Personalized Medicine: Integrating Phenotype and Healthy Habits for Treatment Individualization

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Abstract: In today's world, personalized medicine is transforming treatments by adapting them to individuals' characteristics, such as their phenotype and healthy habits. This project focuses on developing a mathematical model that combines phenotypic variables and healthy habits with high-impact diseases according to their mortality rate in Colombia, utilizing 2023 Death Statistics data from DANE. The model will be constructed through an extensive literature review to identify the predominant phenotypic characteristics and healthy habits associated with each disease. These will be compiled into a table, and association rules will be created using logical propositions. Subsequently, a table will be generated for each disease, randomly linking the criteria from the initial table with assigned weights. The diseases to be considered include ischemic heart disease, tuberculosis, respiratory infections (especially SARS-CoV-2), chronic kidney disease, and cerebrovascular diseases. The primary objective is to create a personalized medicine model tailored to each patient, integrating phenotypic data and healthy habits with the aforementioned diseases. This model aims to offer more effective and individualized treatments by creating patterns that relate phenotype, healthy habits, and diseases, enabling patient categorization and more precise care. It will serve as a clinical decision support system through predictive modeling. This approach is expected to lead to improved health outcomes and quality of life for patients by reducing medical diagnostic errors. According to the World Health Organization (WHO) in 2019, around 134 million people suffer from avoidable medical errors annually, resulting in 2.6 million deaths. With a validated model, a considerable reduction in these errors is projected, promoting precision healthcare.

Overall, this project represents a promising step towards personalized medicine, leveraging advanced mathematical modeling and data analysis techniques to provide tailored treatments and improve patient outcomes.

Keywords: Personalized medicine; Phenotype 2; Healthy habits 3; Diseases 4; Mathematical model 5.

La medicina personalizada: Integración del fenotipo y hábitos saludables para la individualización del tratamiento.

Resumen: En el mundo actual, la medicina personalizada está transformando los tratamientos al adaptarlos a las características individuales de las personas, como su fenotipo y hábitos saludables. Este proyecto se enfoca en desarrollar un modelo matemático que combine variables fenotípicas y hábitos saludables con enfermedades de alto impacto según su tasa de mortalidad en Colombia, utilizando datos de Estadísticas Vitales de Defunciones del DANE de 2023. El modelo se construirá a través de una extensa revisión de literatura para identificar las características fenotípicas predominantes y los hábitos saludables asociados a cada enfermedad. Estos se compilarán en una tabla y se crearán reglas de asociación mediante proposiciones lógicas. Posteriormente, se generará una tabla por enfermedad, vinculando aleatoriamente los criterios de la tabla inicial con pesos asignados. Las enfermedades a considerar incluyen cardiopatía isquémica, tuberculosis, infecciones respiratorias (especialmente SARS-CoV-2), enfermedad renal crónica y enfermedades cerebrovasculares. El objetivo principal es crear un modelo de medicina personalizada adaptado a cada paciente, integrando datos fenotípicos y hábitos saludables con las enfermedades antes mencionadas. Este modelo busca ofrecer tratamientos más efectivos e individualizados al crear patrones que relacionen fenotipo, hábitos saludables y enfermedades, permitiendo la categorización de pacientes y una atención más precisa. Servirá como un sistema de apoyo a la decisión clínica a través del modelado predictivo. Se espera que este enfoque conduzca a mejores resultados de salud y calidad de vida para los pacientes al reducir los errores de diagnóstico médico. Según la Organización Mundial de la Salud (OMS) en 2019, alrededor de 134 millones de personas sufren errores médicos evitables anualmente, resultando en 2,6 millones de muertes. Con un modelo validado, se proyecta una reducción considerable de estos errores, promoviendo la atención médica de precisión.

En general, este proyecto representa un paso prometedor hacia la medicina personalizada, aprovechando técnicas avanzadas de modelado matemático y análisis de datos para brindar tratamientos adaptados y mejorar los resultados de los pacientes.

Palabras clave: Medicina personalizada; Fenotipo2; Hábitos saludables3; Enfermedades4; Modelo Matemático5

Introduction

Personalized medicine is revolutionizing healthcare by tailoring treatments to individual characteristics, including genetics, lifestyle, and disease markers. This approach requires the development of a phenotypic model that integrates specific variables for each individual, ensuring personalized care.

Subsection A: Importance of Personalized Medicine

According to the National Institutes of Health (NIH), personalized medicine utilizes an individual's genetic profile to guide medical decisions, optimizing the efficacy of healthcare delivery [1]. As emphasized by the World Health Organization (WHO), a significant number of patients suffer preventable harm during healthcare delivery, resulting in millions of annual deaths, particularly pronounced in low- and middle-income countries [2]. Investing in preventing such harm not only generates economic savings but also significantly improves patient outcomes. Several studies have demonstrated the potential of personalized medicine to improve clinical outcomes and reduce healthcare costs.

By focusing on the patient, personalized medicine shifts the emphasis from diseases to individuals, recognizing unique responses to illness and treatment. This requires addressing the needs of each patient individually. The 2023 Vital Statistics Report by the National Administrative Department of Statistics (DANE) of Colombia identifies cerebrovascular diseases, cardiovascular diseases, chronic respiratory diseases, and tuberculosis as the leading causes of mortality in the country [3].

Subsection B: Mathematical Modeling Approach

Integrating phenotypic data and healthy lifestyle habits into mathematical models is crucial for developing more effective treatment strategies tailored to individual needs. These models consider not only genetic factors but also lifestyle, habits, and disease markers in these aspects. Several studies have explored the use of mathematical models and machine learning techniques to integrate multimodal data in disease prediction and treatment selection.

For instance, in the study "Symptom Clusters in Acute SARS-CoV-2 Infection and Long COVID Fatigue in Male and Female Outpatients," multivariable logistic regression models and mutually adjusted log-linear regression models were employed to investigate the associations between different symptoms and fatigue in patients with Long COVID. These models allow for analyzing how various variables or symptoms are related to the presence and severity of fatigue in Long COVID patients, both in males and females [4].

In another study titled "Machine Learning Prediction of Treatment Response to Inhaled Corticosteroids in Asthma" [5], machine learning techniques, specifically LASSO regression and random forest models, were utilized to predict the response to inhaled corticosteroid treatment in asthma patients. The LASSO regression performed variable selection and regularization, retaining 89 out of 271 SNPs and achieving an AUC of 0.71. The random forest models, ensembles of tree-based classifiers, retained 270 SNPs and achieved an AUC of 0.74. Both models were optimized to maximize the AUC and evaluated on an independent test set, enabling the identification of genetic variants associated with treatment response.

While these studies are promising, gaps remain in the research. Few studies have addressed high-impact diseases in Colombia, such as those mentioned, and most have focused on genomic data with limited integration of phenotypic and lifestyle variables. The high mortality rates from these diseases in the country [3] highlight the need for personalized approaches to improve health outcomes.

In this project, we aim to develop a comprehensive mathematical model that combines phenotypic variables, healthy lifestyle habits, and high-impact diseases in Colombia. This model will serve as a clinical decision support system, enabling accurate patient categorization and personalized treatment selection, leveraging advanced modeling techniques to improve health outcomes and reduce diagnostic errors. By doing so, phenotype-guided personalized medicine offers a paradigm shift in healthcare delivery, embracing individual variability and tailoring treatments accordingly

Methodology

This type of research is a recent initiative, strengthening significantly in the last decade, evidenced in a large number of texts and scientific articles that have chosen to use it. Thus, existing, scientifically proven methodologies are used as a starting point and the specific aspects corresponding to the object of the research under study will be carried out.

Therefore, this research will use mixed methods by integrating the quantitative approach with the qualitative approach, allowing the possibility of carrying out a comprehensive analysis of the problem to be defined, understood as a mixed methodological approach; whose central postulate is to provide an interrelation of qualitative and quantitative methods immersed in a coherent and specific methodological perspective, which allows a sufficient level of understanding of the object of research and the obtaining of results in accordance with the complexity of the phenomenon under study.

In its qualitative component, the research is developed from the descriptive approach to establish the foundation of the academic processes of educational institutions of higher education, which is consolidated from the interpretation of texts, applications and generation of theories.

The research is non-experimental because it lacks an independent variable; instead, the researcher observes the context in which the phenomenon develops and analyzes it to obtain information.

The research was carried out with exploratory and descriptive methods to define, classify, catalog or characterize the object of study with the idiographic purpose of describing the state and behavior of the variables that are the object of study.

The first, exploratory part carried out the collection of all possible information corresponding to traditional medicine versus advances in personalized medicine, with the objective of knowing and compiling the requirements and problems that are the origin of the opportunity for improvement. Following this, it is necessary to apply the second part of the methodology, where in the descriptive section we begin to analyze and present the information that has been collected in order to identify the current patterns and solutions in order to propose a solution based on the phenotypes and the Healthy habits.

Added to this is the analytical methodology where we proceed to continue with the formulation of the solution, where statistical applications will begin to be able to create the models presented as a result. Thus, the construction of the prototype began, to then carry out the correct checks and unit tests, before deploying it in the exposed context and evaluating the performance variables of this research.

Results

A phenotypic model encompassing variables associated with healthy habits and the most prominent diseases in Colombia, noted for their high mortality rates, is being developed, as mentioned in the introduction: cerebrovascular, respiratory, cardiovascular, renal, and tuberculosis. Therefore, it has been decided to focus on these diseases for the model's creation.

In the initial stage of model development, an exhaustive search was conducted across various scientific works and reliable websites to gather precise information on the phenotypic characteristics and healthy habits related to these diseases. This will enable us to understand which phenotypic and healthy habit aspects are more likely to influence the occurrence of these diseases. Subsequently, the compilation of phenotypic data for these diseases is presented.

Table 1. Diseases vs Phenotypic Aspects

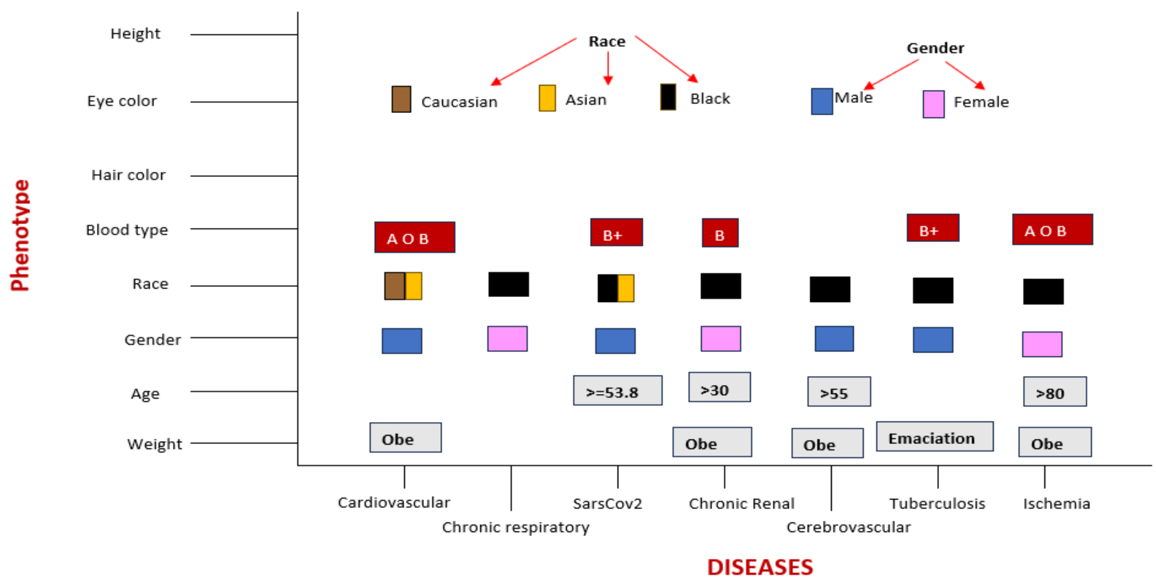
	DISEASES						
PHENOTYPE	**Cardiovascular**	**Chronic Respiratory**	**SarsCov2** [13]	**Chronic Renal**	**Cerebrovascular** [18]	**Tuberculosis**	**Ischemia**
Rh factor	A o B [6]		B+	B [6].		B+ [20]	A o B [6]
Race	Caucasian or Asian [7,8]	Black [11]	Black or Asian	Black [14].	Black	Asian [21]	Black [23]
Gender	Male [9]	Female [12]	Male	Female [15]	Male [19]	Male [22]	Female [9]
Age			>=53.8	>30 [16]	>55		>80 [9]
Weight	>=30 [10]			>=30 [17]	>=30	<18.5[21]	>=30 [9]

Source: The authors

In Table 1, upon analyzing the gathered information, certain significant patterns related to different health conditions can be observed. For instance, concerning cardiovascular diseases, it is notable that individuals with blood type A or B, of Caucasian or Asian ethnicity, male gender, and a body mass index (BMI) equal to or greater than 30 have a higher predisposition to develop these diseases. Additionally, focusing specifically on ischemic cardiovascular disease, it is found that women have a higher incidence compared to men, especially those over 80 years old.

A noteworthy finding from the research is that, in the case of tuberculosis, Black men with blood type B+ and a BMI exceeding 18.5 are more susceptible to contracting this disease. Furthermore, it is highlighted that, for every two affected men, only one woman suffers from tuberculosis. For a more visual comprehension of these findings, the following Figure is presented:

Figure 1. Representation: Diseases vs Phenotypic Aspects



Source: The authors

In Figure 1, diseases are depicted on the x-axis, and their corresponding phenotypic characteristics are represented on the y-axis. Upon close examination, it is evident that obesity and advanced age, particularly over 60 years old, are common factors associated with many of these diseases. Additionally, it is noteworthy that the majority of the diseases appear to be more prevalent among individuals with blood type B.

In Table 2, the direct impact of healthy habits on the incidence of these diseases is clearly evident. While, in the case of respiratory diseases, smoking habit stands as the primary factor, in cerebrovascular and cardiovascular

diseases, healthy habits become more relevant. For a more visual understanding of this relationship, it is necessary to graphically represent the data.

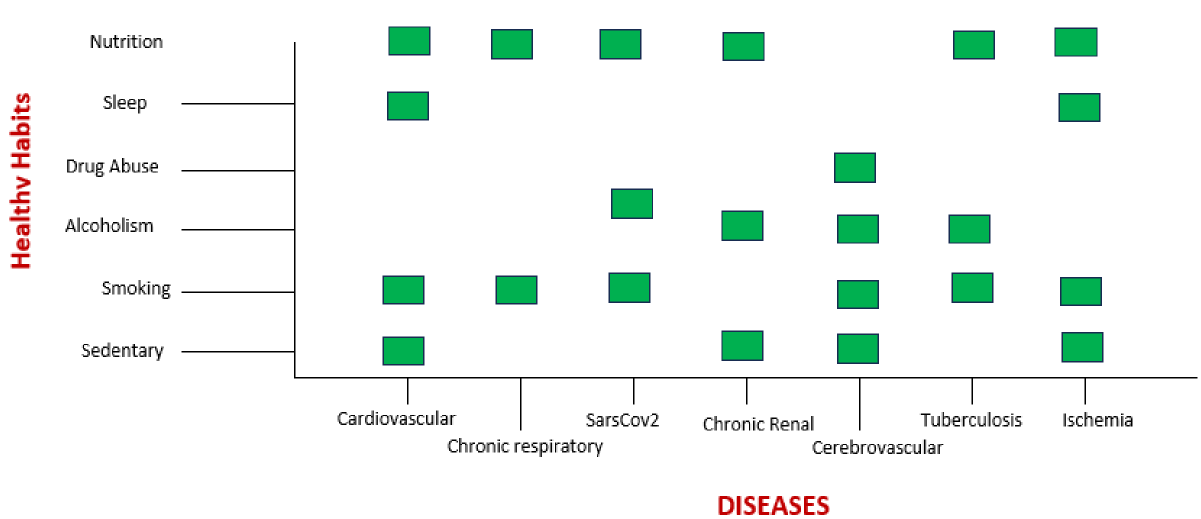
Table 2. Comparative analysis between Diseases vs Healthy Habits

Healthy Habits	DISEASES: Cardiovascular [24]	Chronic [25] Respiratory	SarsCov2 [26]	Chronic Renal [27]	Cerebrovascular [28]	Tuberculosis [21]	Isquemic [29]
Nutrition	X	X	X	X		X	X
Sleep	X						X
Drug Abuse				X	X		
Alcoholism			X		X	X	
Smoking	X	X	X		X	X	X
Sedentary	X			X	X		X

Source: The authors

In Figure 2, the presented results illustrate how various healthy habits affect the incidence of the mentioned diseases. It is noteworthy that individuals leading a sedentary lifestyle, smoking, experiencing sleep problems, and having poor dietary habits are more prone to these diseases. Additionally, those who combine smoking with alcohol consumption, a sedentary lifestyle, and drug use also exhibit a higher propensity for these diseases.

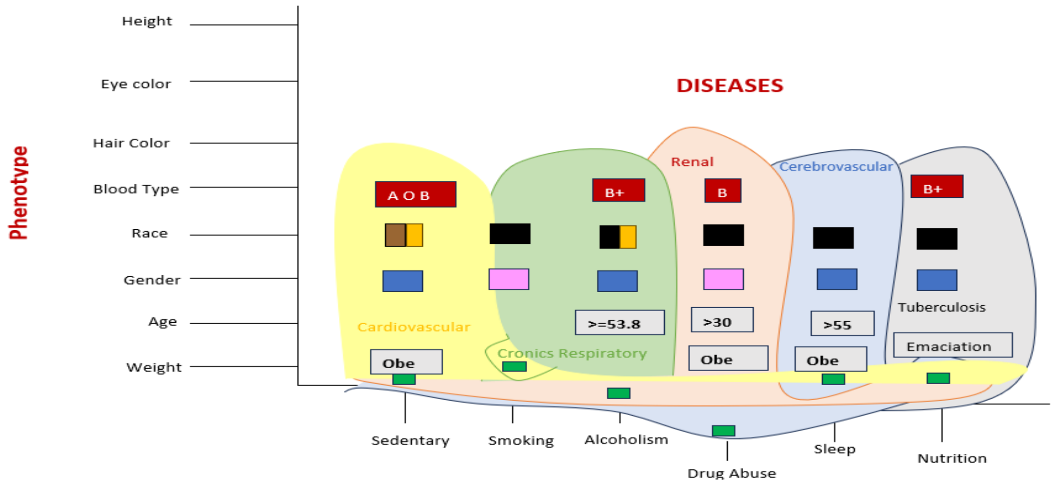
Figure 2. Representation: Diseases vs Healthy Habits.



Source: The authors

However, at this point, the model still does not provide a comprehensive description of how healthy habits and phenotype influence susceptibility to these diseases. To address this issue, Figure 3 has been created:

Figure 3. Intersection Representation Healthy Habits, Phenotypic Factors, and Diseases.



Source: The authors

Upon analyzing the intersections between diseases, phenotypes, and healthy habits, it becomes evident that men, in general, exhibit a higher susceptibility or propensity to suffer from these diseases. Furthermore, it is clear that the habit of smoking is strongly associated with all of these diseases, with the exception of renal diseases. This characteristic consistently manifests across all cases.

Although nutrition and sedentary behavior may not be present in all diseases, their influence is notable. Weight and age also play a significant role in the onset of these diseases. Additionally, Black race and blood type B+ appear to increase the predisposition to these diseases in all cases.

However, it becomes challenging to verify the cross-breeding patterns of each disease concerning phenotype and healthy habits. Therefore, proportional logic methods were employed to create specific patterns for each combination of disease, phenotype, and healthy habit, yielding the following results:

First, the characteristics of each disease were identified based on the phenotype and healthy habits.

Table 3. Character references according to variables

Diseases	Phenotypic Data	Healthy Habits	Symbol
$c = Cardiovascular$ $chr = Chronic\ Respiratory$ $sar = SarsCov2$ $R = Chronic\ Renal$ $Cer = Cerebrovascular$ $Tub = Tuberculosis$ $Isq = Ischemia$	$N = Black$ $A = Asiatic$ $M = Male$ $F = Female$ $O = Obesity$	$MA = Nutrition$ $AD = Drug\ Abuse$ $Alc = Alcoholism$ $Fum = Smoking$ $S = Sedentary$	$\wedge = And$ $\leftrightarrow = Only\ if$ $\vee = Or$

Source: The authors

In the Table 3 displays the characters that will be used to symbolize each parameter of the variables, allowing us to illustrate the relationship of the data according to phenotype and healthy habits:

a. Blood Type:

$$c \wedge Isq \leftrightarrow A \vee B \quad 1$$

The first preposition indicates that cardiovascular and ischemic diseases occur only if one has blood type A or B.

$$sar \wedge R \wedge Tub \leftrightarrow B \quad 2$$

The second preposition indicates that SarsCov2 and Chronic Renal and Tuberculosis diseases occur only if one has blood type B.

b. Race:

$$chr \wedge sar \wedge R \wedge Cer \wedge Tub \wedge Isq \leftrightarrow N \quad 3$$

The third preposition occurs only if one is of Black race

$$c \wedge sar \leftrightarrow A \quad 4$$

The Fourth preposition occurs only if one is of Asiatic race

c. Race + Blood Type:

$$Tub \wedge sar \leftrightarrow N \wedge B \quad 5$$

The fifth preposition for the diseases applies only if one is of Black race and has blood type B

d. Gender:

$$c \wedge chr \wedge R \wedge sar \wedge Cer \wedge Tub \leftrightarrow M \quad 6$$

The sixth preposition is general and applies solely when the gender is masculine

$$R \wedge Isq \leftrightarrow F \quad 7$$

The seventh preposition is general and applies solely when the gender is feminine

e. Race+Gender

$$c \wedge sars \wedge chr \wedge Tub \leftrightarrow N \wedge M \quad 8$$

In the eighth preposition, race and gender form the second pattern, which only exists if the diseases occur in the male gender and their race is Black.

f. Race+Blood Type+Gender

$$sars \wedge Tub \leftrightarrow N \wedge B \wedge M \quad 9$$

The ninth preposition represents the third pattern, indicating that SARS and tuberculosis diseases occur only if the patient is of Black race, has blood type B, and is male.

g. Weight

$$c \land R \land Cer \land Isq \leftrightarrow O_{10}$$

The tenth preposition is general and indicates which diseases have the habit of being associated with obesity.

h. Weight +Gender+Race

$$c \land Cer \leftrightarrow O \land M \land N_{11}$$

The eleventh preposition conforms to the fourth pattern, indicating that cardiovascular and cerebrovascular diseases occur only if the patient suffers from obesity and is male and of Black race.

i. Nutrition

$$c \land R \land Isq \land Tub \leftrightarrow MA_{12}$$

The twelfth preposition applies generally to diseases that are associated with poor nutrition

j. Race+Nutrition:

$$c \land R \land Tub \land Isq \leftrightarrow N \land MA_{13}$$

The thirteenth preposition conforms to the fifth pattern, indicating that diseases such as cardiovascular, renal, tuberculosis, and ischemic are present only if the patient is of Black race and has poor nutrition

k. Race +Gender+Weight+Nutrition:

$$c \land Cer \leftrightarrow N \land M \land O \land MA_{14}$$

The fourteenth preposition conforms to the sixth pattern, indicating the relationship between Black race, male gender, weight in the context of obesity, and suffering from poor nutrition, which may result in diseases such as cardiovascular and cerebrovascular.

l. Sleep+ Weight

$$c \land Isq \leftrightarrow O \land DB_{15}$$

The fifteenth preposition conforms to the seventh pattern, relating to cardiovascular and ischemic diseases that occur only if the patient shows signs of obesity and does not sleep well.

m. Drug Abuse+ Weight+Gender+Race

$$R \land Cer \leftrightarrow AD \land O \land M \land N_{16}$$

The sixteenth preposition conforms to the eighth pattern, indicating the relationship between drug abuse, suffering from obesity, being male, and being of Black race, resulting in the potential occurrence of chronic kidney diseases and cerebrovascular diseases.

n. Alcoholism:+Race+Gender

$$Tub \wedge Cer \leftrightarrow Alc \wedge N \wedge M_{17}$$

The seventeenth preposition conforms to the ninth pattern, given by diseases such as Tuberculosis and cerebrovascular diseases, which occur if and only if they are related to alcoholism, Black race, and male gender.

o. Smoking :+Gender

$$c \wedge chr \wedge R \wedge sar \wedge Cer \wedge Tub \leftrightarrow M \wedge Fum_{18}$$

The eighteenth preposition conforms to the tenth pattern and is established by the relationship between patients who smoke and the female gender, resulting in six possible diseases that can be suffered through these habits.

p. Sedentary

$$c \wedge R \wedge Cer \wedge Isq \leftrightarrow S_{19}$$

The nineteenth preposition is general, resulting in diseases that have sedentary behavior as a healthy habit, potentially leading to conditions such as cardiovascular, renal, cerebrovascular, and ischemic diseases

q. Final prepositions:

$$Sar \wedge Tub \leftrightarrow B \wedge Fum \wedge M \wedge N_{20}$$

The twentieth preposition belongs to the eleventh pattern, which relates blood type, the smoking habit, male gender, and Black race, resulting in diseases such as tuberculosis and SARS-CoV-2.

$$c \wedge Isq \leftrightarrow O \wedge MA \wedge DB \wedge Fum \wedge S \wedge (A \wedge B)_{21}$$

The twenty-first preposition is related to weight, poor nutrition, lack of sleep, smoking habit, sedentary lifestyle, and having blood type A or B to establish the twelfth pattern for the possibility of having cardiovascular and ischemic diseases

$$R \wedge Isq \leftrightarrow N \wedge F \wedge O \wedge MA \wedge DB_{22}$$

Finally, the twenty-second preposition relates to Black race, female gender, patient being obese, having poor nutrition, and not sleeping well to have the possibility of suffering from chronic kidney and ischemic diseases

Conclusions

The findings of this research reveal a complex interplay between phenotypic factors, lifestyle habits, and the development of high-impact chronic diseases in Colombia. The results confirm that certain risk factors such as obesity, smoking, poor nutrition, and sleep disturbances are closely linked to the onset of cardiovascular, renal, cerebrovascular, respiratory, and other conditions. However, the analysis also highlights the need to consider additional variables such as race, gender, and specific disease types when comprehensively assessing risks in the population.

Specifically, in the case of cardiovascular and ischemic diseases, twelve distinct patterns were identified relating them to factors such as blood type A or B, Caucasian or Asian race, male gender, obesity, poor nutrition, lack of sleep, smoking habit, and sedentary lifestyle. For chronic kidney disease, eight associated patterns were found involving Black race, female gender, obesity, poor nutrition, drug abuse, and sedentary habits. Regarding cerebrovascular diseases, nine patterns were determined linking them to Black race, male gender, obesity, poor nutrition, drug abuse, alcoholism, and sedentarism.

Furthermore, for tuberculosis and SARS-CoV-2, three main patterns were established related to blood type B+, Black race, male gender, and smoking habit. Meanwhile, for chronic respiratory diseases, 1 general pattern was identified directly linking them to the smoking habit.

In total, twenty-two logical propositions were formulated, representing diverse patterns of interplay between phenotypes, healthy habits, and specific diseases. These patterns enable categorizing patients according to their individual risk and selecting more precise and personalized treatments. The highest number of patterns was found for cardiovascular, ischemic, renal, and cerebrovascular diseases, demonstrating the complexity of factors influencing the development of these conditions and the importance of a personalized medicine approach.

While these findings represent a promising step towards precision medicine, broader validation of the model in real clinical settings is required to assess its impact on medical practice and improving patients' quality of life. Currently, pilot tests are being conducted, simulating data through rules based on the propositions, generating disease-specific tables that randomly link criteria with assigned weights, to adapt criteria and create decision trees. In the future, it is expected to incorporate additional variables such as genetic, environmental, and socioeconomic factors to achieve an even more comprehensive understanding of individual risks.

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