

Noncommunicable chronic diseases clusters in Brazilian adults and older adults: correlations as multimorbidity

Agrupamento de doenças crônicas não transmissíveis em adultos e idosos brasileiros: correlações como multimorbidade

Marina Christofoletti¹ , Giovani Firpo Del Duca¹ , Jucemar Benedet¹ , Deborah Carvalho Malta² 

¹Universidade Federal de Santa Catarina - Florianópolis (SC), Brasil.

²Universidade Federal de Minas Gerais - Belo Horizonte (MG), Brasil.

How to cite: Christofoletti M, Del Duca GF, Benedet J, Malta DC. Noncommunicable chronic diseases clusters in Brazilian adults and older adults: correlations as multimorbidity. *Cad Saúde Colet*, 2023; 31 (2):e31020184. <https://doi.org/10.1590/1414-462X202331020184>

Abstract

Background: Health has dynamic conditions and overlapping pathophysiological factors. For health prevention and promotion, actions are necessary to understand the most common risk combinations. **Objective:** Describe noncommunicable chronic diseases (NCDs) clusters and investigate specific multimorbidity combinations in Brazilian adults and older adults. **Method:** This study used data from Vigitel 2013 survey held in the Brazilian capitals (52,929 interviews). A self-report of diabetes, dyslipidemia, hypertension, and obesity was used. The analyses were the descriptive cluster of NCDs and an adjusted binary logistic regression (odds ratio [OR]), stratified by age. **Results:** Among adults, the clusters of diabetes, dyslipidemia, hypertension, and obesity (O/E = 18.74) and diabetes, hypertension, and obesity (O/E = 16.83) were higher. There was a higher clustering between diabetes and obesity (O/E = 7.25). Among adults, diabetes was associated with dyslipidemia (OR: 3.04), hypertension (OR: 3.84), and hypertension with obesity (OR: 3.34). In older adults, hypertension was associated with diabetes (OR: 2.79), dyslipidemia (OR: 2.06), and obesity (OR: 2.26). **Conclusion:** Other diseases combined with diabetes and hypertension were more frequent in adults and older adults. It is suggested to combine preventive and control measures for these diseases for the non-occurrence of new diagnoses.

Keywords: chronic disease; related-diagnostic groups; risk index; cluster analysis; cross-sectional studies.

Resumo

Introdução: A saúde apresenta condições dinâmicas e fatores fisiopatológicos sobrepostos. Para ações de prevenção e promoção da saúde é necessário entender as combinações comuns de risco. **Objetivo:** Descrever os agrupamentos de doenças crônicas não transmissíveis (DCNT) e investigar combinações específicas de multimorbidade em adultos e idosos no Brasil. **Método:** Este estudo utilizou dados da pesquisa Vigitel 2013, realizada nas capitais brasileiras (total de 52.929 entrevistas). Foi utilizado um relato de diabetes, dislipidemia, hipertensão e obesidade. Nas análises foram utilizados o agrupamento descritivo de DCNT e uma regressão logística binária ajustada (razão de *odds* [RO]), estratificada por idade. **Resultados:** Entre os adultos, os grupos de diabetes, dislipidemia, hipertensão e obesidade (O / E = 18,74), bem como diabetes, hipertensão e obesidade (O / E = 16,83) foram maiores. Nos idosos, houve maior agrupamento entre diabetes e obesidade (O / E = 7,25). Entre os adultos, o diabetes foi associado à dislipidemia (RO: 3,04) e hipertensão (RO: 3,84), enquanto a hipertensão à obesidade (RO: 3,34). Nos idosos, a hipertensão foi associada a diabetes (RO: 2,79), dislipidemia (RO: 2,06) e obesidade (RO: 2,26).



This is an Open Access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Correspondence: Marina Christofoletti. E-mail: marinachriss@outlook.com

Financial support: Christofoletti M received a master's scholarship grant from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), under finance code 001.

Conflict of interests: nothing to declare.

Received on: Mar. 29, 2020. Accepted on: Mar. 29, 2021

Conclusão: Os agrupamentos de outras doenças combinadas com diabetes e hipertensão foram mais frequentes em adultos e idosos. Sugere-se que além das medidas existentes de prevenção para essas doenças também sejam propostas medidas de controle para a não ocorrência de novos diagnósticos.

Palavras-chave: doença crônica; grupos diagnósticos relacionados; indicador de risco; análise por conglomerados; estudos transversais.

INTRODUCTION

Multimorbidity, or multiple medical conditions in a single individual, is considered a growing global health program¹. Primarily, this health condition's existence was mainly in that older and better health services access¹. However, different income countries increase the multimorbidity reports incidence and better understand the causes, impact, and treatment¹.

A standard disease classification reported around the world that is easily observed in multimorbidity is NCDs². NCDs change the affected systems' physiological processes, which weaken health and expose individuals to other pathologies. Because NCDs are multifactorial diseases³, a new diagnosis can still be linked to modifiable risk factors maintained during more extended periods, which are similar for most NCDs, and favor the appearance of simultaneous diagnosis^{4,5}.

The complexity of individual NCDs promotes patient exposure to new chronic diseases⁶⁻¹¹. For this reason, NCDs should be analyzed according to their pathophysiological and drug and behavioral complexities¹². There are different types of NCDs, and it is crucial to prioritize the investigations of those with more significant economic impact and population prevalence, the vascular-metabolic ones¹³. In adults and older adults, a standard disease classification reported in multimorbidity is also cardio-metabolic².

As mentioned before, the different understanding of causes, impact, and treatment¹ is still lacking in multimorbidity investigation. As an epidemiological approach, cluster analyses can offer the most prevalent combinations between diseases. Health is a complex of dynamic conditions and overlapping pathophysiological factors, resulting in risk factors and comorbidities concomitance¹³, making it necessary to understand the most common combinations. This information could be important for public health direction in primary prevention and prevision of the impact caused by types of treatment, considering that in middle-income countries, these investigations are few¹.

Thus, it is necessary to identify the most grouped diagnosis to direct the necessary measures to prevent multimorbidity. In this context, the aim was to describe noncommunicable chronic diseases (NCDs) clusters and investigate specific multimorbidity combinations in Brazilian adults and older adults.

METHOD

The present study is a secondary analysis of a cross-sectional population-based survey, the National System of Surveillance of Risk Factors and Protection for Chronic Noncommunicable Diseases (Vigitel), carried out between February and December 2013, in the capitals of the 27 federative units of Brazil. The target population was adults (≥ 18 years) who had at least one fixed telephone line at the residence. The sampling process included criteria to estimate the variables of risk factors and protection of NCD with a 95% confidence level and a maximum error of approximately three percentage points, estimating a minimum of 2,000 respondents per capital. The entire process of selecting eligible subjects has been published previously by the Ministry of Health¹⁴ and Monteiro et al.¹⁵. Among 74,005 eligible participants, 52,929 subjects were included (71.5% response rate). There was post-stratification weighting for each interviewee, calculated using the 'rake' method¹⁴. The instrument used was a previously validated questionnaire containing sociodemographic, behavioral, nutritional, and health factors. Data collection was performed via a telephone interview, which relied on computer resources to assist the interviewer in this process.

The outcome and exposure variables were NCDs' occurrences separately and as multimorbidities (≥ 2 diseases)¹. The considered diseases were those included in the survey: diabetes, dyslipidemia, and hypertension, as measured by an affirmative answer to the questions "Has any doctor ever told you that you have diabetes/dyslipidemia/high blood pressure?" Obesity was defined as a body mass index of 30 kg/m² or higher, calculated by the interviewee's self-reported weight and height. The data were allocated using the "hot deck" technique due to blank answers for this variable.

The descriptive analysis included estimating the prevalence and clusters of age-stratified NCDs in which clusters were identified by 16 possible combinations of disease diagnosis (yes or no) in each option presented (diabetes, dyslipidemia, arterial hypertension, and obesity). The observed (O)/expected (E) ratio was calculated between the O and E prevalence, with their respective 95% confidence intervals (95% CIs). The expected prevalence for the independence of NCDs was assumed by multiplying the individual probability of each diagnosis in the study population: $E = (1 - P_{\text{diabetes}}) \times (1 - P_{\text{dyslipidemia}}) \times (1 - P_{\text{arterial hypertension}}) \times (1 - P_{\text{obesity}})$. In the inferential analysis, binary logistic regression was performed, with data expressed as odds ratio (OR) and their 95% confidence interval (95%CI), to identify the association of the coexistence of combinations of existing diseases in the sample. There was the first-level adjustment for sex (male; female), age (continuum variable), marital status (living with or without a partner), skin color (brown/black or white), and demographic macro-regions (South; Southeast; Central West; North East; North); second-level for schooling (<8; 8 to 11; >11 years of study); and third-level for television time per day (≥ 2 hours) and physical activity in leisure-time and commuting per week (>10; 10 to 149; ≥ 150 minutes). The statistical modeling had a critical level of $p \leq 0.20$ for permanence in the regression's hierarchical conceptual model. The significance level adopted for both the crude and adjusted analyses was 5% ($p < 0.05$). Stata® (Stata Corporation, College Station, USA), version 13.0 was used for all analyses. All analyses considered the sample weight as the inverse of the number of existing telephone lines of the domicile and adults living in the interviewee's home.

Free and informed consent was assumed by verbal consent, since it was a telephone survey, upon approval of the National Commission for Ethics in Research for Human Subjects of the Ministry of Health (opinion no. 355.590).

RESULTS

Among 52,929 subjects, most adults and older adults were females (52.9% and 59.5%, respectively). The mean age of adults and older adults was 36.2 ± 11.2 and 69.4 ± 13.3 years, respectively. The most significant proportion of adults reported living without a partner (52.0%), had brown/black skin color (55.1%) predominantly and had 9 to 11 years of education (41.1%). In turn, the majority of the older adults reported living with a partner (56.9%), having a white skin color (61.3%), and 0 to 8 years of education (69.3%). Among NCDs, the majority of adults reported not having diabetes (95.8%), dyslipidemia (82.6%), arterial hypertension (82.4%), or obesity (83.4%), while the majority of older adults reported having arterial hypertension (58.2%).

Table 1 shows the prevalence of 16 different possible clusters of the four NCDs (diabetes, dyslipidemia, hypertension, and obesity). In adults, the most frequent combinations were diabetes and hypertension (3.4%), hypertension and obesity (2.9%), and diabetes and dyslipidemia (2.2%). The observed prevalence of the combination of all four was 18.7-fold higher than the expected prevalence if they occurred independently. For the combination of diabetes, hypertension, and obesity, this value was 16.8-fold the expected; 3.5-fold for diabetes, dyslipidemia, and obesity; 7.1-fold for diabetes and obesity; 3.3-fold for diabetes and dyslipidemia; and, finally, 1.2-fold for hypertension and obesity (Table 1).

Among the older adults (Table 2), the most prevalent pairs combinations were 12.2% (hypertension and obesity) and 6.3% (diabetes and obesity). The combinations of three diseases in older adults included dyslipidemia, hypertension, and obesity (5.6%), followed by diabetes, hypertension, and obesity (4.3%). Considering the NCDs' observation, multimorbidity was the same as those observed in adults, except for diabetes and dyslipidemia.

Table 1. Clustering of different NCDs for multimorbidity in adults. Brazil, 2013 (n=37,947)

Number of NCDs	NCDs				n	% ^a O	% ^a E	O/E (95%CI) ^b
	Diabetes	Dyslipidemia	Hypertension	Obesity				
4	+	+	+	+	215	0.58	0.03	18.74 (13.64;24.46)
3	+	-	+	+	702	1.94	0.12	16.83 (14.12;19.78)
	+	+	-	+	167	0.43	0.12	3.48 (1.32;7.66)
2	+	+	+	-	72	0.21	0.16	1.29 (0.03;7.50)
	-	+	+	+	282	0.7	0.64	1.09 (0.22;3.08)
	+	-	-	+	1,163	3.27	0.46	7.10 (5.72;8.777)
	+	+	-	-	844	2.16	0.65	3.31 (2.22;4.76)
1	-	-	+	+	1,368	2.94	2.40	1.23 (0.72;2.04)
	+	-	+	-	101	0.3	0.61	0.49 (0.00;3.59)
	-	+	+	-	252	0.67	3.40	0.20 (0.01;2.19)
	-	+	-	+	188	0.47	2.57	0.18 (0.00;1.94)
	+	-	-	-	2,597	7.64	2.43	3.14 (2.52;3.90)
	-	+	-	-	2,641	6.65	13.58	0.49 (0.26;0.84)
0	-	-	+	-	3,741	8.5	12.66	0.67 (0.43;0.98)
	-	-	-	+	301	0.8	9.58	0.08 (0.08;2.38)
	-	-	-	-	20,003	62.74	50.58	1.24 (0.08;1.83)

Notes: NCDs – noncommunicable chronic diseases; 95%CI – 95% confidence interval; O – observed values; E – expect values
^aWeighted values ^bConfidence interval of 95% in the weighted sample

Table 2. Clustering of different NCDs for multimorbidity in older adults. Brazil, 2013 (n=14,982)

Number of NCDs	NCDs				n	% ^a O	% ^a E	O/E (95%CI) ^b
	Diabetes	Dyslipidemia	Hypertension	Obesity				
4	+	+	+	+	303	2.70	0.70	3.87 (2.06;6.82)
3	+	-	+	+	533	4.30	1.12	3.83 (2.06;6.82)
	+	+	-	+	222	2.20	0.54	4.08 (1.87;7.56)
2	+	+	+	-	40	0.40	3.41	0.12 (0.00;8.81)
	-	+	+	+	632	5.60	2.97	1.89 (1.00;2029)
	+	-	-	+	689	6.30	0.87	7.25 (5.43;9.46)
	+	+	-	-	175	1.60	2.64	0.61 (0.01;3.14)
1	-	-	+	+	1,693	12.20	4.77	2.56 (18.4;3.41)
	+	-	+	-	74	0.50	5.50	0.09 (0.0;4.86)
	-	+	+	-	580	5.70	14.52	0.39 (0.04;1.24)
	-	+	-	+	206	1.60	2.29	0.70 (0.01;2.67)
	+	-	-	-	407	3.40	4.25	0.80 (0.15;2.14)
0	-	+	-	-	2,330	18.50	11.24	1.65 (1.16;2.23)
	-	-	+	-	1,245	8.10	23.39	0.35 (0.07;0.08)
	-	-	-	+	325	2.50	3.69	0.68 (0.01;2.21)
0	-	-	-	-	3,097	24.40	18.09	1.35 (0.09;1.83)

Notes: NCDs – noncommunicable chronic diseases; 95%CI – 95% confidence interval; O – observed values; E – expect values
^aWeighted values ^bConfidence interval of 95% in the weighted sample

The highest values were the combinations of diabetes and obesity (O / E = 7.25) and diabetes, dyslipidemia, and obesity (O / E = 4.08).

Table 3 presents the odds ratio for adults with specific combinations of two NCDs as a multimorbidity. Pairs of NCDs were the presence of diabetes and dyslipidemia (OR: 3.04), diabetes and hypertension (OR: 3.84), and hypertension and obesity (OR: 3.34).

Table 4 shows the association of multimorbidity combinations in older adults, with a higher odds ratio for diabetes with hypertension (OR: 2.79), dyslipidemia with hypertension (OR: 2.06), and, finally, hypertension and obesity (OR: 2.26).

Table 4. Prevalence of multimorbidity coexistence with two specific NCDs in older adults. Brazil, 2013 (n=14,982)

Variable	(%) ^a	Crude		Model 1		Model 2		Model 3	
		OR ^a (95%IC)	P						
Diabetes and Dyslipidemia	10.7	2.02 (1.69;2.41)	<0.001	2.12 (1.73;2.61)	<0.001	2.00 (1.67;2.39)	<0.001	1.96 (1.63;2.35)	<0.001
Diabetes and Hypertension	16.5	2.92 (2.42;3.52)	<0.001	3.17 (2.56;3.93)	<0.001	2.84 (2.34;3.44)	<0.001	2.79 (2.30;3.39)	<0.001
Diabetes and Obesity	5.7	1.50 (1.19;1.88)	0.001	1.68 (1.30;2.17)	<0.001	1.44 (1.14;1.82)	0.002	1.36 (1.07;1.73)	0.011
Dyslipidemia and Hypertension	25.8	2.16 (1.87;2.51)	<0.001	2.16 (1.82;2.55)	<0.001	2.08 (1.78;2.42)	<0.001	2.06 (1.77;2.39)	<0.001
Dyslipidemia and Obesity	9.0	1.33 (1.09;1.63)	0.005	1.28 (1.01;1.61)	0.041	1.27 (1.03;1.57)	0.025	1.23 (1.00;1.51)	0.051
Hypertension and Obesity	15.4	2.26 (1.81;2.83)	<0.001	2.42 (1.89;3.10)	<0.001	2.36 (1.84;3.04)	<0.001	2.26 (1.76;2.91)	<0.001

Notes: NCDs – noncommunicable chronic diseases; OR – odds ratio; 95%CI – 95% confidence interval. Analysis adjusted for sex, age, marital status, skin color, demographic macroregion (first level), education level (second level), and for physical activity in the commuting and leisure-time domains, and daily television time (third level) ^aWeighted values

Table 3. Prevalence of multimorbidity coexistence with two specific NCDs in adults. Brazil, 2013 (n=37, 947)

Variable	(%) ^a	Crude		Model 1		Model 2		Model 3	
		OR ^a (95%IC)	P						
Diabetes and Dyslipidemia	2.0	4.84 (3.95;5.93)	<0.001	2.90 (2.27;3.69)	<0.001	3.09 (2.48;3.85)	<0.001	3.04 (2.43;3.79)	<0.001
Diabetes and Hypertension	2.4	7.42 (6.05;9.09)	<0.001	4.12 (3.27;5.19)	<0.001	3.87 (3.12;4.79)	<0.001	3.84 (3.10;4.76)	<0.001
Diabetes and Obesity	1.5	3.02 (2.42;3.77)	<0.001	2.14 (1.67;2.75)	<0.001	2.22 (1.77;2.80)	<0.001	2.20 (1.74;2.79)	<0.001
Dyslipidemia and Hypertension	6.4	3.71 (3.32;4.14)	<0.001	2.30 (2.03;2.60)	<0.001	2.33 (2.05;2.64)	<0.001	2.31 (2.04;2.62)	<0.001
Dyslipidemia and Obesity	5.0	2.39 (2.12;2.71)	<0.001	1.94 (1.68;2.24)	<0.001	1.99 (1.75;2.27)	<0.001	1.97 (1.72;2.25)	<0.001
Hypertension and Obesity	6.3	3.97 (3.53;4.48)	<0.001	3.41 (2.98;3.91)	<0.001	3.37 (2.93;3.86)	<0.001	3.34 (2.91;3.83)	<0.001

Notes: NCDs – noncommunicable chronic diseases; OR – odds ratio; 95%CI – 95% confidence interval. Analysis adjusted for sex, age, marital status, skin color, demographic macroregion (first level), education level (second level), and for physical activity in the commuting and leisure-time domains, and daily television time (third level) ^aWeighted values

DISCUSSION

This study aimed to describe NCDs clusters and investigate specific combinations of multimorbidity in adults and older adults in Brazil. The predominantly cluster occurred through the presence of obesity and diabetes in both age groups. The results also indicate that diabetes was associated with dyslipidemia and hypertension and hypertension with obesity in adults. In contrast, hypertension was associated with diabetes and dyslipidemia, and obesity in older adults. It is important to emphasize that in older adults, disease increases more than in adults, and exposure to a new diagnosis, justifies the stratification by age group.

In adults, the most prevalent combination was the absence of NCDs, but the higher impact of diagnostic dependence, visualized from the O/E ratio, was all diseases. The simultaneity was observed 18.7-fold more often than was expected in other combinations. Although the prevalence of NCDs also affected the adult population to a lesser extent than the older adults, it is currently considered a public health concern due to the relative increase in mortality and expenditures in this age group¹⁶. It is worth noting that the National Plan for Combating NCDs and the Global Plan has set goals for the reduction of premature mortality by NCDs among individuals between 30 and 69 years of age, given their importance in national and global scenario¹⁷⁻¹⁹. Like the present study, a survey conducted by Jovic et al.²⁰ found most of the adult population had no NCDs.

In contrast, multimorbidity in adults occurred mainly with cardiometabolic diagnosis⁹, consistent with the present study's findings. In this age group, multimorbidity may occur due to pre-existing diseases, which, over time, generate an overload in the body²¹. In decade-long studies, the highest prevalence of multimorbidity occurred with increasing age, especially between 40 and 60 years of age²².

In general, adults and older adults more often had diabetes and obesity as multimorbidity, which is justified in the literature by physiological determinants; both are also important cardiovascular risk factors^{7,9,21}. Considering that previously the disease exists those are risk factors, which compose the metabolic syndrome²³, the diagnoses promote a long duration of the body's metabolic overload. All of the metabolic changes due to diabetes and obesity^{23,24}, together with the coexistence of risk behaviors such as positive energy balance, increased sedentary behavior, and lack of physical activity, favor the emergence of other diseases dyslipidemias, arterial hypertension, and coronary artery disease¹.

Our findings show that disease clusters in adults are three times more likely when the combination of diagnoses includes diabetes, hypertension, or obesity. It is reasonable to assume that these pathologies may be responsible for a more significant aggregation of diseases, especially their asymptomatic characteristics¹, which can lead to the multimorbidity occurrence without knowing the first disease that originated the others. Nonetheless, Brazil has several programs returning to public health that must be considered, which bring information to those involved in primary health care, such as the Family Health Program²⁵.

In the older adults, the combinations of NCDs multimorbidity were similar to those in adults, with the highest value found for diabetes concomitant with hypertension. Roberts et al.²⁶ observed that an increase in blood pressure is related to an approximately seven-fold increase in the risk for multimorbidity in adults and older adults²⁶. When considering the number of diseases aggregated with hypertension, Sarkar et al.²⁷ reported a mean aggregate value of two per person's multimorbid diseases. In this sense, the older adults in the present study presented a continuity of behavior with that of the grouped diseases identified in adults, indicating that, regardless of age, the combination of diabetes and hypertension is a vital multimorbidity profile. This fact becomes worrying as the advancement of age implies greater exposure to the diseases' adverse effects, mainly attributed to the time of survival of the diagnosis and compromises in progressive functional decline due to the aging process²¹.

The present study has several strengths, including the representativeness of the adult and older adult population, which allows a deeper investigation of the most frequent combinations of diseases to inform future public health measures. The adopted methodology has the reliability that makes it possible to extrapolate the data to the Brazilian population residing in the capitals with a medium-income country's strong sample power.

An analysis was also used to identify the characteristics and magnitudes of the main combinations of diagnosis, leading to inform health promotion and prevention measures. However, some limitations should be considered, such as the self-reporting of diseases in the survey, which requires considering the need for adequate health care to avoid underreporting. In this direction, the BMI missing data needed the hot deck imputation, which required suitable matches of donors to recipients that reflect available covariate information. To minimize that analysis weakness, the sample size and the use of real values should be considered²⁸. A limited number of diagnoses were simultaneously evaluated, combining NCDs, based on the events included in the telephone survey questionnaire, which may have made comparability with studies in other countries difficult. Finally, the diagnosis of NCDs did not consider their severity, a fact that may have been reflected in the findings.

In summary, the analysis of Vigitel data from adults and older adults revealed that NCDs' occurrence had two main potential reasons in both age groups, the presence of obesity and diabetes. In adults, diabetes was associated with dyslipidemia and hypertension and hypertension with obesity. In contrast, hypertension was associated with diabetes and dyslipidemia, and obesity in older adults. Thus, health promotion actions should be encouraged not only for patients without a diagnosis but also for those diagnosed with an illness.

ACKNOWLEDGEMENTS

The authors would like to acknowledge also the logistical and financial contributions of the Health Ministry of Brazil and the study participants.

REFERENCES

1. The Academy of Medical Sciences. Multimorbidity: a priority for global health research. London: The Academy of Medical Sciences; 2018.
2. Violan C, Foguet-Boreu Q, Flores-Mateo G, Salisbury C, Blom J, Freitag M, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One*. 2014;9(7):e102149. <http://dx.doi.org/10.1371/journal.pone.0102149>. PMID:25048354.
3. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee I-M, et al. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43(7):1334-59. <http://dx.doi.org/10.1249/MSS.0b013e318213feff>. PMID:21694556.
4. Wagner K-H, Brath H. A global view on the development of non communicable diseases. *Prev Med*. 2012;54(Suppl):S38-41. <http://dx.doi.org/10.1016/j.ypmed.2011.11.012>. PMID:22178469.
5. Brazil. Plano de ações estratégicas para o enfrentamento das doenças crônicas não transmissíveis (DCNT) no Brasil: 2011-2022. Brasília: Ministério da Saúde; 2011.
6. World Health Organization. Cardiovascular diseases [Internet]. 2023 [cited 2018 Mar 20]. Available from: http://www.who.int/cardiovascular_diseases/en/
7. Strange RC, Shipman KE, Ramachandran S. Metabolic syndrome: a review of the role of vitamin D in mediating susceptibility and outcome. *World J Diabetes*. 2015;6(7):896-911. <http://dx.doi.org/10.4239/wjd.v6.i7.896>. PMID:26185598.
8. Xavier HT, Izar MC, Faria JR No, Assad MH, Rocha VZ, Sposito AC, et al. V Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose. *Arq Bras Cardiol*. 2013;101(4):1-22. <http://dx.doi.org/10.5935/abc.20135010>. PMID:24217493.
9. Stepanova M, Rodriguez E, Biredinc A, Baranova A. Age-independent rise of inflammatory scores may contribute to accelerated aging in multimorbidity. *Oncotarget*. 2015;6(3):1414-21. <http://dx.doi.org/10.18632/oncotarget.2725>. PMID:25638154.
10. Goyal A, Nimmakayala KR, Zonszein J. Is there a paradox in obesity? *Cardiol Rev*. 2014;22(4):163-70. <http://dx.doi.org/10.1097/CRD.000000000000004>. PMID:24896249.
11. Rosario PW, Calsolari MR. Screening for acromegaly in adult patients not reporting enlargement of the extremities, but with arterial hypertension associated with another comorbidity of the disease. *Arq Bras Endocrinol Metabol*. 2014;58(8):807-11. <http://dx.doi.org/10.1590/0004-2730000003314>. PMID:25465601.

12. Mirrakhimov EM, Kerimkulova AS, Lunegova OS, Mirrakhimov AE, Nabiev MP, Neronova KV, et al. The association of leptin with dyslipidemia, arterial hypertension and obesity in Kyrgyz (Central Asian nation) population. *BMC Res Notes*. 2014;7(1):411. <http://dx.doi.org/10.1186/1756-0500-7-411>. PMID:24981337.
13. Whitty CJ, MacEwen C, Goddard A, Alderson D, Marshall M, Calderwood C, et al. Rising to the challenge of multimorbidity. *BMJ*. 2020;368:l6964. <http://dx.doi.org/10.1136/bmj.l6964>. PMID:31907164.
14. Brasil. Ministério da Saúde. Vigitel Brasil 2014: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Brasília: Ministério da Saúde; 2014.
15. Monteiro C, Moura E, Jaime PC, Lucca A, Florindo AA, Figueiredo ICR, et al. Monitoramento de fatores de risco para doenças crônicas por entrevistas telefônicas. *Rev Saude Publica*. 2005;39(1):47-57. <http://dx.doi.org/10.1590/S0034-89102005000100007>. PMID:15654460.
16. Wang H, Dwyer-Lindgren L, Lofgren KT, Rajaratnam JK, Marcus JR, Levin-Rector A, et al. Age-specific and sex-specific mortality in 187 countries, 1970-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2071-94. [http://dx.doi.org/10.1016/S0140-6736\(12\)61719-X](http://dx.doi.org/10.1016/S0140-6736(12)61719-X). PMID:23245603.
17. Malta DC, Morais Neto OL, Silva Junior JB. Apresentação do plano de ações estratégicas para o enfrentamento das doenças crônicas não transmissíveis no Brasil, 2011 a 2022. *Epidemiol Serv Saude*. 2011;20(4):425-38. <http://dx.doi.org/10.5123/S1679-49742011000400002>.
18. World Health Organization. WHO Global action plan for the prevention and control of noncommunicable disease 2013-2020 [Internet]. 2013 [cited 2014 Feb 20]. Available from: <https://www.who.int/publications/i/item/9789241506236>
19. Nações Unidas no Brasil. Os Objetivos de Desenvolvimento Sustentável no Brasil [Internet]. 2015 [cited 2016 Jan 5]. Available from: <https://nacoesunidas.org/pos2015/ods3/>
20. Jovic D, Vukovic D, Marinkovic J. Prevalence and patterns of multi-morbidity in Serbian adults: a cross-sectional study. *PLoS One*. 2016;11(2):e0148646. <http://dx.doi.org/10.1371/journal.pone.0148646>. PMID:26871936.
21. Powers S, Howley ET. *Physiology of exercise: theory and application to conditioning and sports*. Boston: McGraw-Hill; 2009.
22. Pati S, Agrawal S, Swain S, Lee JT, Vellakkal S, Hussain MA, et al. Non communicable disease multimorbidity and associated health care utilization and expenditures in India: cross-sectional study. *BMC Health Serv Res*. 2014;14(1):451. <http://dx.doi.org/10.1186/1472-6963-14-451>. PMID:25274447.
23. Wagner A, Dallongeville J, Haas B, Ruidavets JB, Amouyel P, Ferrières J, et al. Sedentary behaviour, physical activity and dietary patterns are independently associated with the metabolic syndrome. *Diabetes Metab*. 2012;38(5):428-35. <http://dx.doi.org/10.1016/j.diabet.2012.04.005>. PMID:22721723.
24. Banerjee A, Sharma D, Trivedi R, Singh J. Treatment of insulin resistance in obesity-associated type 2 diabetes mellitus through adiponectin gene therapy. *Int J Pharm*. 2020;583:119357. <http://dx.doi.org/10.1016/j.ijpharm.2020.119357>. PMID:32334065.
25. Malta DC, Santos MAS, Stopa SR, Vieira JEB, Melo EA, Reis C. A cobertura da Estratégia de Saúde da Família (ESF) no Brasil, segundo a Pesquisa Nacional de Saúde, 2013. *Cien Saude Colet*. 2016;21(2):327-38. <http://dx.doi.org/10.1590/1413-81232015212.23602015>. PMID:26910142.
26. Roberts KC, Rao DP, Bennett TL, Loukine L, Jayaraman GC. Prevalence and patterns of chronic disease multimorbidity and associated determinants in Canada. *Health Promot Chronic Dis Prev Can*. 2015;35(6):87-94. <http://dx.doi.org/10.24095/hpcdp.35.6.01>. PMID:26302227.
27. Sarkar C, Dodhia H, Crompton J, Schofield P, White P, Millett C, et al. Hypertension: a cross-sectional study of the role of multimorbidity in blood pressure control. *BMC Fam Pract*. 2015;16(1):98. <http://dx.doi.org/10.1186/s12875-015-0313-y>. PMID:26248616.
28. Andridge RR, Little RJ. A review of hot deck imputation for survey non-response. *Int Stat Rev*. 2010;78(1):40-64. <http://dx.doi.org/10.1111/j.1751-5823.2010.00103.x>. PMID:21743766.