Determinants of mental health and abuse of psychoactive substances associated with tobacco use. A case-control study

Abstract This study aimed to estimate the strength of association among smokers with variables regarding mental health, family functionality, and use of other psychoactive substances. This is a case-control observational study developed from March to November 2016. The study was conducted in a Brazilian Midwest municipality with 646 subjects, of which 323 were cases. In the model, the case group comprised subjects with a certain degree of tobacco dependence. The control group included subjects that were not exposed to tobacco. Concerning tobacco use time, the mean exposure of the case group was 25.65 years. In the multiple logistic regression analysis model the following were positively associated: non-white skin color (p = 0.002); years of study ≤ 8 (p < 0.001); having children (p < 0.001); informal work (p = 0.024); not having a health plan (p < 0.001); high family dysfunction (p = 0.007); AUDIT ≥ 8 (p < 0.001); depression (p < 0.001); having illicit drug in lifetime (p < 0.001); living with other people (p = 0.003) and no religion (p = 0.001). This study reinforces the vulnerability of smokers, associating variables correlated to the field of mental health, and innovates by discussing the influence of family relationships on nicotinic dependence.

Key words Tobacco, Family relationships, Mental disorders, Ethnic groups, Illicit drugs
**Introduction**

There is a worldwide consensus that nicotine dependence is a serious public health problem, with an annual mortality of approximately 5.4 million people, higher when compared to lethality from infectious diseases such as AIDS, tuberculosis and malaria. Tobacco is the leading cause of preventable death in the world, with an increased estimate of approximately 8 million deaths per year by 2030. In Brazil, the number of smokers has decreased since the 1990s, but it is estimated that the population of smokers is 27.9 million and that smoking causes 200 thousand deaths annually.

According to the tenth revision of the International Code of Diseases (ICD 10 F-17.2), tobacco use has the potential to induce nicotine dependence and trigger mental and behavioral disorders, including depressive symptoms, bipolar disorder, anxiety, personality disorder and attention deficit disorder. Smokers with nicotine dependence are 2.7 to 8.1 times more likely to develop these disorders, respectively when compared to sporadic smokers, former smokers, and individuals who have never smoked. Thus, tobacco use is classified as a chronic disease, associated with several symptoms that can substantially compromise health conditions.

Tobacco use is an avoidable cause of several chronic health problems, associated with neoplasms, cardiovascular diseases, pulmonary diseases, ophthalmological alterations, among others. Among these comorbidities, the association with other variables is pointed out by researchers, such as males, adulthood, unfavorable economic conditions, unemployment, low level of schooling, low body mass index (BMI), current consumption of alcoholic beverages and residing in rural areas.

The context of family relationships, in particular, family dysfunction, is an important risk factor for the development of psychoactive substance dependence. Some studies with adolescents have shown that living in a dysfunctional family environment is associated with an increased likelihood of becoming a smoker. Although the consequences of nicotine dependence have significant impacts worldwide, investigations regarding the influence of family relationships on tobacco use are still insufficient.

However, associations with other morbidities in the field of mental health and behaviors that would further aggravate the condition of disorders caused by recurrent tobacco use are considered for this study. Given the above, it is hypothesized that psychiatric comorbidities and the use of other psychoactive substances are associated with tobacco dependence, a condition that potentiates chronic health problems and that affects the relationships of these individuals, especially the family.

This study innovated when testing the variable family functionality amidst the vulnerability condition to which individuals with nicotine dependence levels are exposed. This study aimed to estimate the strength of association between characteristics of the smoking group and variables related to mental health, family functionality and the use of other psychoactive substances.

**Methods**

This is an observational, case-control study to investigate the frequency of characteristics in the case group when compared to the control group. In the model, the case group comprised individuals with some degree of tobacco dependence, and the control group included individuals not exposed to tobacco. The field of study took place in a municipality of significant economic and social role in the Midwest of the country.

The case group population consisted of regular smokers (last 30 days), and the control group included non-smokers, both residents in the municipality in question. The sample was calculated in the Stata Software Package (STATA) program, version 14.0, using the *sampsi* .15, 25, power (.80) a (.05) commands. We considered a 15% prevalence of regular smoking in the Brazilian population, a hypothetical increase of 25% for problems related to tobacco use (applied to the case), test power of 80% and a significance level of 5%. We added 20% to the result, providing for losses, resulting 322 individuals in n1 (control) and 323 individuals in n2 (case), totaling 645 individuals to be interviewed.

The whole sample was paired by gender and age to control for possible confounding bias. The criteria for eligibility of cases were to be aged ≥17 years, to be resident in the city where the research was conducted and to have been a regular smoker for a duration of ≥12 months and a result less than or equal to the minimum level of tobacco dependence measured by the Fagerström Test for Nicotine Dependence (FTND). The non-eligible, both for the case and for the control, were nonsmokers who reported congenital cardiovascular diseases without correction and medical diagnosis of psychotic mental disorder.
The sample for the control group was oriented according to the eligibility criteria: ≥17 years old, living in the same municipality as the research, never smoked in their lives (not being current smokers and former smokers) and not living with smokers in the household. We excluded non-smokers who self-reported having congenital cardiovascular problems without correction and evidenced a psychiatric diagnosis of severe and persistent mental disorder (with psychotic symptoms).

Individuals were recruited to the case group by convenience, according to the eligibility criteria in the settings agreed with the university for teaching, extension and research practice. They were community (domiciles, academic and social spaces), Primary Health Care (Basic Health Care Facilities and Family Health Strategy), urgent and emergency care (Emergency Care Unit) and other specialized and medium complexity care (hospitals and testing and counseling centers) mechanisms. The neighborhood criterion was applied as control. Non-smokers were invited to the locations where a smoker was approached, maintaining a similar proportion between the two groups.

The pilot test was a trial that reproduced all the strategies and methods that would be used in the study and was applied to ten individuals (five smokers and five non-smokers) who were in the municipality where the study was performed but did not reside there. The application of the questionnaire in the pilot version aimed to train the team of field researchers and identify the logistic and operational aspects to adjust the data collection tool. This information did not enter into the final data analysis.

Data were collected from March to November of 2016 by field researchers, who were properly trained undergraduate health students.

Interviews were face-to-face, respecting the availability of each, in a reserved place. At that time, they received guidance about the study and signed the Informed Consent Form for individuals aged ≥18 years or Informed Assent Form for those aged 17 fully completed years.

The tool with sociodemographic and historical data was prepared by researchers guided by mental health benchmarks. FTND was applied for the selection of the case group and description of the nicotinic dependence pattern, with six questions that tracked nicotinic dependence. Scores from zero to 2 points were related to very low dependence; from 3 to 4, to low dependence; 5, average dependence; from 6 to 7, high dependence; and from 8 to 10 points, very high dependence.

The family APGAR tool was used to measure family functionality, which, from the index person, allows to evaluate five aspects: adaptation, partnership, growth, affection and resolve. Each initial letter receives a score of zero to 2 points.

High family dysfunction (HFD) is characterized by the 0-4 points score; 5-6 points would indicate moderate family dysfunction (MFD); and 7-10 points, good family functionality (GFF). The Family APGAR tool was developed by Smilkstein in 1978. Its validation in Brazil was carried out through translation and cross-cultural adaptation, with the participation of eight judges in 2001, in addition to a psychometric analysis, through a descriptive, cross-sectional field study with a population of elderly. The Alcohol Use Disorder Identification Test (AUDIT) validated in Brazil in 1999 was used to determine the pattern of risky alcohol use as a screening method for the early detection of alcohol use, consisting of ten questions, in which the maximum score is 40 points. We adopted ≥8 points as cutoff points. Regarding APGAR tools FTND and AUDIT, Cronbach’s alpha reliability test was performed.

The variables were of two levels: I (individual) and II (context). At level I, sample pairing was by gender (female vs. male) and age category (<30 vs. 30-39 vs. 40-49 vs. 50-59 vs. ≥60). The independent variables were self-reported skin color (white vs. non-white), years of study (≤8 years vs. >8 years); children (yes vs. no); marital status (living without partner vs. living with partner); formal work (working regime according to national legislation) vs. informal (self-employed or unemployed); religion (self-referred yes vs. no); not having a health plan (yes vs. no); living with relatives, according to the concept of family vs. other people; HFD – score ≤4 through family APGAR (no vs. yes); depression – has or has had a medical diagnosis of depression (no vs. yes); used illicit drugs in lifetime – has already used drugs such as marijuana, cocaine, crack, lysergic acid diethylamide (LSD) or illegally-marketed inhalants (no vs. yes); AUDIT (score < 8 vs. ≥8) and diagnosis of ischemic heart disease – self-reported by medical diagnosis (yes vs. no).

In level-II variables, the contextual ones were inserted in the multilevel analysis model and oriented by importance in the confounding control, since situations of disease or health are related to contextual factors. The understanding of the health-disease process must be based on...
the exchange between individuals and context. These variables were community vs. PHC services vs. hospitals and specialty services vs. emergency network with effect in the multiple analysis (according to the location of case and control approach). It was a covariate in the analysis of level-II PHC vs. Secondary Care (considering the complexity level of health care corresponding to the four categories of the context variable).

Concerning the statistical analysis of the variables associated to the group, we used software STATA 14.0 and, as a measure of association, the odds ratio (OR), considering 95% confidence interval (CI95%). By obtaining the crude OR, we chose variables with p < 0.10 for the multilevel logistic regression model. At level I, individual variables were inserted following the theoretical model of insertion always adjusted by level II (contextual variable and covariate), as shown in Figure 1.

The quality of fit between the models was evaluated by the –loglikelihood test, and by level-II variance values of the standard error coefficient (SEC), standard error deviation (SE).

The study was developed respecting the ethical principles that guide Brazilian human research and was conducted after authorization from the Research Ethics Committee (CEP).

Results

The study included samples from 322 participants in the control group and 323 participants in the case group. Sample losses were restored by researchers, preserving the sample calculation and pairing by age and gender categories. The control group consisted of individuals with a mean age of 40.22 years (SD of 14.74), while in the case group, the mean age was 40.88 years (SD of 13.21). Regarding the length of tobacco use, the mean exposure of the case group was 25.65 years (SD of 13.87). Information on the sample pairing categories is shown in Table 1.

Crude and adjusted OR are observed in Tables 2 and 3. It should be noted that the adjusted OR was performed in the model with the contextual factor.

In the bivariate analysis, the following variables were positively associated: non-white skin color (p < 0.001, OR 2.65, CI 95% 1.86-3.79); years of study ≤8 (p < 0.001, OR 3.93, 95% CI 2.79-5.52); children (p < 0.001, OR 2.22, 95% CI 1.56-3.16); living with a partner (p = 0.018, OR 1.45, 95% CI 1.06-1.98); informal work (p < 0.001, OR 1.73, 95% CI 1.11-2.70); no health plan (p < 0.001, OR 3.79, 95% CI 2.63-5.46); HFD (p < 0.001, OR 3.20, 95% CI 1.87-5.47); AUDIT ≥ 8 (p < 0.001, OR 4.94, 95% CI 3.30-7.38); depression (p < 0.001, OR 4.15, 95% CI 2.33-7.40); used illicit drugs in lifetime (p < 0.001, OR 7.37, 95% CI 4.15-13.10); living with other people (p < 0.001, OR 2.39, 95% CI 1.56-3.65); no religion (p < 0.001, OR 2.52, CI 95% 1.61-3.96).

Following multiple analysis of logistic regression with contextual factor of interview site, the following variables were positively associated: non-white skin color (p = 0.002, OR 2.08, 95% CI 1.31-3.32); years of study ≤8 (p < 0.001, OR 3.41, 95% CI 2.19-5.31); children (p < 0.001, OR 3.31, 95% CI 1.87-5.86); informal work (p = 0.024, OR 1.97, 95% CI 1.09-3.55); no health plan (p < 0.001, OR 2.92, 95% CI 1.82-4.68); HFD (p = 0.007, OR 2.70, IC 95% 1.31-5.55); AUDIT ≥ 8 (p < 0.001, OR 4.81, 95% CI 2.83-8.18); depression (p < 0.001, OR 3.77, 95% CI 1.88-7.55); used illicit drugs in lifetime (p < 0.001, OR 7.66, 95% CI 3.61-16.25); living with other people (p = 0.003, OR 2.42, 95% CI 1.36-4.31); and no religion (p < 0.001, OR 2.86, 95% CI 1.54-5.29).

| Blank model - Case vs. Control | Model 1* - Case vs. Control - Sociodemographic | Model 2* - Case vs. Control - Sociodemographic - Diagnostic | Modelo 2* - Case vs. Control - Sociodemographic - Diagnostic - Behavioral |
|--------------------------------|-----------------------------------------------|------------------------------------------------------------|---------------------------------------------------------------------|

Figure 1. A conceptual model of multilevel analysis.
In Table 2, the -2loglikelihood test was reduced as models were inserted, giving the analysis better quality of fit as the groups of individual variables were inserted; the best quality of the variation by the level-II fit is expressed in the value greater than double the standard error coefficient in relation to the standard error deviation in the final model. In the multiple studies, the following remained associated to the case group: non-white skin color, years of study ≤ 8 years, children, informal work, no health plan, HDF, AUDIT ≥ 8, diagnosis of depression, illicit drug use in lifetime and no religion.

### Discussion

The main evidence brought about by this study is the association with the smoking group of already known variables (both in the sociodemographic and mental illness realms, as well as those related to the use of other psychoactive and behavioral substances) and another as yet uninvestigated, relative to the family functionality, such as the score of the APGAR evaluation tool for HDF, corroborates mental health implications of the smoking population. We also highlight the application of the context variable in the multiple analysis, in search for broader evidence about the studied phenomenon and control of possible bias.

The limits of the investigation are related to the design of the case-control research, especially about memory and selection of the control group. In an attempt to minimize them, the team was trained to approach and obtain the data reported, and the control individual was as representative as possible regarding gender, age, and neighborhood criteria.

As for skin color, the results suggest that individuals who self-declared themselves to be non-white were at risk for some degree of nicotine dependence. This association can be explained by the time the body requires to metabolize nicotine since white individuals have higher metabolism rates than African American individuals. Therefore, they tend to smoke in smaller quantities and take longer to smoke their first cigarette of the day. According to the FTND, both mechanisms affect scores on the evaluation of nicotine dependence, quantity and first cigarette of the day. Another study performed in a multiracial population showed that the plasma level of cotinine (nicotine metabolite) was six times higher in African American participants with a history of exposure to passive smoking compared to other ethnic groups.

In line with these data from the international literature, recent Brazilian studies show that the prevalence of black self-reported smokers is relatively higher than white self-reported individuals. Data from the Brazilian Institute of Geography and Statistics (IBGE) of 2017 corroborate this finding by affirming the existence of social inequality among these racial groups, with the

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**Table 1. Case and control paired sample data. Midwest, 2016.**

| Categorical variables | Control (n = 322) | Case (n = 323) |
|-----------------------|------------------|---------------|
|                       | N     | %    | N     | %    |
| Gender                |       |      |       |      |
| Female                | 175   | 54.9 | 175   | 53.9 |
| Male                  | 145   | 45.1 | 148   | 46.1 |
| Age group (years)     |       |      |       |      |
| < 30                  | 67    | 21.0 | 67    | 20.7 |
| 30-39                 | 93    | 29.2 | 94    | 29.1 |
| 40-49                 | 85    | 26.6 | 85    | 26.3 |
| 50-59                 | 40    | 12.5 | 44    | 13.6 |
| ≥ 60                  | 34    | 10.7 | 33    | 10.6 |
| Contextual variable   |       |      |       |      |
| Urgent care           | 88    | 49.1 | 91    | 50.8 |
| Community             | 105   | 55.6 | 84    | 44.4 |
| Primary Care          | 55    | 45.8 | 65    | 57.2 |
| Hospitals and specialty services | 72 | 46.4 | 83 | 53.6 |

*Valid number for the box.
The use of tobacco associated with low level of schooling indicates that there is insufficient knowledge about the harm that tobacco products cause to smokers, so much so that there is evidence that residing in areas of difficult access to education favors tobacco abuse.

As for the variable having children, this analysis pointed out that individuals who had chil-
Table 3. Models for multiple logistic regression analysis with interview location contextual factor. Midwest, 2016.

| Level I | Blank Model* | Model 1* | Model 2* | Model 3* |
|---------|--------------|----------|----------|----------|
|         | SEC | SE  | OR | CI95% | P-value | OR | CI95% | P-value | OR | CI95% | P-value |
| Sociodemographic variable | | | | | | | | | | | |
| Non-white skin color | -1.00 | 0.32 | 0.53 | 0.27-1.44 | 0.277 | 0.70 | 0.29-1.65 | 0.419 | 0.62 | 0.25-1.53 | 0.309 |
| Years of study ≤ 8 | 2.29 | 1.54-3.39 | < 0.001 | 2.08 | 1.34-3.24 | 0.001 | 2.08 | 1.31-3.32 | 0.002 |
| Children | 2.70 | 1.85-3.96 | < 0.001 | 3.40 | 2.22-5.21 | < 0.001 | 3.41 | 2.19-5.31 | < 0.001 |
| Living with partner† | 1.47 | 0.96-2.26 | 0.074 | 1.86 | 1.12-3.08 | 0.015 | 3.31 | 1.87-5.86 | < 0.001 |
| Informal employment | 1.79 | 1.08-2.96 | 0.023 | 1.91 | 1.10-3.33 | 0.021 | 1.97 | 1.09-3.55 | 0.024 |
| Does not have a health plan | 3.19 | 2.13-4.76 | < 0.001 | 2.68 | 1.71-4.18 | < 0.001 | 2.92 | 1.82-4.68 | < 0.001 |
| Diagnoses/problems detected | | | | | | | | | | | |
| HFD | 2.96 | 1.49-5.86 | 0.002 | 2.70 | 1.31-5.56 | 0.007 |
| AUDIT ≥ 8 | 7.68 | 4.66-12.65 | < 0.001 | 4.81 | 2.83-8.18 | < 0.001 |
| Depression | 3.72 | 1.91-7.25 | < 0.001 | 3.77 | 1.88-7.55 | < 0.001 |
| Behavioral | | | | | | | | | | | |
| Illicit drug use during lifetime | | | | | | | | | | | |
| Living with other people | | | | | | | | | | | |
| No Religion | | | | | | | | | | | |
| Variance‡ | | | | | | | | | | | |
| SEC 0.221405 | SEC 0.235036 | SEC 0.216696 | SEC 0.208209 |
| SE 7.82006 | SE 0.00002 | SE 0.000051 | SE 0.000022 |
| -2loglikelihood | -447.38 | -373.32 | -318.12 | -289.02 |
| Positive 2loglikelihood | 894.76 | 746.64 | 636.24 | 578.04 |

*Adjustment of the models by the variable and covariate context; †living with other people was controlled for the use of the variable to living with partner; ‡variance: variation of level II of individuals’ interview location (number of location). SEC: standard error coefficient; SE: standard error; OR: Odds Ratio; CI95%: 95% confidence interval; HFD: high family dysfunction; AUDIT: Alcohol Use Disorder Identification Test.
dren tended to smoke more. Conversely, in the literature, another finding is discussed: the fact that children act as a strategy to encourage smoking cessation since parents and children understand that smoking can also affect the health of children in the future. Another finding is that a positive association with the use of alcoholic beverages is identified among individuals with at least one child. However, the variable having children requires more studies, since its role in the association with the use of psychoactive substances is not well understood in the literature.

As for work status, unemployed or self-employed individuals are more likely to consume tobacco when compared to individuals with a formal work. Of these, the group of self-employed professionals showed a greater probability of use. For some working conditions, this relationship can be explained through the control exercised by the employing institution and the imposition of internal anti-smoking rules to workers during the labor process, which substantially limits the time spent in smoking during the period of compliance of working hours. Tobacco use control factors in work environments, as well as irregular physical activity and economic conditions should be considered in future studies to increase knowledge about such aspects related to nicotine dependence.

A condition that complements the previous discussion is the variable not having a health plan, which was positively associated with tobacco use. This situation is inherent to the conditions of acquisition of services in the area of supplementary health and can be articulated with the conditions of work with the legalized employment relationship. However, these are still incipient in tobacco use studies. In Brazil, studies show that sociodemographic conditions are directly related to having a health plan; individuals with low economic status, low schooling level, informal profession and self-declared blacks have less access to health services. By approaching this discussion, it was found that the people attending the health services to which they are linked can receive advice from professionals about tobacco use-related risks, as well as question their habits and provide advice for cessation. This data implies that individuals who have health plans are better assisted, favoring the adoption of a healthy lifestyle. However, this variable requires better exploration for stronger notes.

Tobacco use compromises the individual’s health and affects family relationships, which can lead to estrangement between family members and compromise good family functioning (GFF). Changes in family relationships occur because passive smokers tend to feel stressed and helpless in the family environment, as well as to adopt negative perceptions regarding the role played by relatives within the family system. The opposite can also be seen when any dysfunction (mild, moderate or severe) in the family system makes individuals in this group more prone to the use of psychoactive substances, especially tobacco. Studies with adolescents corroborate this finding by showing that the presence of smokers in the family environment encourages adolescents to use tobacco, either by reproducing tobacco-positive behavior due to exposure to cigarette smoke, resulting in increased sensitivity to nicotine dependence.

At the same time, living with people other than family members increases the likelihood of individuals consuming tobacco and other drugs. This association can be explained due to the distancing that occurs about relatives, with consequent decrease and cessation of the protective effect, which previously inhibited deviant behavior of the offspring, in particular, the use of psychoactive substances. This finding evidences the importance of good family relationship as a factor preventing the use of illicit substances, but future discussions in this regard are required to clarify this association further.

Tobacco use contributes to various diseases and may also be associated with an increased risk of developing mental disorders, including depression. In the literature, the causality between smoking and depression is attributed to distinct mechanisms, among which the risk would be directly proportional to the use of tobacco, that is, the greater the use of tobacco products, the higher the probability of developing the disease. Thus, it is suggested that, due to the action of nicotine in neurochemical systems, as well as neuroendocrine functions, an interference in the trend of the pre-pathological state would occur. There is also a reverse causality: depressive individuals are 1.5 times more likely to initiate and maintain the use of tobacco derivatives, and this can be explained by the lack of health condition self-preserving behaviors and by increased pleasurable sensations when smoking.

This investigation evidenced a negative association in the case group with the status of having religion. There is almost a consensus among studies that practicing a religion is a protective factor in this context. Individuals with a high religious bond tend to be less likely to initiate and maintain
tobacco consumption on a daily basis since the guidelines of religious precepts positively reinforce the behavior of nonsmokers and encourage individuals who make persistent use of tobacco products to curb and cease this consumption. Also, it provides individuals with mechanisms of emotional support against stressful factors that have the potential to trigger tobacco use.

When compared to individuals who are not regular smokers, individuals who smoke cigarettes regularly are more likely to initiate illicit drug use early, especially marijuana, and still report prior consumption opportunities. This association may be related to genetic and environmental factors and the presence of problematic behaviors, such as hyperactivity, impulsivity and aggressiveness.

As to the relationship between comorbidities of alcohol use and other drugs, this study does not innovate, but the coexistent causal relationship is robust. Tobacco use and daily consumption of alcoholic beverages are integrated. Individuals with tobacco behaviors are more likely to ingest alcohol, just as individuals who ingest alcohol are also likely to use tobacco products; this association occurs regardless of time of exposure.

Among tobacco users, those with a higher daily consumption are associated with higher AUDIT scores. Studies suggest that the concomitant use of nicotine with ethanol acts to enhance pleasurable sensations of alcohol and reduce its undesirable effects. Some hypotheses allege that the association between tobacco and alcohol would act by activating the mesolimbic dopaminergic system, which, in turn, would increase the sensation of gratification as a positive reinforcement to psychoactive substances’ dependence.

Conclusion

The results of this study indicated an association of variables in the mental health area that reinforce the vulnerability of the smokers investigated, especially for those with low levels of schooling, with no formal employment relationship and about the risk use of alcohol and illicit drugs. Regarding the main finding, high family dysfunction was strongly associated with some degree of nicotine dependence. We emphasize that other realms related to the family setting can corroborate this situation, such as having children and living with non-relatives. When present in the same context, these variables are enhanced, increasing the exposure to comorbidity related to tobacco use and its social, economic and health impact. This study reveals the need to adopt public policies focused on health care that are more effective and comprehensive about family dynamics.
Collaborations

TA Amorim and R Lucchese: conception and planning of the research project, data collection and / or analysis and interpretation, writing of the manuscript, revision of the manuscript; EM Silva Neta, LHB Monteiro, NI Paula and ND Simões: data collection and / or analysis and interpretation, manuscript writing, manuscript review JS Santos and I Vera: research project design and planning, data analysis and interpretation, manuscript writing, manuscript revision.

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