1,12	1,25
Zhubný novotvar tela maternice (C54) *Malignant neoplasm of the corpus uteri (C54)*	1,59	2,52

Zdroj: Prevzaté z Bergström a kol., 2001, str. 425.
Source: *From Bergström et al., 2001, p. 425.*

Graf 1: Počty zomrelých na vybrané zhubné novotvary v Česku podľa pohlavia, 2016
Number of deaths due to selected malignant neoplasms in Czechia by sex, 2016



Zdroj: ČSÚ, 2017.
Source: *ČSÚ, 2017.*

VÝSLEDKY

V českej populácii v roku 2016 zomrelo na zhubné novotvary (MKCH10, dg. C00–C97) 27 261 osôb (15 095 mužov a 12 166 žien). Počty úmrtí na ZN v českej populácii za posledné roky stagnujú. Novotvary, teda dlhodobo zaraďujeme medzi druhú najčastejšiu príčinu úmrtí v Česku, hneď po kardiovaskulárnych ochoreniach a to pre obe pohlavia (*UZIS, 2015*).

Na Grafe 1 môžeme vidieť počty zomrelých v roku 2016 na jednotlivé typy ZN podľa pohlavia, o ktorých sú publikáciami doložené dôkazy, že ich príčinným dôsledkom môže byť práve zvýšená hodnota BMI (*WCRF, 2012*). Zatiaľ čo najviac úmrtí bolo na ZN dolného tráviaceho traktu (C18–C20) ako u mužov (n = 2 042), tak žien (n = 1 358), u ZN pažeráka bol počet úmrtí u mužov 416 prípadov a u žien len 100 prípadov. Počet úmrtí na ZN tela maternice bol 314 prípadov a prsníka 1 685 prípadov (Graf 1).

Odhady priemerného BMI u mužskej populácie v roku 2008 bol 27 kg/m^2. Ženy mali v priemeru index telesnej hmotnosti o niečo nižší ako muži (25 kg/m^2). Celkovo ale môžeme konštatovať, že viac ako polovica respondentov (54 %) trpela zvýšeným indexom telesnej hmotnosti (BMI ≥ 25 kg/m^2). Podľa pohlavia to bolo 62 % mužskej a 47 % ženskej populácie. Zatiaľ čo nadváhou trpelo viac mužov (45 %) v porovnaní so ženami (29 %), prevalencia obezity bola takmer rovnaká (17 % muži; 18 % ženy) (*ÚZIS ČR, 2011*).

V tabuľke 2 môžeme sledovať vplyv nadváhy (BMI ≥ 25kg/m^2) a obezity (BMI ≥ 30kg/m^2) na úmrtnosť vybraných typov ZN v Česku v roku 2016 podľa pohlavia. Odhadujeme, že z celkového počtu úmrtí na zhubné novotvary, 1 902 prípadov z nich by sme mohli pripísať vplyvu vysokého BMI a to za predpokladu 8ročného oneskorenia. To znamená, že 7 % všetkých prípadov ZN bolo spôsobených vysokým BMI, ktorým trpela česká populácia v roku 2008. Podľa pohlavia bol tento podiel (PAF) o niečo vyšší u žien (ženy 8 %, n = 919) ako u mužov (muži 7 %, n = 983). Podľa jednotlivých typov zhubných novotvarov bola najvyššia PAF pre ZN pažeráka (C15). Odhadujeme, že až 50 % z jeho celkového počtu úmrtí by sme mohli pripísať vysokému BMI ako u mužov (n = 208), tak žien (n = 50). Zároveň, približne 1/3 všetkých prípadov úmrtí na ZN močového systému (C64–C68), ako u mužov (33 %, n = 435), tak žien (35 %, n = 230) by sme mohli prisúdiť práve vysokému BMI. Pre ZN dolného tráviaceho traktu (C18–C20) zase 17 % u mužov (n = 340) a 18 % (n = 243) u žien. Pri pozorovaní dvoch najčastejšie vyskytujúcich

7) Obdobie postmenopauzy ženy je veľmi individuálne. Vyskytuje sa z pravidla v rozmedzí 40. až 60. roku veku, pričom priemerný vek je 51 rokov (MenopauseSymptoms, 2018). V našom výskume sme predpokladali, že všetky úmrtí boli v období postmenopauzy, nakoľko až 97 % (n = 1 641) úmrtí v roku 2016 bolo práve vo veku 40 a viac.

Tab. 2: Odhad počtu a podielu úmrtí spôsobených zvýšeným BMI v rámci jednotlivých typov zhubných novotvarov v českej populácii, 2016 / Estimated number and proportion of deaths due to increased BMI in relation to individual types of malignant neoplasms in the Czech population, 2016

Muži / *Males*

Vybrané typy zhubných novotvarov ***Selected malignant neoplasms***	**PAF**	
	n	**%**
Zhubné novotvary dolného tráviaceho traktu (C18–C20) *Malignant neoplasms of the digestive organs (C18–C20)*	340	16,7
Zhubné novotvary močového systému (C64–C68) *Malignant neoplasms of the urinary tract (C64–C68)*	435	33,0
Zhubný novotvar pažeráka (C15) *Malignant neoplasm of the oesophagus (C15)*	208	50,0
Celkom / Total	983	6,5*

Ženy / *Females*

Vybrané typy zhubných novotvarov ***Selected malignant neoplasms***	**PAF**	
	n	**%**
Zhubné novotvary dolného tráviaceho traktu (C18–C20) *Malignant neoplasms of the digestive organs (C18–C20)*	243	17,9
Zhubné novotvary močového systému (C64–C68) *Malignant neoplasms of the urinary tract (C64–C68)*	230	35,1
Zhubný novotvar pažeráka (C15) *Malignant neoplasm of the oesophagus (C15)*	50	50,0
Zhubný novotvar prsníka (C50) *Malignant neoplasm of the breast (C50*	244	14,5
Zhubný novotvar tela maternice (C54) *Malignant neoplasm of the corpus uteri (C54)*	153	48,5
Celkom / Total	919	7,6*

Pozn.: * Podiel odvrátiteľných úmrtí zo všetkých prípadov zhubných novotvarov.
Note: ** The proportion of avoidable deaths in all cases of malignant neoplasms.*

Zdroj: Vlastné výpočty.
Source: *Authors' calculations.*

sa ZN u žien, bola PAF pre ZN tela maternice až 49 % (n = 153) a pre ZN prsníka 15 % (n = 244) (*Tabuľka 2*).

DISKUSIA

V našom predkladajúcom výskume sme analyzovali zaťaženie vysokej hladiny BMI (s 8ročným oneskorením) na úmrtia piatich vybraných typov zhubných novotvarov. Ukázali sme, že 7 % (n = 1 902) z celkového počtu prípadov úmrtí na ZN by sme mohli pripísať chronickej nadváhe a obezite. Podľa pohlavia, z celkového počtu úmrtí na ZN u mužov by sme mohli prisúdiť 7 % (n = 983) prípadov pre vysoký BMI a u žien 8 % (n = 919). Celkovo, najvyššia záťaž v roku 2016 v českej populácii pre vysoký BMI môžeme pozorovať u ZN pažeráka, kde ako u mužov, tak žien je až 50 % prípadov úmrtí zapríčinených vysokou telesnou hmotnosťou. Zároveň, z celkového počtu úmrtí u mužov na ZN močového systému až 33% prípadov bolo zapríčinené vysokým BMI a 35% prípadov u žien. Podobné výsledky uvádza aj jedna z mála štúdií, ktoré sa danou problematikou zaoberala. Vo Francúzku bola PAF vyššia rovnako u žien ako u mužov (PAF, muži = 4 %; PAF, ženy = 7 %), pričom najviac prípadov spojených s vysokým BMI sa taktiež uvádzalo pre ZN pažeráka (37 %) a tela maternice (34 %) (*Arnold a kol., 2017*). Iné štúdie však vo svojich analýzach

ukazujú, že aj ďalšie typy rakovín ako napr. štítna žľaza (*Zakaria a Shaw, 2017*), žlčník alebo pankreas (*Li a kol., 2016; Vainio, 2002*; *Parkin a Boyd, 2011*), ktoré nie sú v tejto štúdii zahrnuté, majú dostatočné dôkazy o spojení s nadmernou telesnou hmotnosťou. Môžeme teda konštatovať, že výsledky atributívnej frakcie zhubných novotvarov zapríčinených vysokým BMI sú pravdepodobne podhodnotené ďalšími typmi zhubných novotvarov, u ktorých sa súvislosť so zvýšenou hladinou BMI zatiaľ nepotvrdila. To môže byť ale zároveň podnet do ďalších analýz.

Podiel úmrtí vybraných ZN u žien, ktorý predstavoval takmer o 1 percentný bod úmrtí viac ako u mužov môžeme pripísať tomu, že chronická obezita negatívne ovplyvňuje dva najfrekventovanejšie novotvary u žien a to ZN tela maternice a prsníka. Potvrdzujeme to nie len v našej analýze, kedy odhadujeme, že vysoká hladina BMI by mohla zapríčiniť až 49 % (n = 153) prípadov úmrtí na ZN tela maternice a 15 % (n = 244) prípadov ZN prsníka u žien, ale aj viacero predošlých štúdií (*Arnold a kol., 2016; Taghizadeh a kol., 2015*). Zatiaľ, čo presný čas oneskorenia medzi expozíciou vysokého BMI a nástupom rakoviny zostáva do značnej miery neznámy, pravdepodobne bude ovplyvnený práve lokalizáciou rakoviny (*Romieu a kol., 2017*). Naopak, pre porovnanie ako zaujímavý poznatok môžeme spomenúť tzv. krátkodobý prírastok hmotnosti. Štúdia *El-Bastawissiho (2005)* uvádza, že vyššia telesná hmotnosť, konkrétne v tehotenstve je naopak skôr ochranným ako rizikovým faktorom pre vznik rakoviny prsníka u ženy. Podobný prípad je uvádzaný aj u fajčiarov, kedy zase môže dôjsť k nárastu hmotnosti v dôsledku ukončenia fajčenia, čo naopak znižuje riziko novotvaru súvisiaceho s fajčením (*Fernández a kol., 2012*).

Obezita je všeobecne považovaná za iniciátor rakoviny. Ide o následok trvalo energetickej nerovnováhy v čase, ktorý je ovplyvnený individuálnymi voľbami nerozlučne spojenými so životným prostredím, čo následne ovplyvňuje kvalitu stravovania a aktivity. Okrem toho je ale chronická obezita kauzálne spájaná aj s funkčnými poruchami organizmu, zníženou kvalitou života a ochoreniami ako napr. diabetes, ktorý taktiež zvyšuje riziko vzniku nádorových ochorení (*Arnold a kol., 2015*). Je teda pochopiteľné, že štúdia sledujúca výskyt nádorových ochorení napr. u diabetikov je už primárne skreslená vysokým podielom obéznych pacientov. Preto identifikovanie fyziologických, environmentálnych a hormonálnych faktorov spájajúcich s obezitu a rakovinou, ktoré sa kumulujú počas dlhšieho obdobia, je dôležité pre následnú identifikáciu prevencií (*Arnold a kol., 2017*).

Za obmedzenie v našej analýze môžeme považovať to, že PAF vychádza z predpokladu účinku vysokého BMI na rakovinu, ktorý nie je nezávislý na iných kauzálnych faktoroch ako je fajčenie, fyzická aktivita, strava alebo diabetes. To sa však vo veľkej miere zohľadňuje pri použití odhadov RR, ktoré sú prispôsobené daným faktorom (*Schmid a kol., 2014*).

Niektorí autori dokonca spochybňujú, že samotný BMI je vhodným indikátorom pre definovanie nadváhy a obezity. Ako hlavný dôvod uvádzajú napríklad to, že BMI neberie do úvahy distribúciu tuku v tele (*Ruhl a kol.,2010; Lumeng a kol., 2011*). Zároveň však uvádzajú, že obvod pásu (WC) by mohol byť vhodný doplnok pre indikovanie rizika obezity (*Janssen a kol., 2005; Petursson a kol., 2011*), čo navrhuje vo svojej správe aj Svetová zdravotnícka organizácia (*WHO, 2011*). Všeobecne však stále platí, že BMI patrí medzi najpoužívanejšiu a zároveň ľahko získateľnú metriku, ktorá definuje nadváhu a obezitu (*Nuttall, 2015*). Ako obmedzenie môžeme považovať aj to, že sme v našom výskume nebrali do úvahy vek, ktorý výrazne koreluje ako s BMI, tak s úmrtnosťou. Je všeobecne známe, že riziko rakoviny s vekom stúpa. Avšak starnutie alebo proces starnutia je možné považovať za prirodzený priebeh, nie za patológiu a nemusí nutne viesť k vývoju rakoviny (*Arnold a kol., 2015*). Zahrnutie veku by preto mohlo byť podnetom do ďalších analýz. V súčasnosti však neexistuje odhad relatívneho rizika pre vznik ZN v dôsledku zvýšeného BMI podľa veku.

PAF je založená na predpoklade, že vzťah medzi vysokým BMI a rakovinou je príčinný (*Arnold a kol., 2017*). Súhrnne teda môžeme konštatovať, že zníženie BMI na úrovni populácie povedie k poklesu výskytu rakoviny a následne úmrtiam, ktoré sú spájané s vysokým BMI v priereze času.

ZÁVER

Záverom analýzy môžeme konštatovať, že podľa nášho odhadu, v Česku v roku 2016 zomrelo 1 902 (7 %) osôb, ktorým bol diagnostikovaný jeden z vybraných typov zhubných novotvarov a to v dôsledku dlhodobo pretrvávajúcej vysokej hladiny BMI. Môžeme pove-

dať, že z celkového počtu úmrtí na ZN pažeráka ako u mužov, tak u žien a celkového počtu úmrtí na ZN tela maternice až polovica prípadov bola pripísaná vysokej hladine BMI.

Na základe našich výsledkov môžeme teda zhodnotiť, že vzhľadom k neustálemu nárastu európskeho trendu obezity (*Breda a kol., 2015*) naše výsledky posilňujú potrebu uprednostňovania prevencie nadmernej hmotnosti a obezity v Česku a jej všeobecné zahrnutie do medzinárodných plánov kontroly rakoviny. Tým by bolo možné potlačiť narastajúcu prevalenciu rakoviny a iných ochorení.

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KATARÍNA ROŽEKOVÁ

Je od roku 2017 absolventkou magisterského štúdia oboru sociálnej epidemiológie na Prírodovedeckej fakulte Univerzity Karlovej v Prahe. Aktuálne pracuje na Rigoróznej práci, súčasťou ktorej je predkladajúca publikácia. Zároveň pracuje v oblasti pracovnolekárskej služby, v rámci ktorej je aj dosiahnutie zdravotnej spôsobilosti, k hodnoteniu ktorej patrí okrem iného aj optimálne BMI ovplyvňujúce celkové zdravie.

MICHALA LUSTIGOVÁ

Absolvovala doktorské štúdium na Katedre demografie a geodemografie na PřF UK. V súčasnej dobe pôsobí ako odborný asistent na Katedre sociálnej geografie a regionálneho rozvoje PřF UK so zamarením na demografiu a geografiu zdravia. Zároveň pracuje ako odborný pracovník v Štátnom zdravotnom ústavu, kde sa zaoberá štúdiom zdravotného stavu českej populácie, vplyvom životného štýlu a životného prostredia na zdravie populácie.

SUMMARY

Based on the analysis of this paper it is estimated that 1,902 deaths (7.0% of the total) in 2016 in Czechia were diagnosed as one of the selected types of malignant neoplasms connected to a long-term high BMI. We can assume that of the total deaths from esophageal cancer, both in men and women, and the total number of cervical cancer deaths, up to half of the cases were attributable to high BMI levels.

Based on our results, we can conclude that, given the ever-growing European obesity trend (Breda et al., 2015), our results strengthen the need to prioritise the prevention of overweight and obesity in Czechia and the general inclusion of this aim in international cancer control plans. This would suppress the increasing burden of cancer and other illnesses that could follow over the years.

Odhadovanie vplyvu nadváhy a obezity na riziko vzniku rakoviny u českej a slovenskej populácie

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SÚHRN

Cieľ práce: Cieľom tejto štúdie je odhadnúť a porovnať počet a podiel úmrtí na vybrané druhy zhubných novotvarov u českej a slovenskej populácie v roku 2016, ktoré možno pripísať nadmernému indexu telesnej hmotnosti (BMI) v roku 2008.
Materiál a metodiky: Odhad vplyvu nadváhy a obezity na riziko vzniku zhubného novotvaru u českej a slovenskej populácie sa vypočíta pomocou populačnej atribulatívnej frakcie (PAF).
Výsledky: Odhaduje sa, že 2 120 prípadov úmrtí v Česku a 1 073 prípadov na Slovensku v roku 2016, by bolo možné prisúdiť práve zvýšenému BMI. Najvyššia PAF bola pre adenokarcinóm pažeráka vo všetkých vekových kategóriách bez rozdielu na pohlavie a sledovanú krajinu.
Závery: Je možné konštatovať, že vysoký index telesnej hmotnosti vplýva na vznik vybraných druhov zhubných novotvarov. Celkovo bola vyššia PAF u žien. Zároveň, je u žien pozorovateľná stúpajúca PAF s vekom. To je možné pripísať tomu, že so starnutím ženskej populácie dochádza aj k nárastu telesnej hmotnosti.

KĽÚČOVÉ SLOVÁ

nadváha a obezita – zhubný novotvar – česká populácia – slovenská populácia – prevencia

ABSTRACT

Rožeková K., Lustigová M.: Estimating the impact of overweight and obesity on cancer risk in the Czech and Slovak populations
Aim: To estimate and compare the 2016 numbers and proportions of deaths from selected types of malignant neoplasms attributable to high body mass index (BMI) from 2008 in the Czech and Slovak populations.
Material and methods: The estimated impact of overweight and obesity on the risk of malignant neoplasms in the Czech and Slovak populations was calculated using the population attributable fraction (PAF).
Results: It is estimated that 2 120 deaths in the Czech Republic and 1 073 deaths in the Slovak Republic in 2016 could be attributable to high BMI. The highest PAF was observed for oesophagal adenocarcinoma in all age categories regardless of sex and country.
Conclusions: It can be stated that high BMI has an impact on selected types of malignant neoplasms. A generally higher PAF was observed for females. At the same time, females showed an increasing PAF with increasing age. This can be explained by weight increase with age in the ageing female population.

KEYWORDS

overweight and obesity – malignant neoplasm – Czech population – Slovak population – prevention

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ÚVOD

Obezita je stav alebo chronické ochorenie, ktoré je charakterizované zmnožením tukového tkaniva v dôsledku pozitívnej energetickej bilancie. Podľa toho, kde sa nadmerné tukové tkanivo v tele ukladá, rozdeľujeme obezitu na abdominálnu a periférnu. U abdominálnej obezity dochádza k ukladaniu nadmerného tukového tkaniva predovšetkým v dutine brušnej. Tento typ obezity sa nazýva aj centrálna obezita a je typická skôr pre mužov. Zároveň ide o typ obezity, ktorý je spájaný s vyšším rizikom vzniku kardiovaskulárnych ochorení (hypertenzie, ischemickej choroby srdca alebo cievnej mozgovej príhody) v porovnaní s periférnou obezitou, ktorá je typická pre ženy. U daného typu obezity ide o nadmerné ukladanie tukového tkaniva prevažne v dolnej časti tela (stehná, zadok a boky) [56].

V súčasnosti sa považuje zníženie výskytu obezity v populácii za jednu zo základných výziev 21. storočia v oblasti verejného zdravia. Prevalencia obezity sa od roku 1980 takmer zdvojnásobila a u niektorých krajín európskeho regiónu dokonca strojnásobila [45]. Napríklad, práve Česko patrí v súčasnosti k jednej z krajín, kde prevalencia obezity u dospelej populácie patrí medzi jednu z najvyšších v Európe. Zatiaľ, čo v roku 1980 bola v Česku prevalencia 17 %, v roku 2016 dosiahla až 29 %. Nepriaznivé výsledky daného rizikového faktora boli preukázané aj na Slovensku, kde došlo k nárastu za rovnaké časové obdobie o približne 12 percentných bodov (z 10 % na 22 %) [44].
Obezita v populácii sa najčastejšie meria pomocou Indexu telesne hmotnosti (Body Mass Index, ďalej BMI). BMI je jednoducho definovaný ako hmotnosť osoby v kilogramoch vydelená druhou mocninou výšky

osoby v metroch (kg/m²) [45]. Zvýšený index telesnej hmotnosti (BMI ≥ 25kg/m²) je možné zaradiť k jednému z hlavných rizikových faktorov, ktorý sa uplatňuje ako u nádorov hormonálne nezávislých (tvorbou adipocytokínu; napríklad karcinóm prostaty, obličiek alebo adenokarcinóm pažeráka) [57, 58, 59], tak hormonálne závislých (napríklad karcinóm endometria, ovárií alebo karcinómu prsníka v období postmenopauzy) [60]. Nádorové ochorenia v súčasnosti predstavujú v rade európskych krajín jednu z hlavných príčin úmrtí [43, 49]. Na základe súčasných trendov sa dokonca predpokladá, že rakovina sa v najbližších desaťročiach stane hlavnou príčinou chorobnosti a úmrtnosti v európskom regióne [50, 51]. Najčastejším typom rakovín je však možné predísť či ich liečiť, pokiaľ sú diagnostikované včas. Primárna prevencia práve v životnom štýle zvyšuje úspech v neustále sa stupňujúcom zaťažení. Dokonca sa uvádza, že 90–95 % prípadov je pripísaných práve faktorom životného štýlu (napríklad fajčeniu, stravou, alkoholom, obezitou, inaktivitou), infekciám alebo znečistenému životnému prostrediu. Iba 5–10 % všetkých prípadov rakovín možno prisúdiť genetickým mutáciám [52]. Aj napriek tomu, že genetika môže zohrávať úlohu pri zvyšovaní alebo znižovaní rizika s exogénnymi karcinómami, oveľa dôležitejšia je expozícia rizikovým faktorom životného štýlu [53].

Na základe existujúcich konzistentných dôkazoch doterajších štúdií je teda možné konštatovať, že nadváha a obezita môže prispievať k incidencii a následne k úmrtiu zhubného novotvaru hrubého čreva a konečníka [23], žlčníka [21, 42], zhubného novotvaru obličiek (česky ledvin) [39] a u žien zhubného novotvaru prsníka [30] alebo endometria [15, 32]. Podobné závery potvrdzujú aj dve významné medzinárodné organizácie venujúci sa výskumu rakoviny. Medzinárodná agentúra pre výskum rakoviny (IARC) taktiež dospela k záveru, že nadváha a obezita prispievajú ako k zhubnému novotvaru hrubého čreva, endometria, obličiek a adenokarcinómu pažeráka (česky jícnu), tak k postmenopauzálnemu zhubnému novotvaru prsníka [37]. World Cancer Research Fund International (WCRF) sa rovnako domnieva, že existuje asociácia, nie len medzi obezitou a zhubným novotvarom konečníka a hrubého čreva, ale aj medzi zhubným novotvarom žlčníka a pankreasu [26, 40]. Udržanie „normálnej hmotnosti“ počas celého života znižuje aj riziko vzniku zhubného novotvaru prsníka [47].

Riziko vzniku spomínaných druhov zhubných novotvarov u populácie so zvýšeným indexom telesnej hmotnosti je podmienené tiež prítomnosťou civilizačných ochorení (ako napríklad kardiovaskulárnych ochorení alebo diabetes mellitus II. typu), pre ktoré je obezita tiež rizikový faktor. Práve inzulínová rezistencia, chronický zápal alebo vysoká hladina pohlavných hormónov sú zaraďované medzi najpravdepodobnejšie mechanizmy, ktorými môžeme vysvetliť asociáciu medzi dlhodobo pretrvávajúcou obezitou a rizikom rakoviny [28].

Okrem pretrvávajúceho pôsobenia obezity pre vznik rakoviny je možné k faktorom ovplyvňujúcim narastajúcu incidenciu a následnú intenzitu úmrtnosti zaradiť aj pohlavie a vek [35]. Niektoré výskumy potvrdzujú, že riziko rakoviny u obéznej populácii s vekom stúpa [4, 17]. Zároveň, prostredníctvom metaanalýz observačných štúdií bolo potvrdené, že jedinci trpiaci obezitou už vo veku do 30 rokov majú vyššie riziko vzniku rakoviny v neskoršom veku [4]. Veľké obavy zároveň tak vyvoláva nárast incidencie u čoraz mladšej populácie. Konkrétne, rapídny nárast incidencie zhubného novotvaru hrubého čreva a konečníka je možné pozorovať už v populácii od veku 45 rokov, a to ako u mužov, tak žien [6].

Nárast počtu pacientov s nádorovým ochorením ovplyvňuje samozrejme aj ekonomické zaťaženie krajiny, predovšetkým zaťaženie zdravotného systému. Je preto dôležité kvantifikovať vplyv modifikovateľných rizikových faktorov a poukázať tak na to, akú časť zhubných novotvarov je možné prisúdiť práve obezite [25]. Česko a Slovensko prešli podobným vývojom zdravotného stavu populácie od začiatku 90. rokov 20. storočia, odkedy v rámci procesu transformácie došlo k enormnému nárastu nadeje dožitia pri narodení a zlepšení úmrtnostných pomerov [54]. Cez toto zlepšenie a priblíženie sa krajinám západnej Európy, obidve krajiny stále vykazujú vysokú mieru úmrtnosti na ochorenia obehovej sústavy a mimo iné sú charakteristické najvyššou intenzitou úmrtnosti na zhubné novotvary v rámci EU28 [48, 54]. Aj preto sa autori tohto článku budú snažiť hodnotiť a porovnať vplyv vysokého BMI na intenzitu úmrtnosti vybraných typov zhubných novotvarov podľa pohlavia, veku v týchto krajinách.

MATERIÁL A METODIKY

V predkladajúcom analyzovanom výskume sa odhadoval vplyv nadváhy a obezity (BMI ≥ 25kg/m²) na riziko úmrtí na vybrané druhy zhubných novotvarov u českej a slovenskej populácie, pričom boli jednotlivé odhady porovnávané podľa pohlavia a jednotlivých vekových kategórií od veku 45 a viacej rokov (konkrétne vo vekových skupinách 45–54, 55–64, 65–74, 75 a viac rokov), a to z dôvodu nízkych počtov prípadov úmrtí na sledované zhubné novotvary v mladších vekových skupinách.

Sledované typy rakovín

Analyzovali sa iba zhubné novotvary, ktorých vznik je spájaný so zvýšeným BMI [41]. Jednotlivé diagnózy zhubných novotvarov boli uvádzané podľa kódov z 10. revízie Medzinárodnej klasifikácie chorôb (MKCH10, dg. C00–C97). Analyzoval sa teda adenokarcinóm pažeráka (C15), zhubné novotvary dolného tráviaceho traktu (C18–C20; C18 – zhubný novotvar hrubého čreva, C19 – rektosigmoidového spojenia, C20 – konečníka), zhubný novotvar žlčníka (C23), pankreasu (C25), prsníka (C50) v období postmenopauzy, tela maternice (C54) a zhubné novotvary močového systému (C64–C68; C64 – zhubný novotvar obličiek okrem obličkovej panvičky, C65 – obličkovej panvičky, C66 – močovodu, C67 – močového mechúra a C68– zhubné novotvary iných bližšie nešpecifikovaných močových orgánov).

Počty úmrtí na jednotlivé typy zhubných novotvarov v roku 2016 boli získané z oficiálnych štatistík obidvoch krajín, a to z Demografickej ročenky 2016 [12] a zo Štatistického úradu SR [34]. Bol zohľadnený aj čas medzi expozíciou nadmernému BMI a úmrtím. Zatiaľ, čo obdobie latencie medzi expozíciou a úmrtnosťou na vybrané zhubné novotvary nie je jednoznačne potvrdené [1, 35], v danej analýze sa predpokladalo, na základe dostupných dát, 8 ročné rozpätie mapujúce prevalenciu

Tabuľka 1. Relatívne riziko vzniku zhubného novotvaru v dôsledku nadváhy a obezity
Table 1. Relative risk of malignant neoplasms due to overweight and obesity

Typy rakoviny	RR/Nadváha	RR/Obezita
Adenokarcinóm pažeráka (C15)[c]	1,55	2,40
Zhubné novotvary dolného tráviaceho traktu (C18–C20)[c]	1,15	1,32
Zhubné novotvary žlčníka (C23)[c]	1,23	1,51
Zhubný novotvar pankreasu (C25)[c]	1,14	1,30
Zhubný novotvar prsníka (C50) v období postmenopauzy[a, b]	1,12	1,25
Zhubný novotvar tela maternice (C54)[c]	1,52	2,31
Zhubné novotvary močového systému (C64–C68)[c]	1,31	1,72

Zdroj:
[a]prevzaté z Bergstrom et al., 2007 [7]
[b]prevzaté z Rehenan et al., 2008 09130]WCRF, 2007
[c]prevzaté z WCRF, 2007 [40]

Source:
[a]taken from Bergstrom et al., 2007 [7]
[b]taken from Rehenan et al., 2008 09130]WCRF, 2007
[c]taken from WCRF, 2007 [40]

BMI v roku 2008 (podľa pohlavia, veku a krajiny) a úmrtí na zhubné novotvary v roku 2016.

Index telesnej hmotnosti (BMI)
Prevalencia nadváhy a obezity v populácii bola stanovená ako BMI rovné alebo vyššie 25 kg/m^2. Pre danú štúdiu boli získané odhady prevalencie nadváhy a obezity v populácii dospelých vo veku 45 a viac rokov pre Česko a Slovensko podľa pohlavia a sledovaných vekových kategórií v roku 2008. Dáta pochádzajú zo štúdie EHIS 2008 (European Health Interview Survey), pričom za Česko boli získané z Ústavu zdravotníckych informácií a štatistiky ČR [36] a za Slovensko zo Štatistického úradu SR [34].

Relatívne riziko (RR)
Neoddeliteľnou súčasťou analýzy je relatívne riziko (RR) špecifické pre vznik zhubných novotvarov v dôsledku vysokého BMI. Relatívne riziko pre vybrané typy zhubných novotvarov, ktoré môžeme sledovať v tabuľke 1, bolo získané z publikovaných metaanalýz Rehenan et al. [30], Bergstrom et al. [7] a WCRF Continuous Update Project (CUP) [40].

Populačná atribulatívna frakcia (PAF)
Odhad vplyvu nadváhy a obezity na riziko vzniku zhubných novotvarov u českej a slovenskej populácie sa vypočítal pomocou populačnej atribulatívnej frakcie (PAF), a to prostredníctvom nasledujúceho vzorca:

Kde premenná *RRi* je relatívne riziko sledovaného javu, v danom prípade úmrtnosti na zhubný novotvar súvisiaci s kategóriou BMI (*i*) a *pi* je podiel populácie v kategórii BMI (*i*). PAF je možné jednoducho vyjadriť ako podiel prípadov (úmrtí), ktorým by sa dalo predísť, keby bola expozícia danému rizikovému faktoru (BMI ≥ 25 kg/m^2) v populácii eliminovaná [46].
Špecifické PAF pre vek, pohlavie a krajinu boli vypočítané pre jednotlivé typy zhubných novotvarov súvisiacich s nadváhou a obezitou. Počet prípadov jednotlivých typov zhubných novotvar v roku 2016, ktoré možno pripísať zvýšenému BMI v roku 2008 sa odvodili vynásobením PAF špecifických pre vek, pohlavie a krajinu.

VÝSLEDKY

Výskyt nadváhy a obezity v Česku a na Slovensku podľa veku a sledovaných vekových skupín v roku 2008 je zachytený v tabuľke 2. Zatiaľ čo medzi Českom a Slovenskom sa veľké rozdiely vo výskytu nadváhy a obezity nepozorujú, medzi pohlavím sú rozdiely znateľné.
U žien s vekom rastie prevalencia zvýšeného BMI až do veku 65–74 rokov, odkedy naopak klesá. Najnižší podiel nadváhy a obezity u žien v obidvoch krajinách bol vo veku 45–54 rokov. U mužov je možné naopak konštatovať skôr klesajúcu tendenciu od veku 55–64 rokov, kedy je podiel zvýšeného BMI najvyšší.
Je možné konštatovať, že u zhruba desiatich krajín Európy patria novotvary už medzi najčastejšiu príčinu úmrtí [49]. V Česku, konkrétne v roku 2016 zomrelo na zhubné novotvary celkom 27 261 osôb (25 % zo všetkých úmrtí), pričom 94 % všetkých úmrtí bolo vo veku 45 a viac rokov (n = 25 679). Na Slovensku v roku 2016 zomrelo celkovo 13 425 osôb (26 % zo všetkých úmrtí). Vo veku 45 a viac rokov to predstavovalo takmer 97 % (n = 12 996) zo všetkých prípadov zhubných novotvarov.
Počet zomrelých na sledované diagnózy, tj. diagnózy súvisiace s nadváhou a obezitou, však nie vo všetkých prípadoch úmrtí súvisia so zvýšeným BMI. Odhaduje sa, že 2 120 prípadov úmrtí v Česku a 1 073 prípadov na Slovensku v roku 2016, by bolo možné prisúdiť práve vysokému BMI. To by odpovedalo 7,8 % všetkých prípadov zhubných novotvarov v Česku (7,1 % u mužov a 8,7 % u žien) a 8,0 % na Slovensku (6,8 % u mužov a 9,5 % u žien).
Podiel prípadov (PAF), ktoré je možné prisúdiť zvýšenému BMI u žien s vekom narastá, ako v Česku, tak na Slovensku. U českých žien z 7,5% vo veku 45–54 rokov na 9,1 % vo veku 75 a viac rokov. Na Slovensku je tento

Tabuľka 2. Výskyt nadváhy a obezity podľa pohlavia a veku v Česku a na Slovensku, 2008
Table 2. Overweight and obesity by sex and age groups in the Czechia and Slovakia, 2008

ČESKO				
Vekové kategórie	Nadváha		Obezita	
	Muži (%)	Ženy (%)	Muži (%)	Ženy (%)
45–54 rokov	48,0	45,0	24,0	20,0
55–64 rokov	51,9	42,9	29,7	29,2
65–74 rokov	53,7	38,5	25,4	36,5
75 a viac	61,4	45,7	9,1	24,7
Celkom	45,2	29,0	17,3	17,5

SLOVENSKO				
Vekové kategórie	Nadváha		Obezita	
	Muži (%)	Ženy (%)	Muži (%)	Ženy (%)
45–54 rokov	53,6	34,0	16,5	17,0
55–64 rokov	53,9	38,8	22,8	30,7
65–74 rokov	46,6	42,2	25,1	33,7
75 a viac	50,4	46,7	14,9	22,5
Celkom	44,5	27,3	14,5	15,7

rozdeľ ešte výraznejší 6,0 % verzus 10,1 %. Naopak, u mužov oboch zemí je tento trend presne opačný. Práve v najmladšej vekovej skupine je možné najväčší podiel prípadov prisúdiť nadmernému BMI (v Česku 7,7 % a na Slovensku 10,8 %); v najstaršej vekovej skupine je to potom 6,4 % prípadov v Česku a 5,6 % prípadov na Slovensku. Celkovo je ale možné sledovať, že od 45 roku veku dochádza celkovo vo všetkých prípadoch u českých aj slovenských žien k nepriaznivo stúpajúcemu trendu podielu úmrtí v dôsledku pôsobenia vysokého BMI. V porovnaní medzi mužmi je tento trend u oboch krajín opačný, teda so stúpajúcim vekom dochádza k postupnému klesaniu celkového počtu úmrtí v dôsledku vysokého BMI.

Podľa vybraných typov zhubných novotvarov bola PAF v dôsledku zvýšeného BMI najvyššia pre adenokarcinóm pažeráka takmer vo všetkých vekových kategóriách, a to ako u mužov a žien, tak v Česku aj na Slovensku. Pohybovala sa okolo 45 % naprieč vekovými kategóriami a zemami. Predsa len najvyšší podel úmrtí na adenokarcinóm pažeráka v roku 2016, v dôsledku pôsobenia vysokého BMI v roku 2008, bol u českých žien vo vekovej kategórii 65–74 rokov (49,1 %) a slovenských žien vo vekovej kategórii 65–74 rokov (48,1 %). PAF pre zhubný novotvar tela maternice bola vo všetkých vekových kategóriách v Česku aj na Slovensku nad 40 %. Podiel atribulatívnych prípadov narastal až do veku 65–74 rokov, kedy najvyšší v Česku bol 47,5 % a na Slovensku 46,5 %, následne podiel atribulatívnych prípadov s vekom opäť klesal.

Najviac zaťaženými skupinami boli vekové skupiny 55–64 rokov a 65–74 rokov u českých i slovenských žien a u slovenských mužov (hodnoty PAF pre jednotlivé diagnózy boli vo väčšine prípadov vyššie v porovnaní s celou populáciou). U českých mužov sa vyššia záťaž ako v celej populácii objavovala už vo veku 45–54 rokov. Naopak, podľa diagnóz u oboch pohlaví a oboch populáciách bol najnižší podiel atribulatívnej frakcie vo veku nad 75 rokov (tab. 3).

DISKUSIA

Za posledné desaťročia sa podiel ľudí s nadmernou telesnou hmotnosťou výrazne zvýšil, a stal sa tak globálnym zdravotným problémom nielen v Európe, ale na celom svete. Nadváha a obezita zvyšuje riziko vzniku okrem kardiovaskulárnych ochorení, diabets mellitus II. typu aj vznik a intenzitu úmrtnosti na rôzne typy rakovín [8]. Daná štúdia sa snažila odhadnúť vplyv zvýšeného BMI na riziko úmrtia vybraných zhubných novotvarov. Cieľom bolo zároveň dané výsledky porovnať medzi českou a slovenskou populáciou, podľa pohlavia a medzi jednotlivými vekovými kategóriami (45–54, 55–64, 65–74, 75 a viac). Zatiaľ, čo v roku 2016 bolo v Česku celkovo odhadovaných 7,8 % úmrtí spôsobených zvýšeným BMI na vybrané typy zhubných novotvarov, na Slovensku boli výsledky viac menej rovnaké (8,0 %). Podľa pohlavia, bola celkovo vyššia PAF u žien, a to ako u českých (8,7 %), tak slovenských (9,5 %) v porovnaní s mužmi (Česko 7,1 %; Slovensko 6,8 %), čo je možné prisúdiť práve zhubným novotvarom charakteristických pre ženy. Podobne napríklad v Spojených štátoch sa odhadovalo, že podiel všetkých úmrtí na rakovinu, ktoré možno pripísať vysokému BMI osobám starším 50 rokov, je vyšší u žien (20 %) ako u mužov (14 %) [9]. Rovnako, dané výsledky potvrdzujú autori Lukanová et al. [22], Bergstrom et al. [7] alebo Pan et al. [24]. Zároveň, je u žien pozorovateľná stúpajúca PAF s vekom. To je možné pripísať tomu, že

Tabuľka 3. Odhad počtu a podielu úmrtí spôsobených zvýšeným BMI v rámci jednotlivých typov zhubných novotvarov v českej a slovenskej populácii, 2016
Table 3. Estimation of number and proportion of deaths due to increased BMI within selected malignant neoplasms in the Czech and Slovak populations, 2016

ČESKO																				
Vekové kategórie	45–54 rokov				55–64 rokov				65–74 rokov				75 a viac				Celkom*			
Typy rakoviny	PAF				PAF				PAF				PAF				PAF			
	Muži		Ženy		Muži		Ženy		Muži		Ženy		Muži		Ženy		Muži		Ženy	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Adenokarcinóm pažeráka (C15)	16	45,5	2	44,8	57	46,2	13	47,2	79	45,1	18	49,1	32	39,7	14	45,9	183	44,0	47	46,5
Zhubné novotvary dolného tráviaceho traktu (C18–C20)	15	17,1	9	16,8	57	17,5	28	18,0	132	18,0	79	18,9	121	14,7	126	17,3	336	16,5	239	17,6
Zhubné novotvary žlčníka (C23)	1	24,4	2	24,0	5	24,9	8	25,6	8	24,2	20	26,8	11	21,0	24	24,7	26	23,5	54	25,1
Zhubný novotvar pankreasu (C25)	6	12,0	5	12,0	25	12,0	19	12,0	52	12,0	42	11,9	30	12,2	55	12,0	128	12,1	122	12,0
Zhubný novotvar prsníka (C50) v období postmenopauzy	-	-	19	13,8	-	-	39	14,7	-	-	72	15,5	-	-	104	14,2	-	-	244	14,5
Zhubný novotvar tela maternice (C54)	-	-	7	43,3	-	-	21	45,7	-	-	50	47,5	-	-	63	44,4	-	-	142	45,0
Zhubné novotvary močového systému (C64–C68)	19	30,9	5	30,4	61	31,5	22	32,3	145	26,6	69	31,2	155	26,6	113	31,2	392	29,8	208	31,7
Celkom**	58	7,7	50	7,5	206	7,3	150	8,1	415	7,2	347	9,1	349	6,4	498	9,1	1065	7,1	1055	8,7

SLOVENSKO																				
Vekové kategórie	45–54 rokov				55–64 rokov				65–74 rokov				75 a viac				Celkom*			
Typy rakovín	PAF				PAF				PAF				PAF				PAF			
	MUŽI		ŽENY		MUŽI		ŽENY		MUŽI		ŽENY		MUŽI		ŽENY		MUŽI		ŽENY	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	N	%	n	%
Adenokarcinóm pažeráka (C15)	15	42,9	1	45,5	43	44,5	14	32,9	31	45,9	1	48,1	10	42,7	7	45,2	98	43,1	17	46,2
Zhubné novotvary dolného tráviaceho traktu (C18–C20)	12	16,0	9	17,1	48	16,7	22	18,4	54	17,3	34	18,4	49	15,9	72	17,0	192	16,1	139	17,5
Zhubné novotvary žlčníka (C23)	3	22,8	-	-	11	23,9	5	26,1	12	24,7	11	26,2	5	22,7	13	24,3	7	23,0	30	24,9
Zhubný novotvar pankreasu (C25)	4	12,1	2	12,0	13	12,1	8	11,9	11	12,0	14	11,9	9	12,1	21	12,0	51	12,1	46	12,0
Zhubný novotvar prsníka (C50) v období postmenopauzy	-	-	4	14,0	-	-	31	15,1	-	-	44	15,1	-	-	55	14,0	-	-	146	14,3
Zhubný novotvar tela maternice (C54)	-	-	6	43,9	-	-	20	46,5	-	-	34	46,5	-	-	38	43,7	-	-	99	44,7
Zhubné novotvary močového systému (C64–C68)	21	28,9	2	30,9	83	30,2	14	32,9	86	31,2	21	33,0	63	28,8	42	30,7	166	29,1	82	31,5
Celkom**	55	10,8	24	6,0	198	10,5	101	8,9	194	7,6	161	9,8	136	5,6	249	10,1	514	6,8	559	9,5

*Podiel odvrátiteľných úmrtí zo všetkých prípadov zhubných novotvarov a to bez ohľadu na vek.
**Podiel odvrátiteľných úmrtí zo všetkých prípadov zhubných novotvarov a vo všetkých vekových kategóriách.

*The proportion of avoidable deaths from all cases of malignant neoplasms, regardless of age.
**Proportion of avoidable deaths from all cases of malignant neoplasms and in all ages.

so starnutím ženskej populácie dochádza aj k nárastu telesnej hmotnosti a zmene lokalizácie ukladania tuku v tele, obzvlášť v období menopauzy. Zmena lokalizácie ukladania tuku v tele je ovplyvnená taktiež zmenou hladiny hormónov (estrogénov), čo následne vedie k spomaleniu metabolizmu, syndrómu polycystických ovárií alebo tiež k rôznym stupňom inzulínovej rezistencie [55].

V danej štúdii sa preukázalo, že celkovo najvyššia PAF bola práve u zhubného novotvaru tela maternice (C54) – Česko 45,0 %; Slovensko 44,7 %. Pričom je možné sledovať práve stúpajúci trend do 75. roku veku. Nie len táto analýza ukazuje nežiadúce účinky zvýšeného BMI na zhubný novotvar tela maternice (C54), ale aj rada iných epidemiologických štúdií [10, 22, 37]. Tento nepriaznivý účinok BMI môže byť ovplyvnený taktiež zníženou syntézou progesterónu pred menopauzou a zo zvýšenou cirkuláciou estrogénu po menopauze [19, 20, 37].

U zhubných novotvarov postihujúcich ako mužov, tak ženy boli najvyššie odhadované hodnoty PAF u adenokarcinómu pažeráka (C15), ktorý skoro vo všetkých vekových kategóriách v Česku aj na Slovensku presahoval 40 %. Obdobné výsledky ukazuje aj štúdia vykonávaná vo Francúzku [2] alebo vo Veľkej Británii [26]. Autori Pearson-Stuttard et al. [27] dokonca uvádzajú, že v roku 2012 bol celosvetovo približne jeden zo štyroch adenokarcinómov pažeráka spôsobený práve vysokým BMI a diabetom II. typu. Čo potvrdzuje teóriu, že nie len vysoký BMI, ale aj diabetes sa čoraz častejšie uvádza ako rizikový faktor pre vznik rôznych typov rakovín. Zároveň, obezita zvyšuje riziko vzniku diabetu [27]. Bolo by preto vhodné do nasledujúcich štúdií zahrnúť aj tento faktor, čím by bolo možné bližšie špecifikovať a aplikovať optimálne prevencie a skríning, ako pre populáciu, tak jednotlivých pacientov.

Je zaujímavé, že zatiaľ čo viaceré štúdie [1, 3, 18, 22] uvádzajú vyššiu PAF pre zhubné novotvary močového systému (C64–C68) v dôsledku pôsobenia vysokého BMI u mužov, v predkladajúcej analýze bola vyššia PAF takmer vo všetkých vekových kategóriách u žien. Jedine u českých mužov bola PAF vyššia vo vekovej kategórii 45–54 rokov. Dané výsledky naopak ale podporujú napríklad autori Calle a Thun [10]. Tento stav je možné opäť prisúdiť práve tomu, že u žien v porovnaní s mužmi bola prevalencia obezity vyššia takmer vo všetkých vekových kategóriách. Práve vo vekovej kategórii 45–54 rokov bola prevalencia obezity vyššia u českých mužov, čo by potvrdzovalo naše výsledky.

Štúdia má však aj určité obmedzenia. Za jeden zo základných limitov je možné považovat to, že relatívne riziko nie je zhodné naprieč populácii. Riziko sa líši podľa pohlavia, veku ale samozrejme aj podľa doby pôsobenia rizikového faktoru. V predkladajúcej analýze bolo relatívne riziko rozdelené, na základe dostupných dát, len podľa jednotlivých diagnóz a BMI. Rovnakú metodiku analýzy však zvolili aj iní autori ako napríklad Arnold et al. 2015 [1], Pearson-Stuttard et al. [27] alebo Parkin a Boyd [26]. Okrem toho, neskúmala sa 8 ročná doba latencie medzi vysokým BMI a úrovňou úmrtnosti. Analyzoval sa výskyt zvýšeného BMI v populácii roku 2008 a následne sa odhadovala úmrtnosť v roku 2016 na vybrané zhubné novotvary v dôsledku vplyvu vysokého BMI. Teda sa predpokladalo, že vysoký BMI u populácie pretrvávala počas celého obdobia. Neanalyzovala sa ani prítomnosť iných ochorení (ako napríklad diabetes), ktorých vznik by mohla ovplyvniť práve obezita. To však do značnej miery zohľadňuje práve RR [33]. Taktiež je možné konštatovať, že nakoľko sú BMI u sledovanej populácie získavané na základe sebadeklarácie, hodnoty nadváhy a obezity môžu byť reálne vyššie ako respondenti v dotazníkovom šetrení uvádzali.

Na základe prekladajúcich výsledkov je možné očakávať, že v prípade pretrvávajúceho nárastu podielu osôb s nadmerným BMI sa následky v blízkej budúcnosti prejavia vo forme ďalšieho zvyšovania ako prevalencie, tak intenzity úmrtnosti na zhubné novotvary súvisiace s obezitou. Dôležité je, že na základe viacerých výskumov, sa nie len zvyšuje prevalencia úmrtnosti na zhubné novotvary, ale ich výskyt sa posúva do čoraz mladšieho veku [5, 11, 13, 14, 29]. Autori Se et al. [31] na základe štúdie vykonanej v Kórei dokonca uvádzajú, že najvyššia prevalencia vybraných zhubných novotvarov v dôsledku pôsobenia vysokého BMI je u jedincov, čo sú obézni už od veku 30 až 39 rokov. Takže je možné konštatovať, že populácia trpiaca nadváhou a obezitou v mladej dospelosti má zvýšené riziko vzniku nádorového ochorenia v neskoršom veku. (Pozn.: Mladú dospelosť je možné vekovo ohraničiť od 20 do 40 roku veku [38]). Teda dlhé latentné obdobie vysokého BMI predchádza následnej diagnostike nádorových ochorení [31].

Veľká záťaž zhubného novotvaru spôsobené vysokým BMI, nie len v Česku a na Slovensku, poukazuje na dôležitosť programov kontroly hmotnosti u populácie. Je preto dôležité poukázať na potrebu výskumov v oblasti intervencií na kontrolu prírastku telesnej hmotnosti, aby sa predišlo ďalšiemu rastu zhubných novotvarov súvisiacich s obezitou. Je podstatné zároveň implementovať kontrolné opatrenia na riešenie modifikovateľných rizikových faktorov (inaktivita, racionálne stravovanie) spolu s diagnostikovaním vysokého indexu BMI a chronických ochorení (diabetes alebo kardiovaskulárnych ochorení). Stratégie založené na prevenciu vysokého BMI majú veľký potenciál, pretože ide o prekrývajúci sa rizikový faktor s inými chronickými ochoreniami ako napríklad kardiovaskulárnymi. Medzi prvoradé intervencie by mali patriť také, ktoré riešia hlavne základné faktory ako je fyzická aktivita a stravovanie. Povedzme formou dostupnosti možností pre podporu fyzickej aktivity v okolí domova (ako napríklad budovaním športovísk, parkov, cyklistických chodníkov, podporovanie bezpečnosti ako cyklistov, tak chodcov…), dostupnosti „zdravých“ potravín v bytových oblastiach, možnosť racionálneho stravovania v okolí biznis centier, v školských jedálňach. Zároveň, podporovať opatrenia, ktoré sú zamerané na zmenu v zložení potravín, aby sa znížil obsah pridaného cukru, soli, transmastných kyselín, nasýtených tukov, ako aj energetický obsah. V neposlednom rade je dôležitá samotná edukácia v oblasti zdravého životného štýlu detí, mládeže a rodičov.

ZÁVER

Dané zistenia ukazujú zaťaženie zhubným novotvarom spôsobené vysokým BMI v Česku aj na Slovensku. Odhalilo sa, že 2 120 prípadov úmrtí na zhubné novotvary v Česku a 1 073 prípadov na Slovensku v roku 2016, by bolo možné prisúdiť práve vysokému BMI. U ženskej

populácie je zároveň pozorovateľná stúpajúca PAF s vekom. To je možné pripísať tomu, že so starnutím ženskej populácie dochádza aj k nárastu telesnej hmotnosti. Zistenia ďalej potvrdzujú potrebu úsilia na zmiernenie rastúcich trendov obezity na úrovni populácie. Ak súčasný trend prírastku hmotnosti obyvateľstva bude aj naďalej pretrvávať je možné predpokladať zvyšujúce sa zaťaženie rakovinou. Táto štúdia tiež informuje o potrebe implementácie preventívnych programov, ktoré by znižovali BMI u populácie.

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Manuscript Details

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Title	Prevalence of Diabetes and Prediabetes and its Risk Factors in Adults aged 25-64 in the Czech Republic: A Cross Sectional Approach
Article type	Research Paper

Abstract

the Czech population aged 25–64 years and to evaluate the relationships with various cardiometabolic, sociodemographic, and lifestyle risk factors. Methods: This was an epidemiological study with a stratified, crosssectional, random sampling design. Sociodemographic, lifestyle, and anamnestic data were collected through interviewer-administered questionnaires, medical examination, and biochemical assays. Results: Among the 1,189 participants, 114 were diagnosed with DM (9.6%), 330 with prediabetes (27.8%) and 745 were non-diabetes/non-prediabetes individuals (62.7%). Logistic regression analysis showed that overweight, general and abdominal obesity, hypertension, and lower level of HDL (increased risk) significantly increased the risk of both prediabetes and DM, while living in the cities diminished risk of DM. Among lifestyle variables the significant increased risk of prediabetes and DM was found for smokers and ex-smokers. In other lifestyle variables (marijuana lifetime prevalence, physical activity and frequency of alcohol drinking) the significantly higher or lower risk for prediabetes or DM was not found. Conclusions: The study shows a high prevalence of DM and prediabetes in the Czech population of age between 25-64, providing data on their association with several risk factors.

Keywords	diabetes; prediabetes; EHES; Czech population; risk factors
Taxonomy	Diabetes, Medicine, Cardiovascular Disease Risk Factor
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Data will be made available on request

Dear Colleagues,

We kindly request that you consider publishing our article concerning the issue of diabetes and prediabetes and its risk factors among the population of the Czech Republic.

There is only a very limited amount of information related to this topic in post-communist central-east European countries, so we believe that the results of our cross-sectional survey bring valuable insight into this important topic.

As we consider our data important, obtained from a representative sample of patients, we hope that you find our article worth to be considered for review process in your journal.

Looking forward to your reply,

Sincerely yours,

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Prevalence of Diabetes and Prediabetes and its Risk Factors in Adults aged 25-64 in the Czech Republic: A Cross-Sectional Study

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Aims: The aim of this study is to establish the prevalence of diabetes (DM) and prediabetes in the Czech population aged 25–64 years and to evaluate the relationships with various cardiometabolic, sociodemographic, and lifestyle risk factors.

Methods: This was an epidemiological study with a stratified, crosssectional, random sampling design. Sociodemographic, lifestyle, and anamnestic data were collected through interviewer-administered questionnaires, medical examination, and biochemical assays.

Results: Among the 1,189 participants, 114 were diagnosed with DM (9.6%), 330 with prediabetes (27.8%) and 745 were non-diabetes/non-prediabetes individuals (62.7%). Logistic regression analysis showed that overweight, general and abdominal obesity, hypertension, and lower level of HDL (increased risk) significantly increased the risk of both prediabetes and DM, while living in the cities diminished risk of DM. Among lifestyle variables the significant increased risk of prediabetes and DM was found for smokers and ex-smokers. In other lifestyle variables (marijuana lifetime prevalence, physical activity and frequency of alcohol drinking) the significantly higher or lower risk for prediabetes or DM was not found.

Conclusions: The study shows a high prevalence of DM and prediabetes in the Czech population of age between 25-64, providing data on their association with several risk factors.

Keywords: diabetes, prediabetes, EHES, Czech population, risk factors

Introduction

Diabetes mellitus (DM) is nowadays one of the most frequent metabolic disorders in the world, and its prevalence among adults has been increasing globally over the last few decades [1, 2]. An estimation of 451 million persons (aged 18–99 years) with DM worldwide in 2017 was suggested by International Diabetes Federation [3]. The amount is expected to increase to 693 million by 2045 [3]. Type 2 diabetes (T2DM) accounts for more than 90 percent of all DM patients (4).

The term "prediabetes" was defined by the American Diabetes Association (ADA) as a state of increased level but non-diabetes glycemia as indicated by a fasting plasma glucose (FPG) value of 5.6–6.9 mmol/L (impaired fasting glucose, IFG), a plasma glucose value of 7.8–11.0 mmol/L in a 2-h oral glucose tolerance test (OGTT) or an HbA1c value of 5.7–6.4% (39–47 mmol/mol) [5]. The identification of individuals with prediabetes provides an opportunity for intervention through lifestyle modification and pharmacological interventions to prevent progression to DM [6,7]. The number of persons diagnosed with DM among the Czech population in 2016 was 929 945 (prevalence rate 8.8%), but detailed information about DM risk factors are not known as well as about those related to prediabetes (8,9). The high prevalence of DM is not only the result of population ageing, but prediabetes and DM appear also among young adult and middle-aged population as was already showed by Žejglicová et al. (10). Prevalence of DM was found among 2.5% of young adult (25–44 years of age) and among 12% of middle-aged population (45–64 years of age) and prediabetes among 15% resp. 40% (10).

Methods

Study subjects

Data from Czech EHES (European Health Examination Survey) 2014 were used. Main goal of the survey was to obtain actual and relevant information about the non-communicable diseases and its risk factors among the Czech middle-aged population.

The study subjects were recruited among the study population of the European Health Interview Survey (EHIS). EHIS study was cross-sectional survey conducted in the Czech Republic in 2014 on the representative sample of 6737 participants. It consisted of four modules on health status, health care use, health determinants and socio-economic background variables. The data were collected by professional interviewer administered questionnaire. Among the other

variables EHIS covered the following topics: 1) Background variables on demography and socio-economic status; 2) Health determinants such as smoking, alcohol consumption, etc. The EHIS study design including the complete set of variables obtained is available elsewhere (11).

Respondents (in age group 25–64 years) of the EHIS were further asked to participate in EHES survey. This participation in EHES survey was offered to 3850 respondents and 1220 participants were examined (the respondence rate was 32%). The health examination (EHES 2014) involved repeated measure of blood pressure, anthropometric measures and blood sample analysis, including total cholesterol blood level, HDL-cholesterol blood level and glycated hemoglobin.

Ethical considerations

Written informed consent was obtained from all EHES study participants before they underwent any study-specific procedures. The EHES study was conducted according to the applicable International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP) standards and the World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants and was approved by The National Institute of Public Health of the Czech Republic.

Health outcome

The main health outcome was the ***prevalence of DM or prediabetes***. The glucose metabolism impairment phenotypes (DM, prediabetes) were defined according to the 2012 American Diabetes Association (ADA) guidelines (5). We divided the study population (age 25–64 years of age) into three groups according to the glycated hemoglobin level and prevalence of DM as follows **nondiabetic** (HbA1c $\leq$ 5.6% (38 mmol/mol)), **prediabetic** (HbA1c $\geq$ 5.7% and < 6.5% ($\geq$ 39 and < 48 mmol/mol)) and **diabetic** group (HbA1c $\geq$ 6.5% (48mmol/l)) and/or already diagnosed with DM).

Covariates

Information regarding sociodemographic characteristics (age, sex, area of living, education level), lifestyle characteristics (smoking habits, physical activity, marijuana lifetime prevalence, alcohol consumption), and anamnestic data (personal medical history of DM, hypertension, dyslipidemia, current antidiabetic, antihypertensive, or lipid-lowering therapy) were collected through health questionnaires. Blood pressure, blood cholesterol level, level of glycated hemoglobin (HbA1c) and obesity were based on medical examination.

Sociodemographic and lifestyle covariates

Education was categorized as primary, vocational, secondary or university. *Area of living* (degree of urbanization) was based on EUROSTAT variable and methodology (see https://ec.europa.eu/eurostat/web/degree-of-urbanisation/methodology). Our sample was split into two categories: Cities and Towns/suburbs/rural areas. Participants were classified according to smoking status (variable *smoking habits*) as non-smokers (participants who never smoked), current smokers (participants who had smoked more than one cigarette per day, daily or occasionally and had not stopped smoking), and ex-smokers (participants who had quit smoking). Further, the variable *Non-smoking lifetime prevalence* was constructed to evaluate the effect of smoking through life. *Marijuana lifetime prevalence* was dichotomised covariate. *Physical activity* was categorised, according to the number of days with at least 10 min period of physical activity per week, into three categories (0, 1–2, 3 and more days). *Frequency of alcohol drinking* was categorised according to the number of days per week with alcohol consumption into three categories (5–7, 1–4, less days).

All these covariates were obtained from health questionnaires based on subjective responses.

Clinical and biochemical measurements

During the physical examination, the following measurements were made using standard procedures: weight, height, *waist circumference* (low risk: < 94 cm in women and < 102 cm in men), and systolic and diastolic blood pressure (SBP and DBP), respectively. *Body mass index* (BMI) was calculated, participants with BMI of 25–29.9 kg/m^2 were categorized as being overweight and those with BMI ≥30 kg/m^2 were considered obese.

Hypertension was defined as systolic blood pressure (SBP) (mean of the second and the third measurements taken 1 min apart) ≥140 mmHg and/or diastolic blood pressure (DBP) (mean of the second and the third measurements taken 1 min apart) ≥90 mmHg and/or taking antihypertensive treatment (12). The risky level for total cholesterol (TC) was defined as ≥5 mmol/l and/or lipid lowering therapy and for high-density lipoprotein (HDL) ≥ 1,2 mmol/l in men and ≥1mmol/l in women and/or lipid lowering therapy. All biochemical analyses were performed at the Czech Institute of Accreditation officially certified laboratories according to standardized procedures.

Statistical analysis

One-way analysis of variance (ANOVA) was used to compare means of three groups of respondents (non-diabetic, prediabetic and diabetic group). Further, the χ^2-test was used to compare prevalence rates between non-diabetic and prediabetic and non-diabetic and diabetic group in categorical variables. Finally, the binary logistic regression was used to estimate the odds ratio for set of sociodemographic, metabolic and life-style explanatory variable. The metabolic and life-style variables were controlled for age and sex. The dependent binary variables were set as prediabetes (1) vs. non-diabetes (0) and similarly DM (1) vs. non-diabetes (0). STATA 14 was used for data processing and for all data analyses.

Results

A total of 1220 patients were enrolled in the study, incomplete laboratory and demographic data were found in 31 subjects. The final eligible sample consisted of 1,189 patients (97.5%), 476 were men (40%) and 713 women (60%).

The overview of clinical characteristics of the participants is shown in Table 1. Among the 1,189 participants, 114 were diagnosed with DM (9.6%), 330 with prediabetes (27.8%) and 745 were non-diabetes/non-prediabetes individuals (62.7%). The mean ages of the non-diabetic, prediabetic, and diabetic participants were 43.3 (11.5), 52.1 (10.6) and 55.2 (9.0) years of age (mean (SD values); $p<0.001$), respectively. In general, the mean value of followed characteristics was "the worst" among the diabetic group. The mean value of BMI was 26.2 kg/m^2 among non-diabetic group compared to 32.9 kg/m^2 among diabetic group ($p<0.001$). Similarly, the mean waist circumference increased from 88.8 cm in non-diabetic group to 107.8 cm in diabetic group ($p<0.001$). As well, the mean value of systolic BP increased through groups; in diastolic BP the mean value was comparable for prediabetic and diabetic group but significantly higher than among non-diabetic group. The only exception was the mean value of TC, where the lowest mean value was found among the diabetic group (TC=5.03 mmol/l) and the highest among the prediabetic group (TC=5.55 mmol/l).

The number of undiagnosed DM subjects in the whole study group was 19 (16.7%), the proportion of undiagnosed patients was 17.6% (N=13) in the age group of 55–64 years, 23.8% (N=5) in the age group of 45–54 years and 6.3% (N=1) in the age group of 35–44 years.

The prevalence rate of diabetes in adult population (25–64 years) was 9.6% and the prevalence rate of prediabetes was 27.8% (see Table 2). There was not found any significant difference in

male and female prevalence of prediabetes and DM. On the other hand, the prevalence of both, prediabetes and DM, significantly increased with age, the highest prevalence was found in the 55–64 years age group, with 40.1% prevalence of prediabetes and 18.0% prevalence of DM. Further, education was found as a strong determinant for prevalence of DM and prediabetes. Among those with primary education there was 40% of prediabetics and 14.3% of diabetics. Statistically significant difference was also found in prevalence of DM according to the area of living. Among those living in cities the prevalence of DM was 6.7% compared to 10.7% among population living in towns/suburb and rural areas ($p=0.031$).

Further, the prevalence rates of DM and prediabetes were found to increase significantly with BMI, waist circumference, TC and HDL cholesterol level and hypertension.

Smoking habits were similar among non-diabetic and prediabetic group ($p=0.138$), while among diabetic group there was higher proportion of ex-smokers. Prevalence of prediabetes and DM was higher among population with zero physical activity compared to population involving physical activity into their lives (in both $p<0.001$). Frequency of alcohol drinking was not significant with prevalence of prediabetes ($p=0.075$) or DM ($p=0.437$).

Logistic regression analysis showed that overweight, general and abdominal obesity, hypertension, and lower level of HDL (increased risk) significantly increased the risk of both prediabetes and DM (see Table 3), living in the cities significantly diminished risk of diabetes. For instance, among obese population the prediabetes risk (odds ratio) was 2.4 compared to normal weighted population and nearly 10times higher was the risk of DM. Among life style variables the significant increased risk of prediabetes and DM was found for smokers and ex-smokers. While, being a smoker indicated higher risk of prediabetes (OR=1.37, $p=0.05$) and being an ex-smoker the higher risk of DM (OR=2.74, $p<0.001$) compared to lifetime non-smokers. In other life-style variables (marijuana lifetime prevalence, physical activity and frequency of alcohol drinking) the significantly higher or lower risk for prediabetes or DM was not found.

Discussion

The EHES study was the first national study which systematically estimated the prevalence of DM and prediabetes in the adult population (25–64 years) in the Czech Republic and at the same time identified main DM risk factors within this population. The survey showed that the prevalence of DM was 9.6% (8% was already known, but 1.6% was previously unrecognized).

The total diabetes prevalence was higher in men than in woman, but the difference was not significant.

The prevalence of DM was higher than that revealed in post-Monica study (7.1%), a similar survey focused on the same age groups conducted in the six districts of the Czech Republic in the previous decade (2006–2009) (13). The difference is concordant with the overall DM prevalence increase (1), and also with the graduate increase of DM prevalence in the Czech Republic (in absolute numbers 804 987 patients in 2007, 927 373 in 2014) (9). Furthermore, rather more strict definition of DM according to HbA1c levels was used in our study while fasting plasma glucose or DM history was used in the post-Monica study, which could also contribute to this difference (14). The highest increase of DM prevalence among the age groups between the post-Monica study (13) and our survey was found in that of 35-45 years with the increase of 270%. There was 24% increase in DM prevalence in age groups of 54–65 years and almost the same increase in groups of 45–65 years.

A very alarming finding was that 16.7% of DM patients were previously unrecognised, with the 17.6% of previously undiagnosed patients within the age group between 55–64 years and even 23.8% of those in the age group between 45–54 years. Although the total portion of unrecognized DM patients seems to be low in our study group (1.6%) and actually is lower than whole population numbers reported from the other countries (e.g. 1.7% in Slovakia (15), 2.4% in Romania (16) or 6% in Spain (17), still substantial portion of patients of age between 45-64 remain undiagnosed.

The EHES study showed that the prevalence of prediabetes among population of age 25–64 years in the Czech Republic was nearly 28 %. The highest portion of subjects with prediabetes (40 %) was found in the age group 55–64, but substantial portion (35%) was also found in the age group 44–54 years.

The studies dealing with DM and prediabetes prevalence in the Central and Eastern Europe that would focus on the same age groups , are not available, thus a reasonable direct comparison regarding prevalence and other variables is not possible.

Regarding the DM risk factors, this investigation showed that in the single-factor analysis, BMI, central obesity, TC, HDL, hypertension, ever-smoking status, level of physical activity, and level of education were significantly associated with the prevalence rates of DM and prediabetes, while area of living was significantly associated with DM only.

In a multinomial logistic regression model, older age, overweight status, obesity, central obesity, lower HDL level, hypertension, ever-smoker and also ex-smoker status, were risk factors for DM, while living in high density areas and higher level of education than primary or vocational was a protective factor against DM.

In the same model, older age, overweight status, obesity, central obesity, higher TC and lower HDL level, hypertension, current-smoker status and primary education were risk factors for prediabetes, while higher level of education than primary was a protective factor.

Most of the above mentioned risk factor are well known and were found in several other studies (15–18). Apart of them living in the cities (not in towns) we found as an independent DM risk factor. This is concordant with a recent Czech diabetes registry which showed that the lowest regional DM prevalence is in the capital city Prague (7.6%), while the country prevalence is 9.4 % (19). We may speculate that this is due to a higher education associated with people living in the cities as the percentage of university type education is twice higher than country average (38% vs. 19% in 2018).

We found high level of TC to be a risk factor in prediabetes but not in DM, what is very probably result of TC screening in DM patients followed with successful treatment. The highest portion of ever-smokers as well as ex-smokers among the three analysed groups was in DM patients suggesting that this medical condition is in a way a strong reason to quit smoking. This fact very probably explains why current-smoker status is a risk factor for prediabetes but not for DM. Ex-smoker status only was found as a risk factor for DM in a Romanian PREDATORR study (16) while in a Chinese study (18) current-smoker status was a risk factor for both prediabetes and DM.

Marijuana use of higher frequency was found to be associated with prediabetes in one study (20) but not with DM (20, 21). We analysed this possible association in our data but no association was found significant. However, the risk even insignificant ($p=0.688$) of prediabetes was by 12% higher in marijuana users than among lifetime non-users.

Even the physical activity and the frequency of alcohol drinking did not play a role in a multinomial logistic regression model, the distribution of categories of these variable were different. Among non-diabetics there were 56% of none physically active ones, while among diabetics this share was almost 80%. Similarly, the highest proportion of daily drinkers was found in diabetic group (18%) and the lowest among non-diabetics (14%). These findings could point out to reserves in the health behaviour of diabetics.

The present study has several strengths. Primarily, it was the first study involving the representative sample of general population of the whole country. Second, the data and sample collection were done under the guidelines and the requirements for the implementation of standardized national health examination surveys (HES) in the European countries. Complex set of covariates including those which are no routinely analysed into this type of studies such as marijuana use, place of living, level of physical activity, were involved.

Also, several limitations of the study need to be considered when interpreting the results. First of all, the data came from cross-sectional study, thus we could not examine the cause-effect relationship between the followed risk factors and prevalence of prediabetes and DM. Second, the data did not allow us to distinguish between type 1 and type 2 DM. Third, respondence rate of EHES survey was 32 %. In last decades, population health surveys have tended toward lower response rates not only among Czech population but also in other countries [13, 22-23]. As several studies [24, 25] have shown a lower level of self-rated health or higher prevalence of chronic diseases among non-respondents, we could assume, that our results of prediabetes and DM prevalence within the Czech population could be even underreported due to selection bias.

Contributors

JB, ML, JM and MN assisted with the conception, design, and analysis of the study and wrote the manuscript draft, ML, KŽ and KR provided the statistical design, performed the analyses, and assisted with writing the manuscript, KK, JU, MJ, MN and MB contributed to the discussion and critically reviewed and provided edits to the manuscript. JB and ML are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1: General characteristics of the sample (groups)

Variable *total=1189*	*Nondiabetic group* *n=745*	*Prediabetic group* *n=330*	*Diabetic group* *n=114*	**ANOVA**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	***Prob>F***
HbA1C (%/mmol/mol)	***5.3(4.9)/34 (3.1)***	***5.9 (0.3)/41 (2.1)***	***7(2.3)/53(18.2)***	<0.001
Completed age (years)	43.3 (11.5)	52.1 (10.6)	55.2 (9.0)	<0.001
BMI (kg/m2)	26.2 (4.7)	28.7 (5.4)	32.9 (7.2)	<0.001
Waist circumference (cm)	88.8 (13.4)	95.1 (14.1)	107.8 (16.8)	<0.001
TC (mmol/l)	5.27 (1.07)	5.55 (1.01)	5.03 (1.18)	<0.001
HDL (mmol/l)	1.59 (0.46)	1.51 (0.43)	1.29 (0.37)	<0.001
systolic BP (mmHg)	121.4 (16.4)	127.3 (17.0)	132.8 (19.4)	<0.001
diastolic BP (mmHg)	78.9 (10.5)	82.5 (10.5)	82.3 (10.7)	<0.001

Notes: BMI - Body mass index, TC - serum total cholesterol, HDL high-density cholesterol, BP - blood pressure

Table 2: Prevalence of prediabetes and diabetes in the adult population (aged 25–64), Czechia, 2014

Risk factor/variable		*nondiabetic group*		*prediabetic group*		*diabetic group*		*p-value 1*	*p-value 2*	*p-value 3*
		n	***%***	***n***	***%***	***n***	***%***			
Total		***745***	***62,7***	***330***	***27,8***	***114***	***9,6***			
Sex	Male	297	62,1	126	26,4	55	11,5			
	Female	448	63,0	204	28,7	59	8,3	0.160	0.602	0.090
Age group	25–34	202	86,0	30	12,8	3	1,3			
	35–44	227	78,5	46	15,9	16	5,5			
	45–54	144	56,7	89	35,0	21	8,3			
	55–64	172	41,8	165	40,1	74	18,0	<0.001	<0.001	<0.001
Education	Primary	32	45,7	28	40,0	10	14,3			
	Vocational	244	58,5	114	27,3	59	14,1			
	Secondary	297	65,6	127	28,0	29	6,4			
	University	172	69,1	61	24,5	16	6,4	<0.001	<0.001	<0.001
Area of living/	Cities	216	65,9	90	27,4	22	6,7			
Degree of urbanization	Towns/suburb/rural areas	529	61,4	240	27,9	92	10,7	0.097	0.564	0.031
BMI categories	Normal	334	78,0	84	19,6	10	2,3			
	Overweight	270	62,4	127	29,3	36	8,3			
	Obese	141	43,0	119	36,3	68	20,7	<0.001	<0.001	<0.001
Waist circumference	Low risk	496	73,9	150	22,4	25	3,7			
	Increased risk	238	47,1	179	35,4	88	17,4	<0.001	<0.001	<0.001
Blood cholesterol level	Low risk	327	72,5	88	19,5	36	8,0			
	Increased risk	418	56,6	242	32,8	78	10,6	<0.001	<0.001	0.013
High-density cholesterol	Low risk	687	65,1	287	27,2	81	7,7			
	Increased risk	58	43,6	42	31,6	33	24,8	<0.001	0.010	<0.001
Hypertension	Yes	213	47,1	155	34,3	84	18,6			
	No	528	72,3	173	23,7	29	4,0	<0.001	<0.001	<0.001
Smoking habits	Non-smoker	394	67,1	153	26,1	40	6,8			
	Ex-smoker	139	55,4	68	27,1	44	17,5			
	Smoker	212	60,4	109	31,1	30	8,5	<0.001	0.138	<0.001
Non-smoking	Non-smoker	394	67,1	153	26,1	40	6,8			
lifetime prevalence	Smoker or ex-smoker	351	58,3	177	29,4	74	12,3	0.001	0.048	<0.001
Marijuana	yes/ever	86	78,9	21	19,3	2	1,8			
lifetime prevalence	no/never	659	61,0	309	28,6	112	10,4	<0.001	0.009	0.001
Physical activity	0 days	414	56,5	231	31,5	88	12,0			
number of days with 10 min PA	1–2 days	203	74,6	52	19,1	17	6,3			
	3 and more days	128	69,6	47	25,5	9	4,9	<0.001	<0.001	<0.001
Frequency of alcohol drinking	5–7 days	103	59,9	49	28,5	20	11,6			
days per week	1–4 days	272	67,2	97	24,0	36	8,9			
	0 days	370	60,5	184	30,1	58	9,5	0.179	0.075	0.437

Notes: p-value 1 – p-value for the difference between groups;
p-value 2 – p-value for the difference between prediabetic and nondiabetic groups;
p-value 3 –p-value for the difference between diabetic and nondiabetic groups

Table 3: Risk factors for prediabetes and diabetes in the adult population (aged 25–64), Czechia, 2014
crude OR for sex, age, education and degree of urbanization, other variables controlled for age and sex

Variables		***Prediabetes risk***			***Diabetes risk***		
		OR	CI95%	p-value	OR	CI95%	p-value
Sociodemographic variables							
Sex	Male	*1*			*1*		
	Female	1.073	0.823–0.140	0.602	0.711	0.497–1.056	0.091
Age group	25–34	*1*			*1*		
	35–44	1.364	0.829–2.224	0.221	4.746	1.363–16.525	0.014
	45–54	4.162	2.612–6.630	<0.001	9.819	2.874–33.543	<0.001
	55–64	6.459	4.164–10.019	<0.001	28.969	8.972–93.531	<0.001
Education	Primary	2.467	1.374–4.429	0.002	3.359	1.399–8.063	0.007
	Vocational	1.317	0.913–1.901	0.141	2.599	1.446–4.670	0.001
	Secondary	1.205	0.843–1.726	0.306	1.049	0.554–1.988	0.882
	University	*1*			*1*		
Area of living/ Degree of urbanization	Cities	*1*			*1*		
	Towns/suburb/rural areas	1.088	0.815–1.454	0.564	1.706	1.045–2.791	0.033
Metabolic variables							
BMI categories	Normal	*1*			*1*		
	Overweight	1.419	1.007–1.200	0.046	2.700	1.280–5.690	0.009
	Obese	2.401	1.666–3.461	<0.001	9.864	4.817–20.200	<0.001
Waist circumference	Low risk	*1*			*1*		
	Increased risk	1.812	1.362–2.411	<0.001	5.387	3.279–8.846	<0.001
Blood cholesterol level	Low risk	*1*			*1*		
	Increased risk	1.418	1.040–1.939	0.027	0.908	0.574–1.439	0.684
High-density cholesterol	Low risk	*1*			*1*		
	Increased risk	2.057	1.306–3.239	0.002	5.397	3.118–9.343	<0.001
Hypertension	Yes	1.430	1.055–1.938	0.021	4.345	2.651–7.123	<0.001
	No	*1*			*1*		
Life style variables							
Smoking habits	Non-smoker	*1*			*1*		
	Ex-smoker	1.203	0.831–1.741	0.326	2.735	1.647–4.544	<0.001
	Smoker	1.374	1.002–1.886	0.049	1.457	0.859–2.471	0.162
Non-smoking lifetime prevalence	Non-smoker	*1*			*1*		
	Smoker or ex-smoker	1.306	0.989–1.723	0.060	1.996	1.290–3.088	0.002
Marijuana lifetime prevalence	yes/ever	1.118	0.649–1.925	0.688	0.317	0.073–1.370	0.124
	no/never	*1*			*1*		
Physical activity *number of days with 10 min PA*	0 days	0.979	0.655–1.465	0.921	1.684	0.792–3.580	0.175
	1–2 days	0.632	0.392–1.020	0.060	1.098	0.458–2.634	0.834
	3 and more days	*1*			*1*		
Frequency of alcohol drinking	5–7 days	0.725	0.471–1.115	0.143	0.686	0.362–1.300	0.247

days per week	1–4 days	0.771	0.600–1.060	0.110	0.861	0.528–1.404	0.548
	0 days	*1*			*1*		

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2. Surname (Last Name): Brož
3. Date: 2/24/2020

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5. Manuscript Title: Prevalence of Diabetes and Prediabetes and its Risk Factors in Adults aged 25-64 in the Czech Republic: A Cross-Sectional

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Marek | Brabec | 2/24/2020

4. Are you the corresponding author? ☐ Yes ☑ No

5. Manuscript Title

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Michael | Jenšovský | 2/24/2020

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1. Given Name (First Name): Michala
2. Surname (Last Name): Lustigová
3. Date: 2/24/2020

4. Are you the corresponding author? ☐ Yes ☑ No

5. Manuscript Title: Prevalence of Diabetes and Prediabetes and its Risk Factors in Adults aged 25-64 in the Czech Republic: A Cross-Sectional

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Jana | Malinovská | 2/24/2020

4. Are you the corresponding author? ☐ Yes ☑ No

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Marisa | Nunes | 2/24/2020

4. Are you the corresponding author? ☐ Yes ☑ No

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Katarína | Rožeková | 2/24/2020

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Jana | Urbanová | 2/24/2020

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