Simultaneity of chronic noncommunicable diseases in 2013 in Brazilian state capital cities: prevalence and demographic profile*

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Abstract

Objective: to describe the prevalence and sociodemographic profile of chronic noncommunicable disease (CNCDs) simultaneity in adults and elderly people resident in Brazilian state capital cities. 

Methods: Chronic Non-communicable Disease Risk and Protection Factor Surveillance System Survey 2013; simultaneity was considered to be two or more CNCDs (diabetes mellitus, dyslipidemia, hypertension, and obesity).

Results: of the total 52,929 participants, 13.7% of adult participants and 42.9% of elderly participants had CNCD simultaneity; hypertension and diabetes mellitus simultaneity was greater in adults, while hypertension and obesity simultaneity was greater in the elderly; simultaneity was more prevalent in women, in those between 50 and 59 years old, with partners and up to eight years of schooling; the cities with the lowest and highest prevalence in adults were São Luís and Cuiabá, respectively, while in the elderly, the cities were Belém and Manaus, respectively.

Conclusion: simultaneity was identified nationwide; prevention measures should be directed especially toward treatment of hypertension.

Keywords: Chronic Disease; Diagnosis-Related Groups; Socioeconomic Factors; Cross-Sectional Studies.

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Introduction

In Brazil, chronic noncommunicable diseases (CNCDs) accounted for 73% of general deaths and 17% of early deaths recorded in 2017. These data reflect high prevalence of these diseases and are due to the so-called “epidemiological transition”; a fact that can involve high cost for the public health system, early retirement and absenteeism.

Each CNCD promotes an organic overload in affected body systems, due to changes in physiologic processes, debilitating health status and favoring other diseases. In the United States and Canada 26.0% and 12.9% of the adult population, respectively, was found to have two or more diagnosed CNCDs in the period between 2014 and 2015. Treatment with medication exposes the population to possible side effects of drug interactions, while the collective impacts are linked to health service expenditure. Disease simultaneity, defined as multimorbidity, consists of the existence of diagnosis of two or more diseases occurring jointly in the same individual. This condition is of concern for Public Health, given health access inequalities and health service overload resulting from, for instance, continuous use of drugs, specialized medical services and hospitalizations.

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The context of population aging reveals the need for Public Health to promote better quality of life after CNCD diagnosis. Disease simultaneity may be considered a reality to be investigated, because it requires more health care, especially in relation to patient survival after diagnosis.

Investigation as to the prevalence of disease simultaneity in population studies has been widely explored in the Brazilian context, especially in regard to the investigation of associated factors. However, few studies include a broad age range, especially adults, as well as behavior of disease aggregation. The presence of diabetes mellitus, dyslipidemia, hypertension and/or obesity is considered to be an important cardiovascular risk indicator, according to the Ministry of Health’s “Strategic Action Plan for Addressing CNCD”; and this reinforces the importance of approaching these diseases and treating health as a comprehensive dynamic ensemble, and not exclusively as the absence of diseases. This understanding should also consider sociodemographic characteristics, such as age, sex and economic indicators, capable of interfering in greater probability of the occurrence and severity of CNCD simultaneity.

With the purpose of contributing to the comprehension of CNCD simultaneity and possible indicators of this health condition, this study aimed to describe the prevalence and the sociodemographic profile of CNCD simultaneity in adults and the elderly living in the Brazilian state capital cities.

Methods

This study consists of analysis of data obtained via the Chronic Noncommunicable Disease Risk and Protection Factor Surveillance System (VIGITEL), a national survey conducted annually since 2006 in all 27 capital cities of the Brazilian Federative Units.

Data collection took place from February to December 2013 with people aged 18 or over living in households with a landline telephone. The sampling process considered the criteria of CNCD risk and protection factor variable estimates taking a 95% confidence level and maximum error of 3 percentage points, leading to a minimum sample size of 2,000 interviews.

Definition of landlines eligible for the sample took place in three stages: (i) selection stratified by postcode, (ii) reconnaissance of eligible landlines concomitantly with interviews, and (iii) selection of the survey participant to be interviewed from among all adults living in the household. The full description of this process is contained in the report published by the Ministry of Health. The post-stratification weight for each individual in the sample was calculated by the rake method. The data were collected by means of telephone interviews and computer resources used at the same time.

The questionnaire used had been validated in previous pilot-studies. The outcome variable was CNCD simultaneity. Considering that the VIGITEL System has a limited number of questions about...
diagnosis, we opted to include the following CNCDs and risk factors: diabetes mellitus, dyslipidemia, arterial hypertension and obesity. These CNCDs were measured by an affirmative answer to the question:

*Has a doctor ever told you that you have diabetes/dyslipidemia/high blood pressure?*

Or, in the case of obesity, when body mass index (BMI) was greater than or equal to 30kg/m², calculated based on interviewee self-reported weight and height. Data imputation was done using the hot deck technique for blank answers (8.8%) in relation to this second variable. This technique identified missing answers and their association with the “age”, “sex”, “education level” and “ethnicity/skin color” variables. Subsequently, we defined groups according to similarities between characteristics, including those with and without an answer to the question about weight and/or height. We randomly chose one participant per capital city who had answered one or both of these questions and repeated their data when other respondents had left them blank, considering prior existence of similar characteristics. More details on the methodology can be found in another publication.

The simultaneity variable was dichotomized between absence of simultaneity (0 or 1 disease) and presence of simultaneity (≥2 diseases). We also analyzed the amount of accumulated diseases (2 diseases, 3 diseases or 4 diseases). The exposure variables were:
- sex (male; female);
- age (in years: 18 to 29; 30 to 39; 40 to 49; 50 to 59; 60 to 69; 70 to 79; 80 to 89; ≥90);
- marital status (had a partner; did not have a partner);
- ethnicity/skin color (white; black/brown);
- education level (in years of schooling: up to 8; 9 to 11; 12 or more);
- demographic macro-region (Midwest; Northeast; North; Southeast; South); and
- the 27 capital cities of the Federative Units.

For the purposes of description we used absolute and relative frequencies with 95% confidence intervals (95%CI). We stratified the data according to sex, age and reported CNCD simultaneity. Our interpretation of the findings took the 95% CIs into consideration. We used Stata® version 13.0 (Stata Corporation, College Station, USA) to perform the analyses. All analyses considered the sample weight, weighted in the process by two factors: the inverse of the number of telephone landlines in the household interviewed and the number of adults living in the household interviewed.

Free and Informed Consent was audio recorded given that this was a telephone survey. This study was approved by the National Committee for Ethics in Human Research (CONEP) which is subordinated to the National Health Council/Ministry of Health, as per Report No. 355,590.

Results

Out of 74,005 eligible individuals, 52,929 interviews were completed (71.5%). Most of the sample was represented by women (53.9% [95%CI 53.1;54.8]), people without a partner (50.6% [95%CI 49.7; 21.5]), brown/black ethnicity/skin color (52.7% [95%CI 51.8;53.6]) and 9 to eleven years of schooling (37.3% [95%CI 36.3;38.2]). Regarding CNCDs, diabetes mellitus prevalence was 6.9% (95%CI 6.5;7.3), 20.3% (95%CI 19.6;21.0) reported dyslipidemia, 24.1% (95%CI 23.4;24.8) arterial hypertension and 17.5% (95%CI 16.9;18.2) obesity.

The number of answers having the outcome of this study was 47,218 (89.2%). Among them, CNCD simultaneity prevalence was 18.2% (95%CI 17.5;18.9). When considering the score for accumulated diseases, we found that 12.6% (95%CI 12.0;13.2) of the sample had two, 4.7% (95%CI 4.3;5.1) had three and 0.9% (95%CI 0.8;1.1) had four CNCDs. When the results were stratified according to age, the prevalence rates of disease simultaneity in adults and the elderly were 13.7% (95%CI 12.7;14.1) and 42.9% (95%CI 41.0;44.9), respectively. The most frequent combinations in adults were diabetes mellitus and hypertension (3.3%), hypertension and obesity (2.9%) and diabetes mellitus and dyslipidemia (2.2%). In the elderly, the most frequent combination of two CNCDs was hypertension and obesity (12.2%) and diabetes mellitus and obesity (6.3%); and with regard to simultaneity of three diseases, 5.6% had dyslipidemia, hypertension and obesity, and 4.3% had diabetes mellitus, hypertension and obesity.
Table 1 considers reported disease simultaneity according to sociodemographic indicators. In respondents without disease simultaneity, the estimates were similar between men and women, with greater prevalence among younger adults (18 to 29 years of age [33.7% – 95%CI 32.8;34.8]), people without a partner (52.9% [95%CI 51.9;53.9]), black or brown ethnicity/skin color (52.7% [95%CI 51.6;53.8]), 9 to 11 years of study (40.5% [95%CI 39.5;41.5]), and those living in the Brazilian Southeastern region (44.3% [95%CI 43.2;45.4]). In the case of respondents with disease simultaneity, there was no distinction between the proportions of black/brown and white ethnicity/skin color. CNCD simultaneity was more prevalent among women (56.0% [95%CI 53.8;58.1]), those aged 50 to 59 (27.2% [95%CI 25.3;29.1]), those with partners (64.4% [95%CI 62.4;66.3]), those with up to 8 years of schooling (56.3% [95%CI 54.3;58.3]), and those living in the Brazilian Southeastern region (50.6% [95%CI 48.5;52.6]).

CNCD simultaneity showed variation according to age group (Figure 1). Having two CNCDs was more prevalent with effect from 30 years old, while having three diseases was concentrated mainly between the 50 to 89 age groups; simultaneity of four diseases was more evident in the first decade of the elderly age group (60 to 69 years of age). Greater prevalence of three and four diseases was found in those aged 50 to 59; while prevalence of three or four diseases was lower in those aged over 90 when compared to the other elderly age groups.

CNCD simultaneity among adults in the Brazilian state capital cities behaved similarly. Capital cities with lower prevalence of disease simultaneity in adults were São Luís (9.7% [95%CI 8.1;11.7]), Florianópolis (10.4% [95%CI 8.7;12.5]) and Porto Velho (11.0% [95%CI 9.1;13.0]). While Cuiabá (16.8% [95%CI 14.1;20.0]), Maceió (16.4% [95%CI 13.9;19.2]) and Aracaju (15.4% [95%CI 13.02;18.1]) stood out by having the highest prevalence of CNCD simultaneity when compared to the other capital cities (Figure 2).

In the elderly, the cities of Belém (34.1% [95%CI 28.6;40.1]), São Luís (34.6% [95%CI 28.4;40.5]) and Palmas (35.4% [95%CI 26.4;45.5]) had lower prevalence of CNCD simultaneity, while Manaus (57.1% [95%CI 40.7;53.5]), Belo Horizonte (56.7% [95%CI 41.5;52.0]) and Aracaju (36.5% [95%CI 40.1;53.0]) had the highest prevalence rates (Figure 3).

**Discussion**

We found an important difference in the prevalence of CNCD simultaneity in the Brazilian state capital cities when comparing adults (13.7%) and elderly people (42.9%). Being in the 40 to 59 age group, being a woman, living with a partner, having low education level and living in the Brazilian Southeast region contributed to higher proportional presence of CNCDs in the health outcome framework. Furthermore, the occurrences of disease simultaneity were similar in the Brazilian state capital cities investigated.

The prevalence of CNCD simultaneity among adults identified in this study was similar to the rates presented in results of studies carried out in high-income countries, such as Canada and England. The elderly had higher rates than the 30% estimated for high-income countries. This result has already been found when taking CNCD prevalence separately. CNCDs have also been found to be more prevalent in low- and middle-income country populations when compared to high-income country populations.

Studies carried out in Australia in 2005 and in Canada between 2003 and 2009 found disease simultaneity prevalence rates in adults similar to those found in this research, with 32.6% and 28.2% prevalence, respectively. In both countries mentioned, CNCD simultaneity variation was also close to that found in this study, namely 8.2% to 14.7% for two CNCDs, 1.9% to 3.9% for three CNCDs and 0.5% to 1.1% for four or more CNCDs, respectively. Regarding these two countries, two other studies also identified a proportional increase in these prevalence rates as age increased. Nevertheless, a survey carried out in India associated the fact of having CNCD with higher schooling and income, possibly due to more opportunities for accessing health services. Brazil is similar to high-income countries with regard to disease simultaneity. It is possible that these similarities may be due reduction in health inequalities as a result of the actions of the Brazilian National Health System (SUS), since SUS facilitates diagnosis and access to health services for people.
### Table 1 – Description of sociodemographic characteristics, stratified by the existence of simultaneity of chronic non-communicable diseases (CNCDs) (n=47,218), Brazil, 2013

<table>
<thead>
<tr>
<th>Sociodemographic characteristics</th>
<th>Without simultaneity (0 to 1 disease) (n=36,717)</th>
<th>With simultaneity (2 to 4 diseases) (n=10,501)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15,281</td>
<td>49.3</td>
</tr>
<tr>
<td>Female</td>
<td>21,436</td>
<td>50.7</td>
</tr>
<tr>
<td>Age (in years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29</td>
<td>8,666</td>
<td>33.7</td>
</tr>
<tr>
<td>30-39</td>
<td>7,071</td>
<td>24.5</td>
</tr>
<tr>
<td>40-49</td>
<td>7,300</td>
<td>18.7</td>
</tr>
<tr>
<td>50-59</td>
<td>6,276</td>
<td>12.3</td>
</tr>
<tr>
<td>60-69</td>
<td>4,158</td>
<td>6.3</td>
</tr>
<tr>
<td>70-79</td>
<td>2,360</td>
<td>3.2</td>
</tr>
<tr>
<td>80-79</td>
<td>801</td>
<td>1.2</td>
</tr>
<tr>
<td>≥90</td>
<td>85</td>
<td>0.05</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did not have a partner</td>
<td>18,149</td>
<td>52.9</td>
</tr>
<tr>
<td>Had a partner</td>
<td>18,256</td>
<td>47.1</td>
</tr>
<tr>
<td>Ethnicity/skin color</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>15,600</td>
<td>47.3</td>
</tr>
<tr>
<td>Black/brown</td>
<td>17,069</td>
<td>52.7</td>
</tr>
<tr>
<td>Education level (in years of schooling)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-8</td>
<td>7,518</td>
<td>29.3</td>
</tr>
<tr>
<td>9-11</td>
<td>14,211</td>
<td>40.5</td>
</tr>
<tr>
<td>≥12</td>
<td>14,707</td>
<td>30.2</td>
</tr>
<tr>
<td>Brazilian macro-regions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midwest</td>
<td>5,459</td>
<td>12.0</td>
</tr>
<tr>
<td>Northeast</td>
<td>11,865</td>
<td>24.8</td>
</tr>
<tr>
<td>North</td>
<td>9,933</td>
<td>10.2</td>
</tr>
<tr>
<td>Southeast</td>
<td>5,367</td>
<td>44.3</td>
</tr>
<tr>
<td>South</td>
<td>4,093</td>
<td>8.7</td>
</tr>
</tbody>
</table>

a) Percentage in the weighted sample.

b) Confidence interval 95% in the weighted sample.
Demographic profile of disease simultaneity in Brazilian state capital cities

**Figure 1** – Prevalence of accumulated chronic non-communicable diseases (CNCD), according to age group (n=52,929), Brazil, 2013

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>0 a 1 disease</th>
<th>2 disease</th>
<th>3 disease</th>
<th>4 disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 a 29</td>
<td>10.2</td>
<td>12.2</td>
<td>10.8</td>
<td>5.3</td>
</tr>
<tr>
<td>30 a 39</td>
<td>10.4</td>
<td>12.1</td>
<td>10.6</td>
<td>5.3</td>
</tr>
<tr>
<td>40 a 49</td>
<td>10.0</td>
<td>11.9</td>
<td>10.7</td>
<td>5.3</td>
</tr>
<tr>
<td>50 a 59</td>
<td>10.1</td>
<td>11.5</td>
<td>10.6</td>
<td>5.3</td>
</tr>
<tr>
<td>60 a 69</td>
<td>10.3</td>
<td>11.3</td>
<td>11.2</td>
<td>5.3</td>
</tr>
<tr>
<td>70 a 79</td>
<td>10.5</td>
<td>10.8</td>
<td>11.4</td>
<td>5.3</td>
</tr>
<tr>
<td>80 a 89</td>
<td>10.2</td>
<td>10.4</td>
<td>11.6</td>
<td>5.3</td>
</tr>
<tr>
<td>≥ 90</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>5.3</td>
</tr>
</tbody>
</table>

a) Weighted values.

**Figure 2** – Prevalence of number of diagnosed chronic non-communicable diseases (CNCDs) in adults in the sample, stratified per capital cities of the Federative Units (n=37,947), Brazil, 2013

a) Weighted values.
with CNCDs. Nonetheless, studies based on the Brazilian National Health Survey have identified that although people with CNCDs have more access to health services than people without these diseases, having a lower education level leads to greater incapacity and, consequently, lower healthy life expectation.

With regard to the elderly, our results were different from those of the study carried out in Canada, where disease simultaneity prevalence was 76.8% and prevalence of two, three and four diseases was 21.5%, 20.6% and 34.7% respectively. This discrepancy may be attributed to the number of diseases investigated in the studies and, given the fact that Brazil and Canada provide public health services, it may also be attributed to the influence of different social determinants.

Considering that disease simultaneity leads to hospitalization rates 5.6 times higher in the elderly population, those who have had better access to Education, which is the case of high-income countries, have more disease control and consequently, better survival quality. This is a possible justification for the difference observed.

It is also known that health service expenditure on disease simultaneity is 5.5 times greater, and that lack of resources for monitoring may not allow proper treatment, increasing the risk of early mortality. It is believed that people with disease simultaneity who have longer survival are those who have higher education levels, while those with less education die earlier.

The decrease in disease simultaneity observed in the last decades of life, in both men and women, should not be interpreted as more advanced age being a protection factor, since such simultaneity is due above all to the fact that people with multimorbidity are more likely to die earlier. The study conducted by Britt et al. with Australian citizens identified an increasing trend in the number of simultaneous diseases according to age group in adults, mainly among those aged between 40 and 60 years old. After this considerable appearance of more simultaneous diseases, in the years that follow a decrease can be seen simultaneity rates. This simultaneity behavior may be due to survival bias, whereby risk of mortality is higher among individuals with more than one CNCD because of the conditions that each of the diseases create in the human body over time. That is to say, for an adult, with effect from diagnosis of the first CNCD, exposure to simultaneity will be higher, and consequently the risk of diagnosis of other CNCDs will be greater, thus increasing the possibility of early mortality. Therefore, elderly people without multiple CNCD simultaneity will be those represented in investigations of the elderly group age profile. The strategies adopted in primary health care are determinants of mortality risk control, and
should put into practice after identification of a health profile – or lack of health – that allows identification of a human body vulnerable to exposure.\textsuperscript{17} Aging, for both men and women, means being more exposed to CNCD simultaneity with effect from adulthood.\textsuperscript{13} Men and women show similar behavior in the first decades of life, when there is an increase in exposure to CNCDs, up until reaching the elderly age group. In the adult phase, disease simultaneity occurs more in in men, whereas among the elderly, women are more affected. This suggests that it has not yet been established in which sex disease simultaneity is more evident, regardless of age: sometimes disease simultaneity is more prevalent in men, sometimes it is more prevalent in women. This variation found in the literature may be justified by the characteristics of the diseases investigated, which behave differently in men and women, during the course of the life cycle.\textsuperscript{13} The peak found for both men and women coincides with reaching the elderly age group, which is a time of life when morphofunctional, behavioral and emotional changes are more intense.\textsuperscript{22}

Disease simultaneity was more prevalent among respondents who had partners. Investigations into the existence of simultaneity, without attributing difference to the accumulation of diseases, found similar results in the elderly.\textsuperscript{23} This fact may be justified by the transition of marital status from single to living with partners and adopting unhealthy behaviors, such as reduction in physical activities, poorer diet and sleeping patterns.\textsuperscript{24}

There was no distinction between the prevalence of black/brown and white ethnicity/skin color in the population living in the Brazilian state capital cities. Although it is considered an investigation variable,\textsuperscript{25} the fact that there is no adjustment of other factors to indicate association may raise discussion about the complexity of diagnosis in relation to different ethnicities/skin colors, beyond sociocultural aspects such as education level and income. In statistical analysis, ethnicity/skin color may be considered as a residual confounding variable of socioeconomic factors, which may reflect a discriminatory process during the course of history while they are identified as risk of a given health condition.\textsuperscript{26}

The relation between income and health is established in the literature: a better social position is reflected in better health.\textsuperscript{27} Level of education, in turn, is adopted as an important marker of social inequalities, and association with disease simultaneity has already been found in those with lower schooling.\textsuperscript{8}

Regarding the demographic information, this study found CNCD simultaneity prevalence of 18.2\% in the total sample, this being lower than the 23.6\% found by a national survey carried out in the same year throughout the entire Brazilian territory. Considering the urbanization indicator, it is known that people living in urban areas are less exposed to disease simultaneity when compared to those living in urban/rural areas.\textsuperscript{28, 29}

In relation to the Brazilian macro-regions, the Southeast had higher prevalence, possibly due to aspects such as demographic density.\textsuperscript{27} There was a relatively low percentage point variation in CNCD simultaneity prevalence in adults (6.8\%) and the elderly (13\%), between the different Brazilian state capital cities. This fact may be attributed to similar Human Development Index (HDI) scores among these capital cities, even if they have unequal budgets regarding health expenditure, for example.\textsuperscript{29} It is important to mention that HDI is measured by a combination of factors which include health, education and sanitation conditions.

Finally, the cities of Manaus, Belo Horizonte, Aracaju, Cuiabá and Maceió had the highest CNCD simultaneity prevalence rates. This finding may be the result of certain social determinants,\textsuperscript{13} such as demographic transition, urbanization process, economic and social growth, besides differences in investments in health services. In the same year as the survey was carried out, the public health budget of the states in which the capital cities mentioned above are located and the health cost per inhabitant,\textsuperscript{29} except for the Brazilian states of Amazonas and Sergipe, were in the lowest tercile of the Brazilian scenario. This study stands out due to its descriptive investigation of the profile of Brazilian adults and elderly people with CNCD simultaneity. The occurrence of disease simultaneity during the course of life and its behavior according to different age strata enabled the detailed description of the CNCD profile in the country. This may favor future Brazilian National Health System measures for prevention and health promotion in Primary Care.

The capital cities of the Federative Units of all macro-regions were analyzed separately, thus allowing understanding of how multimorbidity is distributed in Brazil. The reliability of the methodology applied, in turn, enables data interpretation in relation to the general...
population given the considerable sample size. It also includes this study in the international epidemiological scenario as an investigation with data representing the situation of a middle-income Latin American country.

However, some limitations should be pointed out, such as measurement of self-reported sociodemographic indicators and disease diagnosis, usually applied in cross-sectional studies, in which values may be overestimated or underestimated depending on the interviewees’ knowledge. Brazil has diverse Public Health State programs, which define and inform actions of Primary Care professionals, such as the Family Health Strategy. Furthermore, this analysis considered a limited set of diseases, without including other cardiovascular, musculoskeletal, mental and respiratory diseases for example. However, the diseases we investigated stand out in the national scenario and are recognized in the health guidelines as important cardiovascular risk indicators. Finally, even though it is a Brazilian population sample, the survey only covered people living in the state capital cities who had a landline telephone and this restricts extrapolation of the findings. Vigitel performs data weighting, in order to reduce the effects of this bias.

We conclude that CNCD simultaneity in all Brazilian capital cities is similar to the world epidemiological scenario. The period of transition from adulthood to the elderly age group represented the most critical phase for the occurrence of simultaneity of these diseases in the life cycle considered, both for men and women. For future practical applications, we suggest that characteristics and lifestyle be monitored throughout the entire adult phase, with the aim of preventing or minimizing complications expected for the elderly age group in people with unhealthy habits. We also point out the need to provide guidance to Brazilians with diagnosis of chronic non-communicable diseases, recommending behavior change and a healthier lifestyle, together with prescribed medical treatment.

Authors’ contributions

Christofoletti M, Del Duca GF and Malta DC contributed to the conception and design of the study. Christofoletti M analyzed and interpreted the data. Christofoletti M, Del Duca GF, Gerage AM and Malta DC contributed with drafting the manuscript, undertaking relevant critical revision of the intellectual content and approving the final version of the manuscript to be published. The authors have approved the final version and declared themselves to be responsible for all aspects of the study, ensuring its accuracy and integrity.

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