THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Alcohol consumption behaviour of the Hungarian general and Roma populations and the effect of taste preference-related gene polymorphisms on alcohol consumption patterns

by Ali Abbas Mohammad Kurshed

UNIVERSITY OF DEBRECEN

DOCTORAL SCHOOL OF HEALTH SCIENCES

DEBRECEN, 2023

THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Alcohol consumption behaviour of the Hungarian general and Roma populations and the effect of taste preference-related gene polymorphisms on alcohol consumption patterns

by Ali Abbas Mohammad Kurshed

Supervisor: Judit Diószegi, MD, PhD

UNIVERSITY OF DEBRECEN

DOCTORAL SCHOOL OF HEALTH SCIENCES

DEBRECEN, 2023

Table of contents

LIST OF ABBREVIATIONS

ADH	alcohol dehydrogenase
ALDH	aldehyde dehydrogenase
APC	alcohol per capita consumption
AUDIT	Alcohol Use Disorder Identification Test
AVI	alanine-valine-isoleucine
CA6	carbonic anhydrase 6
CD36	Cluster determinant 36
CHRM2	cholinergic receptor, muscarinic 2
CHRNA5	cholinergic receptor, nicotinic, alpha 5
CI	confidence interval
COMT	catechol-O-methyltransferase
DALY	disability-adjusted life years
DAT	dopamine transporter
DNA	deoxyribonucleic acid
DRD2	dopamine D2 receptor gene
EDTA	ethylenediaminetetraacetic acid
ENaC	epithelial sodium channel
EU	European Union
GABA	γ-amino butyric acid
GABRA	γ-amino butyric acid receptor A
GNAT3	G protein subunit alpha transducin 3
GP	General Practitioner
GPMSSP	General Practitioners' Morbidity Sentinel Stations Programme
GRM8	glutamate receptor, metabotropic 8
GWAS	genome-wide association study
HG	Hungarian general population
HR	Hungarian Roma population
5-HTT	5-hydroxytryptamine transporter
HWE	Hardy-Weinberg equilibrium

MAOA	monoamine oxidase A
NCD	noncommunicable disease
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B cells 1
NPY2R	neuropeptide Y receptor Y2
OPRK1	opioid receptor, kappa 1
OPRM1	opioid receptor, mu 1
OECD	Organisation for Economic Co-operation and Development
OR	odds ratio
PAV	proline-alanine-valine
PCR	Polymerase chain reaction
PDYN	prodynorphin
PRH1	proline-rich protein HaeIII subfamily 1
PRH1-TAS2R14	proline rich protein HaeIII subfamily 1 - taste 2 receptor member 14
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PROP	6-n-propylthiouracil
PRR4	proline rich 4
PTC	phenylthiocarbamide
SNP	single nucleotide polymorphism
TACR3	tachykinin receptor 3
TAS1R2	taste 1 receptor member 2
TAS1R3	taste 1 receptor member 3
TAS2R10	taste 2 receptor member 10
TAS2R13	taste 2 receptor member 13
TAS2R14	taste 2 receptor member 14
TAS2R16	taste 2 receptor member 16
TAS2R19	taste 2 receptor member 19
TAS2R20	taste 2 receptor member 20
TAS2R3	taste 2 receptor member 3
TAS2R9	taste 2 receptor member 3
TAS2R31	taste 2 receptor member 31
TAS2R38	taste receptor type 2 members 38

TAS2R39	taste 2 receptor member 39
TAS2R4	taste 2 receptor member 4
TAS2R40	taste 2 receptor member 40
TAS2R41	taste 2 receptor member 41
TAS2R43	taste 2 receptor member 43
TAS2R46	taste 2 receptor member 46
TAS2R5	taste 2 receptor member 5
TAS2R50	taste 2 receptor member 50
TAS2R60	taste 2 receptor member 60
TAS2R7	taste 2 receptor member 7
TAS2R8	taste 2 receptor member 8
TRPA1	transient receptor potential cation channel subfamily A member 1
WHO	World Health Organization

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Harmful alcohol intake has been documented as a principal risk factor for illness, disability, and mortality at global level (1). Though previous research suggests that moderate consumption of alcohol may be beneficial to health via decreasing cardiovascular diseases' risk and overall mortality (2-4), excessive intake of alcohol may lead to the development of several diseases. Over 200 illnesses and/or health-related conditions are directly or indirectly linked to alcohol consumption among which alcohol dependence, liver cirrhosis, cancers and injuries are the predominant ones (5). It was also revealed that during the first year of COVID-19 pandemic, the intake of alcohol as well as associated harms increased (6).

1.1 Global alcohol situation

In 2016 around 2.3 billion people 15 years or older were recorded as current drinkers. Among them, the average pure alcohol consumption increased from 5.5 to 6.4 litres from 2005 to 2010, while from 2010 to 2016 the level of consumption remained the same at 6.4 litres. When compared to males, females drink fewer quantities of alcohol worldwide and are less likely to be characterized as heavy drinkers (7). It has been estimated that in 2016 harmful alcohol consumption accounted for 5.3% (3 million) of all deaths and 5.1% (132.6 million) of all disability-adjusted life years (DALYs) worldwide, whereas 28.7%, 21.3% and 19% of these alcohol attributable deaths were due to injuries, digestive and cardiovascular diseases, respectively. Additionally, infectious diseases and cancers were responsible for 12.9% and 12.6% of alcohol-related deaths, respectively. Furthermore, noncommunicable, and mental health conditions accounted for 49% and injuries for 40% of DALYs associated with alcohol intake. Moreover, 7.2% of global all premature mortality was attributable to alcohol (7).

The frequency and amount of alcohol consumption varies among different World Health Organization (WHO) regions. Countries of the WHO European Region can be characterized by the highest levels of per capita intake of alcohol. Though the substantial differences in alcohol consumption among the countries of this region, the average alcohol intake decreased from 12.3 litres in 2005 to 9.8 litres in 2016 (7). Alcohol per capita (APC) trend analysis depicted that among European Union's (EU) inhabitants (15 years or older) pure alcohol intake has fallen

from 11.5 litres in 2010 to 11.3 litres in 2016, and in 2016 average consumption was four times higher among males compared to females (males 18.3 litres: females: 4.7 litres). In 2016 alcohol intake led to 5.5% of all deaths in the EU resulting from cancer (29%), liver cirrhosis (20%), cardiovascular disease (19%) and injury (18%). In addition, over 10.3 million DALYs were linked to alcohol use, where alcohol use disorders (AUDs) contributed to 93% of all DALYs.

In Hungary, pure alcohol consumption changed from 12.1litres in 2010 to 11.4 litres in 2016, and the average alcohol consumption varied from 19.1 litres for males to 4.5 litres for females (7). Although there has been a decreasing trend of alcohol consumption in Hungary, the consumption level was still higher compared to the Organisation for Economic Co-operation and Development (OECD) average and this country was among those which reported yearly per capita pure alcohol consumption of more than 11 litres (8). Additionally, the reported prevalence of heavy episodic drinking among Hungarian citizens aged over 15 years was 33.5% which is much higher than the global prevalence of 18.2%. Furthermore, Hungary had a significantly higher prevalence of alcohol use disorders (21.2% in Hungary versus 8.8% in Europe) and alcohol dependence (9.4% in Hungary, while 3.7% in Europe) compared to the average of the WHO European Region's (7). Moreover, standardized mortality rates related to alcohol intake were the highest in Hungary among European countries (9).

1.2 Ethnic-specific disparities in health behaviour and alcohol consumption

Health behaviour together with alcohol consumption patterns may vary not only across populations but also between different races and ethnicities (10). Findings of earlier studies demonstrated that prevalence rates of overweight, poor diet and physical inactivity were higher among black women compared to white women, while among black and white men differences were less both in magnitude and consistency (11-13). Additionally, though there is a contradiction, results of several other studies indicated that compared to Mexican Americans, white women had a lower prevalence of overweight and physical inactivity levels (14-16). Furthermore, Winkleby et al. illustrated that ethnicity had a significant association with health behaviours, among black and Mexican American women the odds of obesity and physical inactivity were significantly higher than among white women. The research group also

demonstrated that for men, the odds of smoking and physical inactivity were significantly higher among black individuals compared to white males (17).

Alcohol consumption levels may not only show regional differences but may also differ between ethnic minority groups. For instance, in one study among individuals above or equal to 12 years of age, American whites demonstrated higher (57.4%) alcohol consumption than other ethnic/racial groups (18). It was also observed that Native Americans (both men and women) and Hispanic men have had the highest prevalence of weekly and daily heavy drinking, respectively, while the lowest rates of weekly and daily heavy drinking were reported by Asian-American, Hispanic and Asian-American and African American women, respectively (19). Additionally, among adolescents (12–17 years), alcohol consumption varied across ethnic groups while the prevalence of 30-day alcohol use and binge drinking ranged from highest among whites to lowest among Asians (20). Besides, findings from the study of Borrell and colleagues represented a positive relationship between experiences of ethnic discrimination and drinking status. Hispanics, who were subjected to ethnic discrimination had a 62% greater odds of drinking heavily (21). Moreover, among several studies trying to elucidate ethnic-specific variations of alcohol-related harms, Hasin et al. presented that in the United States whites (13.8%) were more likely to develop alcohol dependence than blacks (13.8%) and Hispanics (13.8%) in their lifetime (22). Contradictory findings were obtained from another study stating that in the case of low levels of drinking, black and Hispanic adult drinkers reported more alcohol dependence symptoms and social consequences from drinking compared to white drinkers, while heavy drinking problems were similar for all the groups (23). Furthermore, the results of another study elucidated that the persistence of alcohol dependence was greater among blacks and Hispanics than non-Hispanic whites (24).

1.3 Roma population and alcohol consumption

Roma is acknowledged as the largest and most widely distributed ethnic minority population in the European Union. Linguistic, cultural, anthropological, and genetic evidence suggested that Roma individuals came from the Indian subcontinent and entered Eastern Europe around 1000 years ago (25-32). Later, they spread all over Europe by the end of the fifteenth century (25).

Though, due to inadequate documentation, worry about stigmatization as well as disinclination to self-identification, the exact number of Roma remains unspecified (33). It is estimated that about 10-12 million Roma are inhabited in the European Region, where the majority of them are concentrated in Central and Eastern Europe (34). In most Central, Eastern, and Southern European countries representation of Roma individuals exceeds 5% of the total population (35). Among the countries with the highest representation of Roma, in Romania, this minority group accounted for 1.2–2.5 million (8.3% of the population), while in Bulgaria Roma represented 10.3% (700,000–800,000) of all individuals living in the country (34). Hungarian Roma represents 8.9% of the country's population with an estimation of 876,000 inhabitants and the number is rising continuously (36).

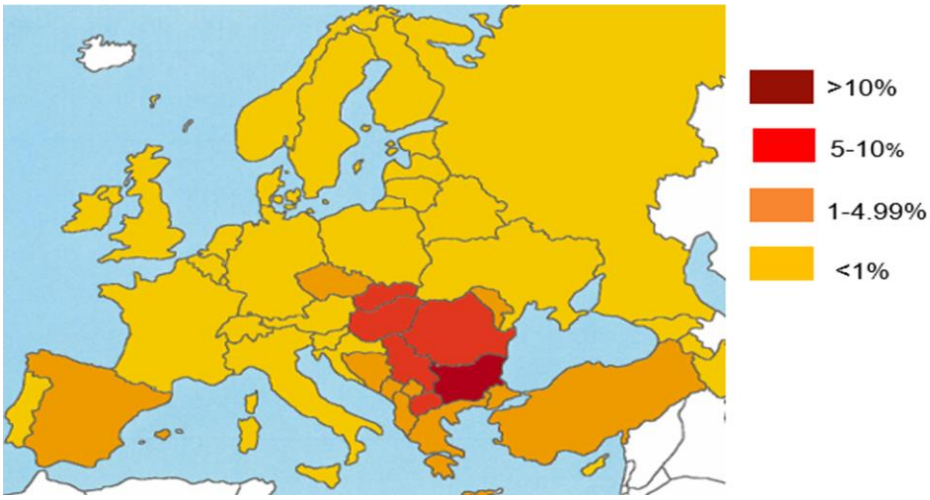

Figure 1. Percentage of Roma of the total population in Europe
(Source: Council of Europe, Roma and Travellers Division, 2010)

All over Europe, compared to mainstream populations, Roma individuals faced generations of discrimination and oppression which is manifested in racism, marginalisation in the formal labour market, poor education as well as inadequate access to healthcare services (37-43). Besides, several studies comparing Roma to the general majority populations revealed that along with worse health and well-being, the majority of Roma suffered from increased rates of communicable and non-communicable diseases, and higher mortality rates compared to non-Roma (44).

In Europe, numerous studies were conducted to compare patterns of alcohol consumption behaviour between Roma and the majority populations. Among them, a study conducted by Zelko et al. on the Roma and non-Roma populations of Slovenia is the only study where an AUDIT questionnaire was applied to evaluate drinking patterns. Results of the study demonstrated that for abstainers (Roma: 39.0%; non-Roma: 16.0%) and non-hazardous drinkers (Roma: 38.0 %; non-Roma: 64.0 %), there were significant differences between participants of Roma and non-Roma (45). One of the Slovak studies did not find any difference in overall alcohol consumption among males of Roma and non-Roma but in the case of binge drinking the rate was higher among Roma females than non-Roma (46). Additionally, a study on Roma and non-Roma mothers in Slovakia revealed that during pregnancy, Roma mothers had a greater risk of alcohol intake. The odds of alcohol drinking were 11.7 times higher for non–Roma mothers ($p<0.001$) (47). Though results from another study in Slovakia indicated that Roma adolescents drank less frequently than non-Roma (48). Findings of a study in Moldova represented that compared to non-Roma, Roma families spent more (116% of the non-Roma) on alcohol and tobacco, where the expenditure for essential goods among Roma was significantly lower than among non-Roma (49). In comparison with non-Roma, a higher proportion of Roma children in Lithuania and Latvia were daily alcohol users, though the differences were not statistically significant (50). Results of a study conducted on the Roma social workers in the Czech Republic showed that substance use including regular excessive alcohol intake was 2–6 times higher among Roma than that of the general population (51). Similar findings were also obtained from another study conducted in Spain stating that Roma women had significantly higher levels of alcohol consumption compared to non-Roma women (52). Gender-specific results were obtained from another study in Spain, it illustrated that young Roma men were more likely to drink alcohol compared to other young men, but among women, the frequency of alcohol consumption was lower among Roma than in the general population (53). Furthermore, a study conducted in Turkey demonstrated that compared to other strata of society, Roma individuals differed not only in traditions, livelihood and job opportunities but also suffered from excessive alcohol intake, where alcohol intake was 3.2 times higher compared to others (54).

Both daily alcohol consumption and drunkenness were more common among Roma adolescents in Hungary (55). Another study conducted among Hungarian Roma and non-Roma adolescents revealed that Roma ethnicity was significantly associated with the lifetime prevalence of alcohol intoxication (56). Besides poorer socioeconomic conditions, higher consumption of sweets and soft drinks, children living in Roma settlements in Hungary could also be characterized by earlier initiation of alcohol consumption and at the age of 11 years and trying alcohol was also more prevalent among Roma boys than non-Roma ones (57). Another Hungarian study described that between 2003 to 2014 there were negative changes regarding alcohol intake among Roma individuals and in comparison, with the general population, the gap was widened for alcohol consumption. From this study, it was articulated that during the surveys of 2014/2015 for both men and women and all age groups between 18 and 64 years, the percentage of heavy drinking was higher among Hungarian Roma than that of the general population (58). On the other hand, Kosa et al revealed that the prevalence of abstainers was significantly higher among Roma compared to the Hungarian general adult population (59).

1.4 Genetic factors influencing alcohol consumption and related phenotypes

Both patterns and the amount of alcohol consumed are accountable for the adverse health outcomes of alcohol intake (60, 61). Numerous factors comprising both genetic variations and non-genetic variables influence the quantity and patterns of alcohol consumption (62-64). Nongenetic factors include gender (65), age (66), duration of involuntary unemployment, extent of poverty (67) and relevant lifestyle factors like smoking and inadequate physical activity (68).

Several genes, particularly those coding for enzymes involved in alcohol metabolism have a substantial influence on alcohol consumption. Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are the two important enzymes responsible for the degradation of alcohol in the oxidative pathway. ADH is responsible for the oxidation of ethanol to acetaldehyde, which is further oxidized to acetate by aldehyde dehydrogenase ALDH (Figure 2). This toxic by-product of hepatic oxidation is responsible for the unpleasant effects of alcohol consumption. Thus, individuals with isoforms of ADH and ALDH that oxidize ethanol at a faster rate and acetaldehyde at a slower rate, respectively, are protected against the risk of alcohol dependence due to the accumulation of acetaldehyde (69).

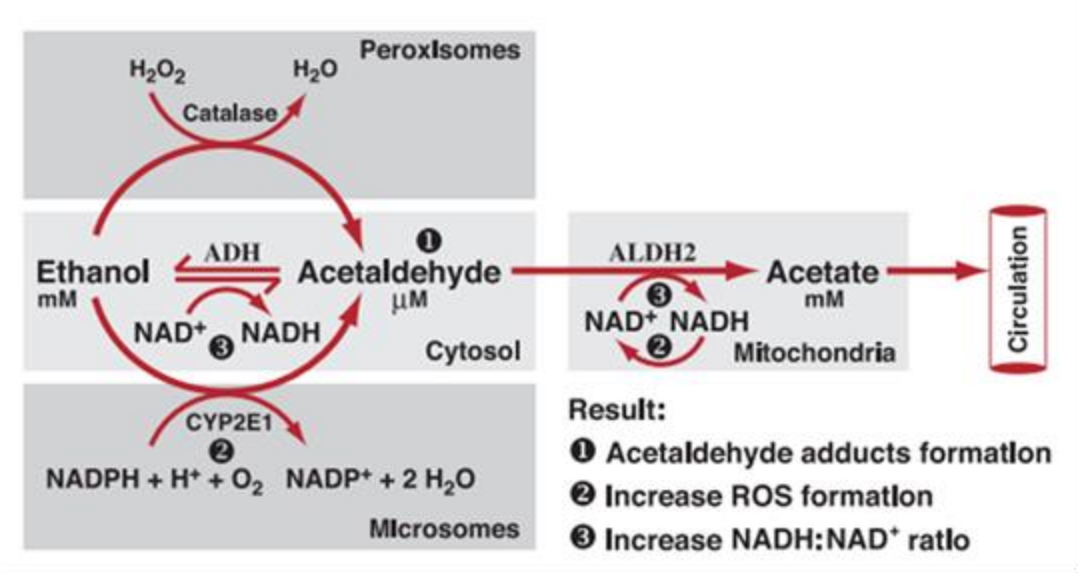

Figure 2. Oxidative pathways of alcohol degradation

(*Source: Zakhari, S., Overview: how is alcohol metabolized by the body? Alcohol Res Health, 2006, 29(4): p. 245-54.)*

Additionally, a statistically significant association was found between GABRA2 (γ-amino butyric acid receptor A2) gene polymorphism and alcohol dependence (70), where the finding was repeated in individuals of different European (71-74) as well as African ancestries (75). Furthermore, numerous genes related to neurotransmitter pathways involved in the mediation of positive reinforcing effects of alcohol such as the cholinergic receptor, muscarinic 2 (CHRM2); cholinergic receptor, nicotinic, alpha 5 (CHRNA5); catechol-O-methyltransferase (COMT); glutamate receptor, metabotropic 8 (GRM8); solute carrier family 6, member 4 (5-HTT); nuclear factor of kappa light polypeptide gene enhancer in B cells 1 (NFKB1); monoamine oxidase A (MAOA); neuropeptide Y receptor Y2 (NPY2R); opioid receptor, kappa 1 (OPRK1); opioid receptor, mu 1 (OPRM1); prodynorphin (PDYN); and tachykinin receptor 3 (TACR3) were also found to be associated with certain alcohol consumption-related phenotypes (76).

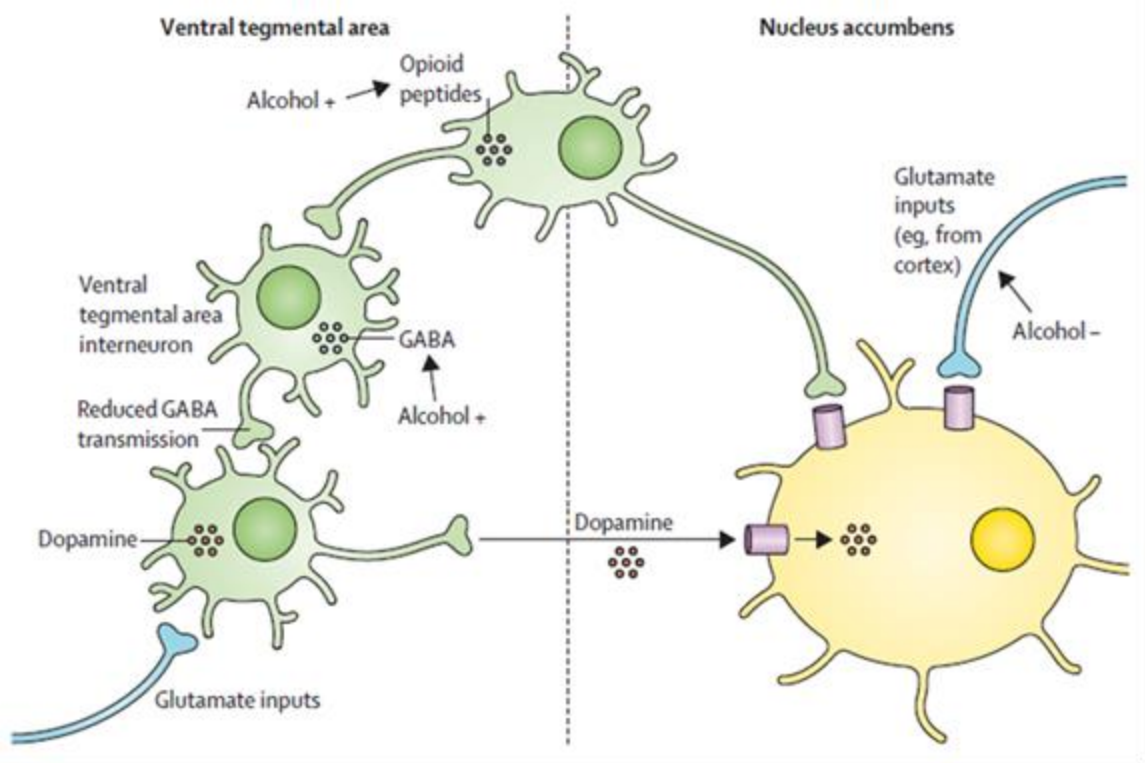

Figure 3. Effects of alcohol on neurotransmitter systems

(Source: Connor, J.P., Haber, P.S., Hall, W.D., Alcohol use disorders. The Lancet, 2016, 387(10022): p. 988-98.)

Besides alcohol metabolizing and neurotransmitter genes, taste preference-related genetic variants may also influence drinking behaviours. Perceived taste is one of the sensory components assumed to influence alcohol intake. Based on concentration, the taste profiles of alcohol comprise bitter and sweet sensations (77). Furthermore, along with ethanol, alcoholic beverages usually contain several active-tasting compounds such as sugars, acids, proteins and polysaccharides which may either increase or mask the bitterness of the alcoholic drinks (78). Alcohol consumption was found to be negatively influenced by the degree of responsiveness towards bitter component 6-*n*-propylthiouracil (PROP), while sweet taste sensitivity is assumed to increase preference for alcoholic beverages. Individuals with higher bitter taste perception are supposed to consume fewer alcoholic beverages compared to those with a lower perception of bitter taste (77, 79).

Human taste bud cells can be classified into four categories based on their morphological characteristics and three of those express taste receptors (Figure 4), type I, II and III being involved in salty, sweet-umami-bitter and sour taste perception, respectively (80). Numerous known genes are responsible for mediating bitter taste perception and many of them belong to the superfamily of G protein-coupled receptors of the TAS2R family (89, 90). The TAS2R family in humans is capable of interacting with several substances belonging to various taste qualities. Bitter-tasting compounds are linked to 25 different bitter taste receptors functioning as monomers (Figure 4) of the TAS2R gene family (81) among which TAS2R38 is the most studied one. Different variants of the TAS2R38 gene are linked to variation in responsiveness towards two bitter-tasting compounds called phenylthiocarbamide (PTC) and PROP (82, 83), and are associated with preferences for numerous foods such as brassica vegetables, other bitter-tasting foods, sweets, spicy foods and different alcoholic beverages (84-88). Three common variants such rs713598, rs1726866 and rs10246939 of TAS2R38 involved in changes of amino acids sequences and thus, results in two haplotypes, called AVI (alanine-valine-isoleucine) and PAV (proline-alanine-valine) which are liable for variation in human bitter taste sensitivity. Carriers of AVI homozygous are mainly non tasters while heterozygous and PAV homozygous carriers tend to be tasters (82, 83, 89, 90) Additionally, the bitter taste modality is also affected by other genes like TAS2R19 (Taste 2 Receptor Member 19), TAS2R31 (Taste 2 Receptor Member 31), TAS2R4 (Taste 2 Receptor Member 4), TAS2R5 (Taste 2 Receptor Member 5), TAS2R9 (Taste 2 Receptor Member 9) and CA6 (Carbonic Anhydrase 6) (gustin) (91). Gustin is a protein considered as a trophic factor for the growth and development of taste buds (92) and is linked with the formation and function of fungiform papillae (93).

In humans, receptor proteins of the TAS1R family functioning as heterodimers (Figure 3) are vital for the perception of sweet and umami taste modalities (94). Sweet taste perception is mostly mediated by the activation of TAS1R2 (taste receptor type 1, member 2) and TAS1R3 (taste receptor type 1, member 3) heterodimers and umami are mainly linked to TAS1R1/TAS1R3 heteromers (95). Cluster determinant 36 (CD36) encoding for the fatty acid translocase is responsible for sensation of fat taste (dietary long-chain fatty acids) and the epithelial sodium channel (ENaC) with four subunits and transient receptor potential cation channel subfamily V member 1 (TRPV1) play crucial roles in responsiveness towards salty taste

(96). A sour taste is sensed through acid detection. Though the underlying mechanism is not yet clearly identified, but it is suggested that transient receptor potential channels (TRPs), i.e. the polycystic kidney disease-like (PKDL-like) receptors are involved in sour taste perception (Figure 4) (97, 98). Genetic variants related to the perception of sweet, umami, fat, sour, and salty taste modalities may also contribute to variation in taste perception and consequential food intake, though these sensory pathways other than bitter and sweet are not relevant in terms of alcohol consumption.

Alcohol use disorder is a multifactorial disorder that can be influenced by a wide variety of genetic determinants and social, cultural and personal factors such as more permissive attitudes towards heavy drinking, physical and financial availability of alcohol (99, 100), poor family support (101, 102) parental drinking and individual expectations of alcohol effects may also contribute to AUD (103, 104) ADH1B and ALDH2, two important genes responsible for coding for alcohol-metabolizing enzymes were found to exhibit associations with different levels of alcohol consumption and with potential intermediate phenotypes of alcohol use disorder (AUD) (105). Relevant studies demonstrated that ADH1B rs1229984 and rs2066702 were associated with AUD (106-109) and numerous aspects of alcohol consumption such as alcohol dependence, and hazardous and harmful drinking (107, 110-113). Likewise, highly significant associations were found between ALDH2 and alcohol dependence (114-116) as well as with drinking status (117). These two genes ADH1B and ALDH2 involved in the metabolism of alcohol were found to have the strongest effect on the development of alcoholism. Through the accumulation of acetaldehyde toxic intermediate, which can create unpleasant feelings such as dizziness and nausea and thus have an effect on alcohol consumption (118). Other studies focus on genes and their variants involved in the central nervous system's responses linked to alcohol consumption. Findings from genetic association studies represented that GABRA2 and other GABA-A receptor genes (119-121) were significantly linked with alcohol dependence (70, 72, 74, 75). γ-amino butyric acid (GABA), the major inhibitory neurotransmitter in the vertebrate brain (122) binds to the GABA-A receptor and is involved in regulating brain excitability through changing neuron membrane potential via opening a chloride ion channel. GABA-A receptors are sensitive to ethanol and suppose to mediate many effects comprising anxiolysis, sedation, motor incoordination, tolerance, and dependence (123). Dopamine has been considered to be involved

in the development of alcoholism through the reward system (119) since the mesolimbic dopamine system plays a crucial role in the rewarding effects of alcohol (124, 125). Alcohol consumption leads to the release of neurotransmitters in the limbic system via stimulating dopamine neurons in the mesolimbic system and thus mediates positive reinforcement and reward (126). Dysfunction in the dopaminergic transmission is linked with a craving for ethanol (127) and appears to impact withdrawal symptoms (128, 129). Among 5 dopamine receptors, the dopamine D2 receptor gene (DRD2) controls both the release and synthesis of dopamine (119). Additionally, the dopamine transporter (DAT) affects dopaminergic neurotransmission (130), where a reduction in DAT density was observed among alcoholics (131). Furthermore, two important enzymes called catechol-O-methyltransferase (COMT) and monoamine oxidase A (MAO-A) (132, 133) play important roles to metabolize dopamine to homovanillic acid, which is recognized as a potential indicator for central dopaminergic neuronal activity (134). Serotonin (5-hydroxytryptamine; 5-HT) is also believed to be involved in the mediation of alcohol intake (135). Serotonin transporter (5-HTT) polymorphism located on chromosome 17q11.2 (136) was demonstrated being a functional polymorphism: the shorter allele exhibiting lower transcriptional efficiency. The association identified between the short allele of HTT and anxiety-related personality traits (137) facilitates the assumption that HTT may be involved in the regulation of alcohol consumption via participation in harm avoidance (138). Variations in kappa opioid receptors, such as opioid receptor kappa 1 (OPRK1) and prodynorphin (PDYN) are strongly linked to alcohol dependence (139). Moreover, 11 SNPs of cholinergic receptor muscarinic 2 (CHRM2) showed statistically significant associations with alcoholism (140)

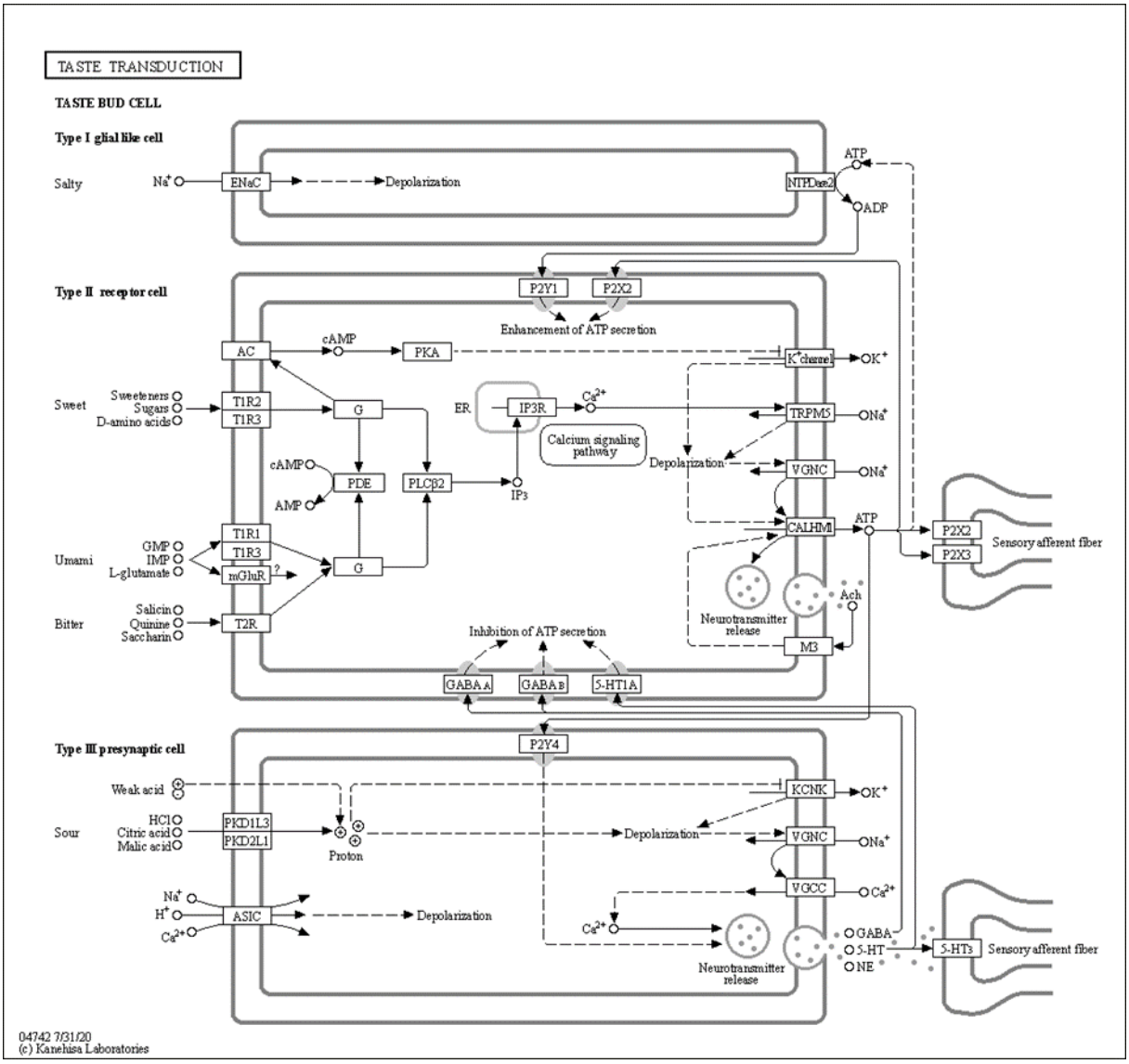

Figure 4 KEGG PATHWAY Database: Taste transduction - Reference pathway

(Source: https://www.kegg.jp/pathway/map=map04742&keyword=taste)

1.5 Genetic studies of alcohol consumption in Hungary and among Roma

Genetic association studies regarding alcohol drinking behaviours of the Hungarian general and Hungarian and other Roma populations are scarce. One Hungarian study illustrated that variations in alcohol consumption patterns among Hungarian general and Roma participants were not linked to the genetic constitution, but rather exposure to different environmental factors and respective cultural values that may have a prominent influence on alcohol intake (141). Another study of Hungarian men exhibited that ADH1B rs1229984 had a significant association with lower odds of drinking frequency (142) and in the case of Hungarian males ADH1C rs1693482/ rs698 alleles enhanced the risk of excessive and problematic drinking, respectively (143). Findings from another study illustrated that the allele frequency of ADH1B rs1229984 did not differ significantly between participants of Roma and Czech populations (144). At the same time, the effect of taste preference genetic variants on different dimensions of alcohol consumption among Roma individuals and in the Hungarian general population has not been investigated yet.

AIM OF THE STUDY

Our study aimed to identify the factors that may influence alcohol consumption behaviours of the Hungarian general and Roma populations of North-East Hungary. The specific objectives were to:

1. Describe and compare alcohol consumption behaviours of the Hungarian general (HG) and Roma (HR) populations.
2. Evaluate the potential effect of taste preference-related gene polymorphisms on alcohol consumption behaviours among participants of HG and HR populations.
3. Synthesize the evidence on the effect of taste preference-related genetic variants on various aspects of drinking behaviours.

MATERIALS AND METHODS

3.1 Study design and sampling

The current research used data derived from a cross-sectional study conducted in 2018 from 17 May to 29 August (145). Within the framework of this three pillar (questionnaire survey, physical examinations, and laboratory analysis) complex comparative health survey, representatives of the HG and HR populations segregated settlements of two counties of North-East Hungary named Borsod-Abaúj-Zemplén and Szabolcs-Szatmár-Bereg, where most of Roma populations are inhabited (146). In the beginning, it was intended to comprise 500 participants from each of the two study groups. The inclusion of study subjects was aided by the pre-determined principle that if somebody was not available to reach, it was acceptable to add another individual, but when anyone denied to participate in the study, it was unacceptable to include another subject for the one who refused to participate. To collect data from study participants of HG and HR groups, questionnaires were administered by practice nurses and Roma field workers, respectively. Through interviews, information on alcohol intake, smoking, eating habits, physical activity, information on demographics, and socioeconomic status was collected. Physical examination included measurements of weight, height and waist circumference, blood pressure, ischiocrural muscle elasticity, and lateral spinal flexion. Furthermore, visual acuity and fitness of cardiovascular tests were also performed. For genetic analysis, blood samples were collected at General Practitioners' (GPs) practices. This study was approved by the Ethical Committee of the Hungarian Scientific Council on Health (61327-2017/EKU). By following the Helsinki Declaration written consent was taken from the study respondents of both groups.

3.2 Sample representative of the Hungarian general population living in Northeast Hungary

Participants for the HG population sample were derived from a population-based disease registry called the General Practitioners' Morbidity Sentinel Stations Programme (GPMSSP). This registry was set up to observe the incidence and prevalence of various chronic non-communicable diseases (diabetes, hypertension, ischaemic heart disease, liver cirrhosis, acute

myocardial infarction, stroke, malignancies of the respiratory tract, colon and rectum, breast, cervix, and prostate). In 1998 the School of Public Health of the University of Debrecen together with the National Public Health and Medical Officer Service founded the GPMSSP (147). Initially, this program encompassed populations from four different counties: Hajdú-Bihar, Szabolcs-Szatmár-Bereg, Győr-Moson-Sopron, and Zala. Afterward, populations from several other regions of Hungary were also included in the GPMSSP (148).

The reference HG population sample for the present study was randomly recruited from the GPMSSP registry. The sample comprised individuals of 20–64 years residing in private houses in two selected counties of Northeast Hungary (Borsod-Abaúj-Zemplén and Szabolcs-Szatmár-Bereg) and registered by GPs involved in the GPMSSP. GPs documented the medical history, conducted physical examinations, and collected blood samples for routine examinations and DNA extraction. At the beginning, it was intended to recruit 25 respondents from each of twenty previously nominated GPs, which ultimately would have accounted for 500 subjects of the general population. Two GPs refused to take part; thus, the final sample size comprised 450 respondents from eighteen GPs. Health-related information was collected at the time of the participants' visits at the GP's practices and practice nurses administered questionnaires in a face-to-face mode.

3.3 Sample representative of the Hungarian Roma population living in segregated colonies in Northeast Hungary

A stratified multistep sampling technique was applied to enrol representative subjects of the Hungarian Roma population from the same two counties (Borsod-Abaúj-Zemplén and Szabolcs-Szatmár-Bereg), where most of the Roma populations are inhabited. Earlier, an environmental survey was conducted in all settlements of Hungary, where Roma field workers were engaged to detect and characterize segregated Roma settlements of no less than, 100 residents and the ethnicity of the individuals of these segregated colonies was authenticated by self-statement (146). Followed by the required validation of this registry, twenty colonies were selected randomly for the present study and 25 households were chosen randomly from each of these selected colonies. Afterward, from each selected household all individuals within the age range

of 20–64 years were identified and one person of this age group from every house was nominated by using a random table for subsequent face-to-face interviews. To avoid probable adversities and mistrust of Roma participants regarding interviewers, skilled Roma university students were engaged to collect information related to health behaviours.

3.4 Sociodemographic and economic variables

Several sociodemographic and economic variables (gender, ethnicity, sex, marital status, highest education level, economic activity, and self-perceived financial status) were used in this study, as predictor variables for different alcohol consumption phenotypes. During this study, different age categories (20-34, 35-49, and 50+ years) were used for describing study participants. The highest educational level was classified as primary or less, secondary, high school, and tertiary school. Based on their marital status the respondents were categorized as married, single, and widow, or divorced, while economic activity was illustrated by categories such as worker, unemployed, and pensioner/other allowance/student. A five-point Likert scale varying from very bad to very good was applied to gather information on participants' self-perceived financial status, and the responses were subsequently converted to three different options: good, satisfactory, and bad.

3.5 Assessment of alcohol consumption patterns

Patterns of alcohol intake were evaluated by utilization of the 10-item Alcohol Use Disorders Identification Test (AUDIT-10) tool, where the total AUDIT score varies between 0 to 40 and total scores of 20 or greater indicate possible alcohol dependence. This tool comprises questions on three important domains of alcohol consumption such as hazardous alcohol use related to the frequency and quantity of drinking, dependence symptoms, and harmful alcohol use describing problems due to alcohol consumption. AUDIT questions 1- 8 have five response options to be chosen, while each response category has a corresponding score varying from 0 to 4. Questions 9 and 10 are scored on either of the three available options such as 0 (no), 2 (yes, but not in the last year), or 4 (yes, during the last year) (149). In our study, the Hungarian version of the AUDIT was applied (158). The first question of the AUDIT questionnaire provides information on

drinking frequency, while questions 2 and 3 gather data on the typical quantity of alcohol consumed and frequency of heavy drinking, respectively. Additionally, a score of more than 0 on questions 4 to 6 indicates the presence of alcohol dependence while points on questions 7 to 10 infer the possibility of alcohol-related harm being experienced. Total scores ≥ 8 out of 40 are generally suggested as an indication of hazardous as well as harmful alcohol use and the possibility of alcohol dependence (149). However, in certain cases improvements (obtaining optimal sensitivity and specificity of assessment) have been done by lowering the cut-off score, depending on the population investigated (149). Results from several other research on AUDIT indicated that for optimal revealing of hazardous and harmful alcohol use among women, lower than the originally suggested cut-off score of 8 is recommended by some researchers (150-154). Findings from another similar type of study revealed that among females, optimal sensitivity and specificity of the assessment of different alcohol consumption behaviours were obtained at AUDIT score cut-off point ≥5 (155). One explanation for this lower cut-off value for females may be the gender-specific differences in alcohol requirement and alcohol metabolism. As females have lower body weight than males, they have less body water to dissolve alcohol which results in more concentrated alcohol in women's bodies compared to men. Additionally, women possess fifty percent less ADH than men and thus more unmetabolized alcohol is passed into their bloodstream which ultimately decreases the alcohol requirement of the females than men to produce equal alcohol concentration in the blood (156). Though we have also included some analyses using the original cut-off score of 8 as well.

During the current study, several alcohol consumption phenotypes, i.e., problematic drinking, hazardous level of alcohol use, alcohol dependence, alcohol-related harm, and past alcohol problems were evaluated as primary outcome variables. To evaluate problematic drinking the following thresholds of total AUDIT score were considered: ≥ 8 points for men and ≥5 points for women (149, 155). Additionally, a score of ≥ 1 on questions 2 or 3 specified a hazardous consumption level, while a score above 0 on questions 4 to 6 indicated alcohol dependence. Furthermore, score on questions 7-10 pointed towards alcohol-related harms being experienced. Finally, the last two questions provided evidence of past problems(149). These domains were also considered separately in our research to gain more insight into several aspects of alcohol-related phenotypes of our two study samples, which might point out ethnic-specific problems and

the need for more tailored interventions. Moreover, for genetic association analysis the first three questions of the AUDIT questionnaire were used as potential outcome variables. The first question ("How often do you have a drink containing alcohol?") and the second question ("How many standard drinks containing alcohol do you have on a typical day when drinking?") of the AUDIT questionnaire measure the frequency of drinking and the typical quantity consumed respectively, while the third question ("How often do you have six or more drinks on one occasion?") indicates the frequency of heavy drinking.

3.6 Selection of genetic polymorphisms

A systematic literature review was conducted to identify single nucleotide polymorphisms linked to different taste preference genes, which are assumed to be associated with various alcohol consumption behaviours. Based on the literature search, SNPs, whose effects regarding bitter and sweet taste preference and/or perception were investigated comprehensively (91) and likely to be related to diverse alcohol intake phenotypes were included in the present study. Four SNPs, TAS1R3 (taste 1 receptor member 3) rs307355, TAS2R38 (taste 2 receptor member 38) rs713598, TAS2R19 (taste 2 receptor member 19) rs10772420 and CA6 (carbonic anhydrase 6) rs2274333 were selected for further analysis. Detailed descriptions of the selected SNPs and their effects on alcohol consumption and taste preferences are illustrated in Table 1.

Table 1. Effect of selected genetic polymorphisms on alcohol consumption behaviour and taste phenotypes

Gene	SNP	Association	No association	Relation to taste phenotypes
TAS1R3	**rs307355**	Soju intake and heavy drinking (≥30 g/day; Individuals with CT genotype tend to be heavy drinkers) (157).	Intake of wine, spirit & beer. (157).	Taste responsiveness towards sucrose (T alleles linked with decreased sensitivity) (158).
TAS2R38	**rs713598**	Daily number of standard drinks (Individuals with P allele: fewer standard drinks, also from spirits and mixed drinks) (159). Frequency of alcohol intake (tasters: higher frequency) (160). Decreased alcohol intake (C allele; first AUDIT question (161).	Intake of Beer & wine (159). 2nd and 3rd AUDIT questions (161). Weekly intake of alcohol (162).	PTC, PROP, thioamide and salicin threshold, taster status, bitterness; preference for bitter vegetables (lower preference, threshold for tasters) (89, 163-172). Preference/threshold of sucrose, preference, and intake of sweet tasting foods (GG lower preference) (173-175).
TAS2R38	**rs713598, rs1726866, rs10246939**	AVI/AVI homozygotes associated with more frequent and more alcohol intake (84, 176). Carriers of AVI/AVI positively associated with being alcoholic (177) Alcohol drinkers had a higher number of AVV homozygotes and were linked with higher alcohol consumption (178). Association between taster haplotype and	Daily intake of alcohol (180, 181). Beer and daily total alcohol intake (157). Alcohol drinker status (182, 183). Amount and frequency of alcohol consumption (184).	PROP phenotype, bitterness of ethanol, cruciferous vegetable preference & intake (taster had lower preference & threshold) (164-167, 170, 172, 185-200). Preference and consumption of sweet-tasting foods (PAV higher preference) (201), (202).

		lower mean of the largest number of drinks (ever having in 24 hours) (179) and Individuals with minimum one PAV haplotype had lower weekly alcohol consumption (162). Subjects with AVI haplotype were less likely to be alcohol drinkers (157).		
TAS2R19	**rs10772420**	--	Alcohol consumption frequency (160). First three AUDIT questions (161). Drinking frequency as well as heavy drinker status of alcohol (203).	Preference, intensity, detection threshold of bitter-tasting compounds, and preference of grape-fruit juice (significant association between A allele and more intense perception of quinine (84).
CA6	**rs2274333**	--	Daily consumption of alcohol (180). Alcohol consumption frequency (160).	PROP (bitter) taster status, threshold (The A allele more common in supertasters (186, 188, 190, 204)

AUDIT: Alcohol Use Disorders Identification Test; AVI: alanine- valine- isoleucine; PAV: proline–alanine–valine; PROP: 6-n-propylthiouracil; PTC: phenylthiocarbamide; *SNP: single nucleotide polymorphism.*

3.7 DNA preparation

DNA extraction was conducted from previously collected ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood samples. To isolate DNA from 500-µl aliquots of blood, the "MagNA Pure LC DNA Isolation Kit – Large Volume" made by Roche Diagnostics of Germany was used.

3.8 Genotype assessment

Genotyping of the selected 4 SNPs was conducted by the Mutation Analysis Core Facility (MAF) of the Clinical Research Center of Karolinska University Hospital of Stockholm, Sweden. Genotype assessment was conducted on the Sequenom Mass Array platform using the iPLEX Gold Chemistry. During the process, initially, a locus-specific polymerase chain reaction (PCR) reaction is carried out, and then a locus-specific primer extension reaction is accomplished, where oligonucleotide primers anneal to the polymorphic site of interest. In the iPLEX assay, both primers and amplified target DNA are incubated with mass-modified dideoxynucleoside terminators. Extended primer mass can be determined by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, when the mass of primer specifies the sequence, thus alleles existing at the specific polymorphic site (205). Furthermore, validation, quality control as well as concordance analysis was carried out by MAF. The success rate of genotyping was over 98%.

3.9 Statistical analysis

Data were analysed by utilizing the statistical software STATA 10 version (Stata Corporation, College Station, Texas). The normality of the age distribution of HG and HR respondents was checked by the Shapiro-Wilk test, while a comparison of mean age and gender distribution of HG and HR respondents was made by execution of the Mann-Whitney U and chi-square ($\chi 2$) tests, respectively. To compare the distribution of different sociodemographic variables between the study populations (HR versus HG) χ^2 and Fisher's exact tests were executed. Furthermore, both crude and gender-stratified distributions of different alcohol consumptions behaviours (problematic drinking, alcohol intake at hazardous levels, dependence syndrome of alcohol, harms associated with alcohol intake, and evidence of past problems related to alcohol consumption) between the two groups were calculated by χ^2 and Fisher's exact tests. To investigate the association between above mentioned sociodemographic variables and different alcohol consumption behaviours included in this study, multiple Poisson, as well as, logistic regression analyses were applied, where outputs of the association analyses were presented as respective odds ratios with corresponding 95% confidence intervals.

When Poisson or multivariate logistic analysis denoted statistically significant differences between HG and HR participants, the decomposition method established by Oaxaca (206) and Blinder (207) was applied to reveal the ethnicity-specific variations in different alcohol intake behaviours that could be described by various socioeconomic variables. This decomposition technique utilizes the output of regression analysis and divides the components of a group difference into the endowments and coefficients. The endowment is resulted from the variations in characteristics between groups, while the coefficient is attributable to the variations in the effects of characteristics. The STATA command "mvdcmp" was applied to run a multivariate decomposition analysis (208).

To assess the deviation from the Hardy-Weinberg equilibrium (HWE) and to calculate allele frequencies of the included SNPs the STATA commands "hwsnp" (209) and "genhw" (210) were executed, respectively. The $\chi 2$ test was used to depict the differences in genotype frequencies between HG and HR populations. Additionally, an association of included genetic variants with different alcohol intake behaviours among HG and HR participants were evaluated by applying "qtlsnp" command in STATA (209). During all association analyses, adjusments were made for potential covariates (age, gender and marital status), and dominant and recessive models were considered (based on corresponding minor alleles). In the case of HWE p-value of <0.001 was applied as a significance threshold (211), while in every other case of analysis $p<0.05$ indicated statistical significance. Additionally, Bonferroni corrected p-values were presented for multiple testing analyses.

3.10 Systematic literature search to identify taste preference genetic variants related to alcohol consumption behaviours

3.10.1 Procedure of literature search and inclusion criteria

To identify articles investigating associations of taste preference-related genetic variants with various aspects of drinking behaviours, a systematic literature search was conducted using three search engines PubMed, Web of Science and, ProQuest Central. Principles of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (212) were followed throughout the search process. During the literature search the following keywords

were applied to ascertain desired articles: ("taste preference" OR "taste perception" OR "taste sensitivity" OR "sweet taste preference" OR "sweet taste perception" OR "sweet taste sensitivity" OR "bitter taste preference" OR "bitter taste perception" OR "bitter taste sensitivity" OR "fat taste preference" OR "fat taste perception" OR "fat taste sensitivity" "salty taste preference" OR "salty taste perception" OR "salty taste sensitivity" OR "sour taste preference" OR "sour taste perception" OR "sour taste sensitivity" OR "umami taste preference" OR "umami taste perception" OR "umami taste sensitivity" OR "taste threshold" OR "sweet taste threshold" OR "fat taste threshold" OR "salty taste threshold" OR "sour taste threshold" OR "umami taste threshold") AND ("genes") AND ("alcohol consumption") NOT ("animal"). From the findings of the literature search articles meeting the desired criteria such as focusing on human samples, written in English, published in peer-reviewed journals, and existing in a full-text format were included for subsequent analysis.

3.10.2 Quality evaluation of selected studies

The validated 11-item quality assessment tool of genetic association studies called the Q-Genie tool was used to assess the quality of the included articles, where a 7-point Likert scale varying from 1 (poor) to 7 (excellent) was applied to evaluate included studies regarding certain quality aspects defined by each item. Depending on the total quality score, selected studies were specified as three quality categories, i.e., poor, moderate, or good. Total scores of ≤ 35, >35 to ≤ 45 and > 45 for studies with control groups, while total scores of ≤ 32, >32 to ≤ 40 and >40 for studies without control groups indicated poor, moderate, and good quality studies, respectively (213).

3.10.3 Data extraction

After the removal of duplicated studies, abstracts of the remaining publications were screened to identify eligible articles for further analysis.

RESULTS

The study comprised altogether 797 respondents from both HG and HR populations: 410 HG and 387 HR subjects, respectively. Data related to different alcohol consumption behaviours were available for all 797 respondents, while for genetic association analysis, a total of 405 HG and 364 HR DNA samples were obtainable. The mean age of HG respondents did not differ significantly from that of HR participants (HG: 44.3 ± 12.3 years, HR: 42.8 ± 12.1 years, p=0.075). Additionally, the output of $\chi 2$ test analysis postulated that the proportion of male respondents was significantly lower in the HR (0.26 vs 0.44, $p<0.001$) than in the HG sample.

4.1 Characteristics of the study populations

The socioeconomic characteristics of respondents of both study groups (HG and HR) are illustrated in **Table 2**. Except for marital status and age categories, all other socioeconomic variables included in the study such as education, economic activity, financial status, and gender differed significantly ($p<0.001$) between the two study groups. Among HR, the majority of the individuals (84.5%) could be characterized by primary educational level or less while for HG, most of the study individuals (33.66%) completed high school. Additionally, 18.29% of HG participants were tertiary-level educated, while for HR this percentage was less than 1%. It is also articulated that the rate of unemployment was almost three times higher (HG: 7.80%; HR: 21.45%) among HR compared to HG. Furthermore, 30.98% and 14.99% of the HG and HR participants, respectively, were in good financial status, while for bad financial status, the percentage was almost three times higher (HG: 11.71%; HR:30.23%) among participants of HR than HG. Moreover, the percentage of female participants was significantly higher among HR (73.9%) compared to HG (56.1%).

Table 2. Characteristics of the Hungarian general (HG) and Roma (HR) populations

Characteristics	Variable	Total n (%)	HG n (%)	HR n (%)	p-value*
Education	primary or less	413 (51.82)	86 (20.98)	327 (84.50)	**<0.001**
	secondary	151 (18.95)	109 (26.59)	42 (10.85)	
	high school	150 (18.82)	138 (33.66)	12 (3.10)	
	tertiary education	76 (9.54)	75 (18.29)	1 (0.26)	
Economic activity	worker	531 (66.62)	303 (73.90)	228 (58.91)	**<0.001**
	Pensioner, other allowance. student	138 (17.31%)	69 (16.83)	69 (17.83)	
	unemployed	115 (14.43)	32 (7.80)	83 (21.45)	
Marital status	married	509 (63.86)	253 (61.71)	256 (66.15)	0.240
	single	166 (20.83)	95 (23.17)	71 (18.35)	
	widow, divorced	115 (14.43)	60 (14.63)	55 (14.21)	
Financial status	good	185 (23.21)	127 (30.98)	58 (14.99)	**<0.001**
	satisfactory	434 (54.45)	227 (55.37)	207 (53.49)	
	bad	165 (20.70)	48 (11.71)	117 (30.23)	
Age category (years)	20-34	209 (26.22)	99 (24.15)	110 (28.42)	0.348
	35-49	308 (38.64)	160 (39.02)	148 (38.24)	
	50+	280 (35.13)	151 (36.83)	129 (33.33)	
Gender	male	281 (35.26)	180 (43.90)	101 (26.10)	**<0.001**
	female	516 (64.74)	230 (56.10)	286 (73.90)	
Total		797 (100)	410 (100)	387 (100)	

**Pearson chi-square and Fisher's exact test. Bold indicates statistical significance.*

4.2 Alcohol consumption patterns of the Hungarian general and Roma populations

4.2.1 Drinking characteristics of study participants

Table 3 demonstrates the alcohol-drinking frequencies of the HG and HR populations. Assessment of how often the study participants in both groups consumed alcoholic beverages was done based on the first question of the AUDIT questionnaire. From the table, it is observed that there is a statistically significant ($p<0.001$) difference in the frequency of having alcoholic drinks between HG and HR. In comparison with HG, a lower proportion of HR participants had alcoholic drinks "2-4 times a month" (HG: 12.01%; HR: 4.17%) and "2-3 times a week or more" (HG: 12.75%; HR: 5.47%). Meanwhile, a higher percentage of HR individuals (37.76%) had alcoholic drinks "monthly or less" compared to HG participants (28.43%). Additionally, after stratification by gender, the frequency of alcohol intake remained statistically significant between HG and HR males ($p=0.007$) and between HG and HR females ($p<0.001$).

Table 3. Drinking frequencies of Hungarian general (HG) and Roma (HR) populations

	never n (%)	monthly or less n (%)	2-4 times a month n (%)	2-3 times a week or more n (%)	p-value*
HG Total	191 (46.81)	116 (28.43)	49 (12.01)	52 (12.75)	**<0.001**
HR Total	202 (52.60)	145 (37.76)	16 (4.17)	21 (5.47)	
HG Male	52 (29.05)	55 (30.73)	28 (15.64)	44 (24.58)	**0.007**
HR Male	22 (21.78)	52 (51.49)	12 (11.88)	15 (14.85)	
HG Female	139 (60.70)	61 (26.64)	21 (9.17)	8 (3.49)	**<0.001**
HR Female	180 (63.60)	93 (32.86)	4 (1.41)	6 (2.12)	

**Pearson chi-square and Fisher's exact test. Bold indicates statistical significance.*

Table 4 recapitulates the number of standard drinks consumed on a typical day and how often 6 or more alcoholic drinks per occasion were consumed by study participants. The table postulates that the number of standard drinks consumed did not differ significantly between the participants of HG and HR. After stratification by gender, consumption of standard alcoholic drinks varied significantly ($p=0.011$) between HG and HR females. From the table, it is observed that 7.0% and 12.1 % of the HG females and HR females, respectively, consumed 3 to 4 standard alcoholic drinks, while in the case of 5 or more drinks it was 0.4% for HG females and 4.3% for HR females.

Additionally, it was also observed that in the case of 6 or more alcoholic drinks, there was no significant ($p>0.05$) difference between participants of both study groups and even after stratification by gender.

Table 4. Number of standard drinks consumed on a typical day and frequency of consuming 6 or more drinks per occasion among the Hungarian general (HG) and Roma (HR) populations

	Number of standard drinks on a typical day				Frequency of six or more alcoholic drinks per occasion			
	1 or 2 n (%)	**3 or 4 n (%)**	**5 or more n (%)**	**p-value***	**Never n (%)**	**Less than monthly n (%)**	**monthly or more often n (%)**	**p-value***
HG Total	341 (83.58)	48 (11.76)	19 (4.66)	0.378	118 (65.56)	43 (23.89)	19 (10.56)	0.872
HR Total	303 (79.74)	55 (14.47)	22 (5.79)		62 (62.63)	25 (25.25)	12 (12.12)	
HG Male	128 (71.5)	33 (18.4)	18 (10.1)	0.106	214 (93.04)	14 (6.09)	2 (0.87)	0.342
HR Male	60 (60.6)	29 (29.3)	10 (10.1)		259 (91.52)	16 (5.65)	8 (2.83)	
HG Female	213 (93.0)	15 (7.0)	1 (0.4)	**0.011**	332 (80.98)	57 (13.90)	21 (5.12)	0.400
HR Female	243 (86.5)	26 (12.1)	12 (4.3)		321 (84.03)	41 (10.73)	20 (5.24)	

**Pearson chi-square and Fisher's exact test. Bold indicates statistical significance.*

4.2.2 Alcohol consumption behaviours of study respondents

Mean AUDIT-C (HG: 1.38 ± 1.86; HR: 1.13 ± 1.89; p=0.063) and AUDIT-10 (HG: 1.60 ± 2.35; HR: 1.65 ± 3.64; p=0.766) scores did not show any significant difference (p>0.05) between respondents of two study groups even after stratification by gender.

Different alcohol consumption behaviours of the HG and HR study populations are presented in **Table 5**. Among the listed five, only two alcohol consumption behaviours such as "alcohol-related harm" and "past problems" differed significantly between participants of the two study groups. Among Roma participants, the frequency of alcohol-related harm was significantly higher (13.33%) than in the HG sample (6.20%). After stratification by gender, the frequency of alcohol-related harm also varied significantly between males of HG and HR (p<0.001) females (p=0.001). Among Roma males experience of alcohol-related harm was more than 2 times higher than among HG males (HG: 12.92%, HR: 30.69%), while for females the experience of harm was nearly 7 times higher among HR compared to HG (HG: 0.89%; HR: 6.93%).

Additionally, past problems related to alcohol consumption differed significantly between respondents of the two study populations. It was observed to be 1.71% and 4.95% among respondents of HG and HR, respectively. The table also represents that after stratification, differences in evidence of past problems remained significant between males of HG and HR (p<0.007) and females (p=0.035) as well. Around 13% of the Roma males reported alcohol-related past problems, while 2.12% of Roma females reported such problems. Furthermore, though none of the HG females experienced past alcohol problems, 2.12% of HR females reported having evidence of past problems. The table also demonstrates that the three listed alcohol consumption behaviours such as problematic alcohol drinking, alcohol intake at hazardous levels and alcohol dependence showed no statistically significant (p>0.05) differences between the two study groups (HG versus HR).

Table 5. Alcohol consumption behaviours of Hungarian general (HG) and Roma (HR) participants

	HG n (%)	**HR n (%)**	**p-value***
Problematic drinking			
Male	13 (7.39%)	14 (14.74%)	0.054
Female	4 (1.79%)	13 (4.78%)	0.084
Total	17 (4.25%)	27 (7.36%)	0.065
Consumption at hazardous level			
Male	77 (43.02%)	46 (47.42%)	0.482
Female	25 (10.92%)	43 (15.30%)	0.147
Total	102 (25.00%)	89 (23.54%)	0.635
Alcohol dependence			
Male	14 (7.82%)	14 (14.14%)	0.094
Female	1 (0.44%)	6 (2.19%)	0.134
Total	15 (3.70%)	20 (5.36%)	0.265
Alcohol-related harm			
Male	23 (12.92%)	31 (30.69%)	**<0.001**
Female	2 (0.89%)	19 (6.93%)	**0.001**
Total	25 (6.20%)	50 (13.33%)	**0.001**
Past problems			
Male	7 (3.89%)	13 (12.87%)	**0.007**
Female	0 (0.00%)	6 (2.12%)	**0.035**
Total	7 (1.71%)	19 (4.95%)	**0.010**

*Problematic drinking: cut-off: men≥8; women≥5. Alcohol consumption at hazardous the level: scores of 1 or more on question 2 or question 3. Alcohol dependence: points scored above 0 on questions 4-6. Alcohol-related harm: points scored on questions 7-10. Past problems: based on the final two questions of AUDIT (Alcohol Use Disorder Identification test). *Pearson chi-square and Fisher's exact test. Bold indicates statistical significance.*

Additional descriptive analysis using a cut-off score of AUDIT ≥8 for both men and women as an indicator of hazardous and harmful alcohol intake is demonstrated in **Table S1**. From the table, it is observed that there was no significant difference (HG: 3.5%; HR: 5.18%; $p>0.05$) in hazardous and harmful alcohol intake between participants of both study groups when AUDIT ≥8 was used as a threshold. Even after stratification by gender, the difference remained insignificant among males and females of HG and HR. The binary logistic regression analysis has also been conducted to elucidate the association between different socioeconomic factors and hazardous and harmful alcohol intake using the AUDIT ≥8 cut-offs for both sexes and the outcome of the analysis is exhibited in **Table S2**. From the table, it is articulated that though gender and the oldest age category showed significant associations with hazardous and harmful alcohol intake, ethnicity and other factors included in the study did not depict any significant associations.

4.2.3 Association of listed socioeconomic variables with various alcohol consumption behaviours

Outcomes of univariate and multivariate logistic regression analyses between various listed socioeconomic variables and different alcohol consumption behaviours are illustrated in **Table 6 and Table 7**. The tables depict the associations of listed socioeconomic variables (ethnicity, educational level, economic activity, marital status, financial status, age categories, and gender) with different alcohol consumption behaviours (total AUDIT score, problematic drinking, hazardous alcohol intake, alcohol dependence, harms related to alcohol intake and evidence of past problems associated with alcohol consumption). Among different predictor variables, ethnicity showed a statistically significant ($p<0.05$) association with alcohol-related harms and evidence of past problems. The odds of having alcohol-related harms were 3.47 times higher (OR: 3.47; 95% CI:1.61-7.49) among respondents of Hungarian Roma compared to Hungarian general. Similarly, the odds of having evidence of past alcohol problems were 4.09 times higher (OR: 4.09; 95% CI:1.02-16.46) among HR participants than those of HG. Additionally, the marital status of the respondents also postulated a significant association with alcohol intake at the hazardous level. In comparison with married respondents, the odds of having hazardous alcohol intake were 1.57 times higher (OR: 1.57; 95% CI:1.00-2.48) among the individuals who were single. Like marital status, the age of the study population was also significantly associated with alcohol consumption at a hazardous level. It was observed that respondents of the oldest age category (≥50 years of age) had lower odds (OR: 0.55; 95% CI:0.32-0.93) of having alcohol intake at the hazardous level compared to the youngest category. Gender was also significantly associated with all the alcohol consumption behaviours analysed in the study. The odds were lower among females compared to male participants for total AUDIT score (OR: 0.27; 95% CI:0.22-0.33), problematic drinking (OR:0.30; 95% CI:0.16-0.60), hazardous alcohol intake (OR:0.18; 95% CI:0.12-0.26), alcohol dependence (OR:0.11; 95% CI:0.04-0.26), alcohol-related harms (OR:0.14; 95% CI:0.08-0.25) and evidence of past alcohol problems (OR:0.12; 95% CI:0.04-0.32).

Table 6. Negative binomial regression to reveal associations of listed socioeconomic variables with total AUDIT scores

Characteristics	Variable	AUDIT OR*(95% CI)
Ethnicity	HG	1.00
	HR	1.29 (0.97-1.73)
Education	Primary or less	1.00
	Secondary	1.09 (0.80-1.48)
	High school	0.98 (0.70-1.39)
	Tertiary education	1.13 (0.75-1.72)
Economic activity	Worker	1.00
	Pension, other allowances, student	1.02 (0.77-1.36)
	Unemployed	1.10 (0.82-1.48)
Marital status	Married	1.00
	Single	1.18 (0.91-1.52)
	Widow, divorced	1.03 (0.77-1.39)
Financial status	Good	1.00
	Satisfactory	1.11 (0.87-1.42)
	Bad	1.34 (0.98-1.83)
Age category (years)	20-34	1.00
	35-49	1.08 (0.83-1.42)
	50+	0.98 (0.73-1.31)
Gender	Male	1.00
	Female	**0.27 (0.22-0.33)**

*HG: Hungarian general population; HR: Hungarian Roma population. AUDIT: AUDIT total scores. OR: odds ratio, CI: confidence interval. *Negative binomial regression.*

Table 7. Binary logistic regression to reveal associations of listed socioeconomic variables with different alcohol consumption phenotypes

Characteristics	Variable	Problematic drinking OR** (95%CI)	Hazardous level OR** (95%CI)	Alcohol dependence OR** (95%CI)	Alcohol-related harm OR** (95%CI)	Past problems OR** (95%CI)
Ethnicity	HG	1.00	1.00	1.00	1.00	1.00
	HR	1.69 (0.71-4.04)	1.14 (0.68-1.90)	1.29 (0.46-3.59)	**3.47 (1.61-7.49)**	**4.09 (1.02-16.46)**
Education	Primary or less	1.00	1.00	1.00	1.00	1.00
	Secondary	1.22 (0.51-2.91)	1.10 (0.65-1.88)	0.74 (0.25-2.21)	0.96 (0.44-2.11)	1.00 (0.26-3.82)
	High school	0.70 (0.21-2.32)	0.83 (0.45-1.54)	0.57 (0.15-2.21)	1.17 (0.46-2.99)	1.31 (0.24-7.24)
	Tertiary education	nc	1.01 (0.48-2.13)	0.24 (0.03-2.24)	0.61(0.15-2.48)	nc
Economic activity	Worker	1.00	1.00	1.00	1.00	1.00
	Pension, other allowances, student	0.83 (0.31-2.22)	0.63 (0.35-1.14)	1.03 (0.33-3.21)	0.65 (0.26-1.62)	0.72 (0.17-2.98)
	Unemployed	0.97 (0.40-2.40)	1.28 (0.75-2.18)	2.46 (9.95-6.42)	1.28 (0.63-2.60)	1.54 (0.52-4.53)
Marital status	Married	1.00	1.00	1.00	1.00	1.00
	Single	1.69 (0.76-3.76)	**1.57 (1.00-2.48)**	1.26 (0.47-3.34)	1.61 (0.86-3.03)	0.95 (0.29-3.16)
	Widow, divorced	1.03 (0.40-2.68)	1.16 (0.67-2.03)	1.13 (0.39-3.33)	0.86 (0.36-2.10)	0.78 (0.20-2.95)
Financial status	Good	1.00	1.00	1.00	1.00	1.00
	Satisfactory	0.89 (0.37-2.16)	1.33 (0.84-2.12)	0.51 (0.20-1.30)	0.95 (0.49-1.85)	0.41 (0.13-1.32)
	Bad	1.68 (0.64-4.43)	1.38 (0.77-2.48)	0.87 (0.30-2.48)	1.24 (0.56-2.74)	1.32 (0.42-4.16)

Age category (years)	20-34	1.00	1.00	1.00	1.00	1.00
	35-49	1.73 (0.66-4.55)	0.73 (0.45-1.18)	1.88 (0.54-6.55)	0.85 (0.43-1.68)	3.94 (0.79-19.68)
	50+	1.70 (0.61-4.74)	**0.55 (0.32-0.93)**	3.13 (0.88-11.09)	0.86 (0.41-1.81)	4.06 (0.77-21.29)
Gender	Male	1.00	1.00	1.00	1.00	1.00
	Female	**0.30 (0.16-0.60)**	**0.18 (0.12-0.26)**	**0.11 (0.04-0.26)**	**0.14 (0.08-0.25)**	**0.12 (0.04-0.32)**

*HG: Hungarian general population; HR: Hungarian Roma population. AUDIT: AUDIT total scores. OR: odds ratio, CI: confidence interval. *Negative binomial regression. Problematic drinking: based on AUDIT scores, where cut-off: men≥8. women≥5. **Binary logistic regression. Alcohol consumption at the hazardous level: scores of 1 or more on question 2 or question 3. Alcohol dependence: points scored above 0 on questions 4-6. Alcohol-related harm: points scored on questions 7-10. Past problems: based on the final two questions of AUDIT. nc: not countable due to low strata-specific numbers. Bold indicates statistical significance.*

4.2.4 Decomposition analysis

The predicted ethnic-specific differences in alcohol-related harms were decomposed by using Blinder Oaxaca decomposition methods for non-linear models. The outcomes of this decomposition analysis are presented in **Table 8**. From the table, it is observed that the single marital status and gender explained -7.90% and -59.86% of the alcohol-related harm frequency gap, respectively, between HG and HR respondents. These findings indicate that equalization of differences explained by gender and marital status may be expected to reduce the gap of alcohol-related harms between the two study groups by about 8% and 60%, respectively. And the effect of endowment coefficient for marital status was statistically significant ($p<0.05$), while for gender the coefficient effect was highly significant ($p<0.01$). For other socioeconomic variables (education, economic activity, financial status, and age category) the coefficient's effect was not statistically significant ($p>0.05$), which implies that the protective or risk effect of these studied variables is as strong for HG as for HR subjects. Additionally, Roma ethnicity had a significant positive effect (13.32%) on alcohol-related harm frequency. In other words, if there was no ethnicity-specific effect, the outcome gap would be 89.24% lower.

The decomposition analysis could not be done for evidence of past alcohol problems due to low stratum-specific numbers (only 7 respondents identified as having past alcohol problems among HG participants).

Table 8. Multivariate decomposition of the group (HG, HR) difference in alcohol-related harm

		Endowments		Coefficients	
		Coef. (95%CI)	**Pct.**	**Coef. (95%CI)**	**Pct.**
Education	Primary or less	1.00			1.00
	Secondary	0.58% (-1.90%;3.05%)	8.18%	-0.22% (-3.56%;3.13%)	-3.07%
	High school	-3.82% (-11.33%;3.69%)	-54.26%	2.58% (-3.47%;8.64%)	36.07%
	Tertiary education	nc	nc	1.06% (-1.23%;3.34%)	14.99%
Economic activity	Worker	1.00			1.00
	Pensioner, student	-0.14% (-0.43%;0.15%)	-2.00	-0.96% (-3.45%;1.54%)	-13.59%
	Unemployed	1.43% (-0.75%;3.60%)	20.25%	0.00% (0.00%;0.00%)	0.00%
Marital status	Married	1.00			1.00
	Single	**-0.56% (-1.01%;-0.10%)**	**-7.90%***	2.57% (-0.19%;5.33%)	36.48%
	Widow, divorced	-0.02% (-0.08%;0.05%)	-0.23%	1.76% (-0.88%;4.40%)	24.98%
Financial status	Good	1.00			1.00
	Satisfactory	0.02% (-0.30%;0.34%)	0.28%	-0.35% 9-6.15%;5.45%)	-4.92%
	Bad	0.43% (-2.30%;3.17%)	6.17%	-0.45% (-1.90%;1.00%)	-6.37%
Age category (years)	20-34	1.00			1.00
	35-49	0.05% (-0.08%;0.17%)	68%	-0.07% (-4.50%;4.36%)	-0.99%
	50+	-0.04% (-0.44%;0.36%)	-0.53%	2.78% 9-2.05%;7.60%)	39.43%

Gender	Male	1.00			1.00
	Female	**-4.21% (-5.94%;-2.49%)**	**-59.86%****	3.98% (-1.75%;9.70%)	56.48%
Subtotal		-6.28% (-15.37%;2.80%)	-89.24%	**13.32% (3.00%;23.64%)**	**189.24%***
	Total	7.04% (3.00%; 11.08%)**			

*HG: Hungarian general population; HR: Hungarian Roma population. Endowments: due to differences in characteristics. Coefficients: due to difference in coefficients. *p<0.05, **p<0.01. Coef. (%) = coefficients multiplied by 100. CI: confidence interval; Pct. = expressed as a percentage. nc: not countable due to low strata-specific numbers. Bold indicates statistical significance*

4.3 Effect of selected taste preference genetic variants on alcohol intake

4.3.1 Genotype and allele frequencies of the selected polymorphisms

From **Table 9,** it is observed that none of the included SNPs deviated significantly ($p<0.001$) from HWE in either of the two study groups (HG and HR).

Table 9. Hardy-Weinberg equilibrium (HWE) test for included genetic polymorphisms among Hungarian general (HG) and Roma (HR) populations

Gene	SNP	Position	Consequence	HG (p-value of HWE)	HR (p-value of HWE)
TAS1R3	rs307355	chr1:1329774	2KB Upstream Variant	0.978	0.996
TAS2R38	rs713598	chr7:141973545	Missense Variant (Ala49Pro)	0.021	0.362
TAS2R19	rs10772420	chr12:11021677	Missense Variant (Arg299Cys)	0.892	0.667
CA6	rs2274333	chr1:8957145	Missense Variant (Ser90Gly)	0.052	0.949

SNP: single nucleotide polymorphism; HWE: Hardy-Weinberg equilibrium; The significance threshold for Hardy-Weinberg equilibrium was 0.001.

The distribution of genotype and allele frequencies of the selected SNPs in HG and HR samples are illustrated in **Table 10**. Genotype and allele frequencies did not differ significantly ($p<0.05$) between HG and HR subjects.

Table 10. Genotype and allele frequencies of selected SNPs in the Hungarian general (HG) and Hungarian Roma (HR) populations

Gene	SNP	Genotype	Genotype frequency		p-value	Allele	Allele Frequency		p-value
			HG % (n)	HR % (n)			HG % (n)	HR % (n)	
TAS1R3	rs307355	CC	81.2 (329)	82.7 (301)	0.864	C	0.90(730)	0.91(662)	0.588
		TC	17.8 (72)	16.5 (60)		T	0.10(80)	0.09(66)	
		TT	1.0 (4)	0.8 (3)					
TAS2R38	rs713598	CC	34.1 (136)	37.1 (134)	0.203	C	0.56(446)	0.60(433)	0.107
		GC	43.6 (174)	45.7 (165)		G	0.44(352)	0.40(289)	
		GG	22.3 (89)	17.2 (62)					
TAS2R19	rs10772420	AA	19.3 (78)	16.4 (59)	0.215	A	0.44(357)	0.40(287)	0.087
		AG	49.6 (201)	46.8 (169)		G	0.56(453)	0.60(435)	
		GG	31.1 (126)	36.8 (133)					
CA6	rs2274333	AA	50.0 (199)	50.3 (182)	0.490	A	0.69(553)	0.71(513)	0.418
		AG	38.9 (155)	41.1 (149)		G	0.31(249)	0.29(211)	
		GG	11.1 (44)	8.6 (31)					

SNP: Single Nucleotide Polymorphism
p-value was calculated by the $\chi 2$ test.

4.3.2 Association analysis of selected genetic polymorphisms with alcohol consumption phenotypes

Associations of included genetic polymorphisms with different alcohol consumption phenotypes in study populations are demonstrated in **Table 11** and **Table 12**. To evaluate alcohol consumption phenotypes, the first three questions (AUDIT 1, AUDIT 2, and AUDIT 3) of the AUDIT questionnaire were used, where AUDIT 1 and AUDIT 3 provide information about the frequency of drinking and frequency of heavy drinking, respectively. AUDIT 2 assesses the number of standard alcoholic drinks on a typical day. During the association analysis dominant and recessive models were used, where models were defined based on the minor allele frequency of the respective SNPs. Adjustments were made for the potential covariates such as age, gender, and marital status.

From **Table 11** it is articulated that except TAS2R38 rs713598, no other selected SNPs showed significant association with any of the alcohol consumption phenotypes of interest in both study groups. Among HG respondents TAS2R38 rs713598 showed a statistically significant association (p=0.028) with AUDIT 2, while in the case of HR participants this variant was significantly (p=0.048) associated with AUDIT 3. **Table 11** also reveals that none of the included SNPs depicted a significant association with AUDIT 1 in either of the study groups. Furthermore, from the recessive model analysis, it is observed that TAS2R38 rs713598 (CC or GC vs GG) was significantly associated with AUDIT 2 (Coef: -0.136; p=0.028) and AUDIT 3 (Coef: -0.170; p=0.049) among HG and HR respondents, respectively (**Table 12**).

Table 11. Association of selected genetic polymorphisms with alcohol consumption phenotypes in the Hungarian general (HG) and Roma (HR) populations

Phenotype (AUDIT question)	Gene, SNP	HG	HR	HG	HR
		Dominant genetic model p-value	Dominant genetic model p-value	Recessive genetic model p-value	Recessive genetic model p-value
AUDIT1	TAS1R3 rs307355	0.500	0.289	0.381	0.416
	TAS2R38 rs713598	0.872	0.205	0.359	0.075
	TAS2R19 rs10772420	0.277	0.862	0.260	0.408
	CA6 rs2274333	0.443	0.195	0.861	0.354
AUDIT2	TAS1R3 rs307355	0.808	0.544	0.637	0.353
	TAS2R38 rs713598	0.402	0.812	**0.028**	0.255
	TAS2R19 rs10772420	0.557	0.525	0.482	0.684
	CA6 rs2274333	0.787	0.494	0.243	0.264
AUDIT3	TAS1R3 rs307355	0.517	0.204	0.543	0.876
	TAS2R38 rs713598	0.523	0.499	0.994	**0.048**
	TAS2R19 rs10772420	0.246	0.693	0.108	0.770
	CA6 rs2274333	0.482	0.072	0.550	0.363

SNP: single nucleotide polymorphism; AUDIT: Alcohol Use Disorder Identification Test; AUDIT1: How often do you have a drink containing alcohol? (0p: never; 1p: monthly or less; 2p: 2 to 4 times a month; 3p: 2 to 3 times a week; 4p:4 or more times a week); AUDIT2: How many standard drinks containing alcohol do you have on a typical day when drinking? (0p: 1 or 2; 1p: 3 or 4; 2p: 5 or 6; 3p: 7 to 9; 4p:10 or more); AUDIT3: How often do you have six or more drinks on one occasion? (0p: Never; 1p: Less than monthly; 2p: Monthly; 3p: Weekly; 4p: Daily or almost daily); Covariates: Gender, age, marital status; Nominally significant p-values are presented in bold.

Table 12. Associations of selected genetic polymorphisms with alcohol consumption behaviours in the Hungarian general (HG) and Roma (HR) populations

Gene, SNP	Phenotype	Population	Genetic model	Reference	Genotype	Coef	p-value
TAS2R38 rs713598	AUDIT 2	HG	Recessive	CC or GC	GG	-0.136	0.028 0.224*
TAS2R38 rs713598	AUDIT 3	HR	Recessive	CC or GC	GG	-0.170	0.049 0.392*

SNP: Single nucleotide polymorphism; Models were defined based on minor alleles; AUDIT2: How many standard drinks containing alcohol do you have on a typical day when drinking? (0p: 1 or 2; 1p: 3 or 4; 2p: 5 or 6; 3p: 7 to 9; 4p:10 or more); AUDIT3: How often do you have six or more drinks on one occasion? (0p: Never; 1p: Less than monthly; 2p: Monthly; 3p: Weekly; 4p: Daily or almost daily); Coef: Regression coefficient; Covariates: age, gender, marital status; Only at least nominally significant results are presented. p-value after Bonferroni correction.*

4.4 Relationship of taste preference genetic variants with different drinking behaviours

4.4.1 Findings of literature search

Overall, 293 publications were identified in our search, among them 18 and 125 articles were derived from PubMed and Web of Science, respectively, while the rest (150) were obtained from ProQuest Central. Initially, 26 duplicated publications were removed, and then 229 articles that were unable to meet the inclusion criteria were excluded. The remaining 38 articles were preliminary selected for full-text assessment. After initial assessment 21 articles were eliminated, which led to the availability of the final 17 publications for extensive analysis. Details of the study selection process are described in **Figure 5.**

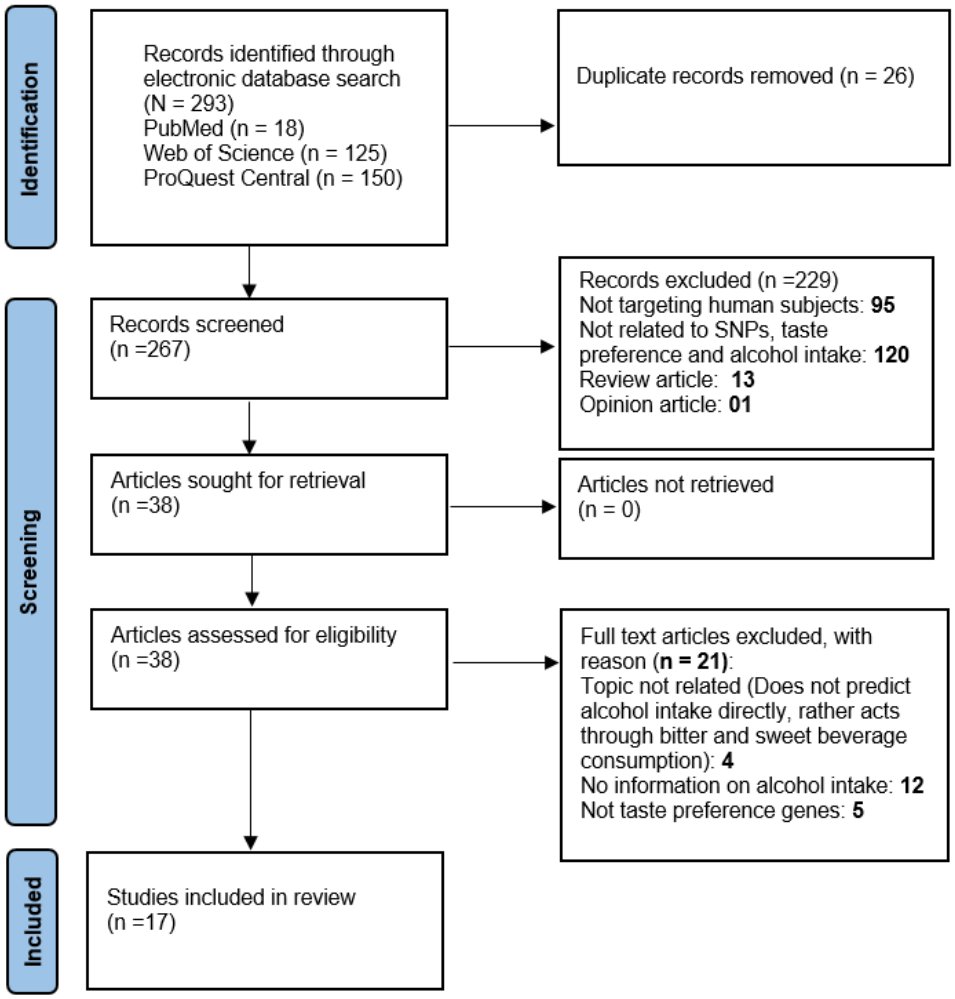

Figure 5 . PRISMA flowchart of the study selection process

(214)

4.4.2 Characteristics of the included genetic association studies

Among the 17 studies selected for the systematic review, 5 (29.4%) articles were of good quality and the rest 12 (70.6%) were rated as moderate quality.

A detailed description of the 17 genetic association studies selected for a systematic review is depicted in **Table 13.**

Table 13. Overview of the genetic association studies included in the systematic review

Publication (First author, Year)	Gene	SNP	Study population Characteristics	Phenotype assessment method	Findings
Beckett (2017) (159)	TAS2R38	rs713598	180 patients at Gosford Hospital, NSW, Australia, who also reported their alcohol consumption information. (51% women; average age 61.6 years).	Alcohol intake was assessed by FFQ, which was then converted to standard drinks (1 standard drink=10ml alcohol).	Individuals with the P allele consumed fewer standard drinks per day than those without P allele. No association with alcohol intake in beer and wine.
Hayes (2011) (84)	TAS2R16	rs846672	96 healthy adults from the University of Connecticut, mostly European ancestry who did not smoke more than 9 cigarettes per week. Average age 40.9 years and 76% were female.	Semiquantitative food frequency survey (standard drinks equaled 12, 5, and 1.5 oz, respectively).	Significant association between rs846672 and frequency as well as quantity of alcohol intake. Carriers of AA consumed alcoholic beverages twice as frequently and drank more compared to other genotypes. TAS2R38 AVI homozygotes consumed more total beverage

					compared to heterozygotes or PAV homozygotes. In comparison with PAV homozygotes, AVI homozygotes drank alcohol more frequently.
	TAS2R38	rs713598, rs1726866, rs10246939			
	TAS2R16	rs1308724			Samples with CC homozygotes of rs1308724 drank alcohol less frequently compared to heterozygotes and GG homozygotes.
Ramos-Lopez (2015) (178)	TAS2R38	rs713598, rs1726866, rs10246939	375 subjects from Mexico (182 women, men 193) without chronic sinus problems and any prescribed medication.	Medical history questionnaire and expressed as: g ethanol = volume mL x % alcohol x 0.8/100. Participants were categorised into drinkers (drank > 2 drinks/occasion) and non-drinkers (drank < 2	Higher frequency of AVV was found among drinkers compared to non-drinkers while AVV/AVV homozygote was significantly associated with alcohol consumption.

				drinks/occasion).	
Duffy (2004) (176)	TAS2R38	rs713598, rs1726866, rs10246939	84 healthy non-smoker adults without a high level of dietary restraint and uncommon haplotypes. Participants were of 21 to 59 years old (53 females and 31 males) and primarily of European ancestry.	Block Food Survey, version 98.1. For consumption frequency range from "never" to "every day" was used while glass, bottle, and serving size were applied for amount/time.	TAS2R38 AVI/AVI homozygotes consumed more alcohol than PAV/AVI or PAV/PAV.
Fu D (2019) (160)	TAS2R38	rs10246939, rs1726866, rs713598	519 subjects in California (52% women; ≥ 21 years of age) mostly European descent (86%).	Frequency of weekly alcohol intake was recorded as "<2 drinks, 2–7 drinks and >7 drinks".	TAS2R38 significantly associated with intake of alcohol while carriers of alleles allowing responsiveness towards bitterness in PTC drank more alcohol. No statistically significant association between CA6 rs2274333, GNAT3 rs1524600, TAS2R16 rs846664, TAS2R16 rs846672, TAS2R19 rs10772420, TAS2R20 rs12226920, TAS2R43 rs71443637, TAS2R46 rs2708377,
	CA6	rs2274333			
	GNAT3	rs1524600			
	TAS2R16 (84, 160, 161, 184)	rs846664, rs846672			
	TAS2R19	rs10772420			
	TAS2R20	rs12226920			
	TAS2R43	rs71443637			
	TAS2R46	rs2708377			
	TAS2R50	rs10772397			
	TAS2R60	rs4595035			

	TAS2R8	rs1548803			TAS2R50 rs10772397, TAS2R60 rs4595035, TAS2R8 rs1548803, TRPA1 rs11988795 and frequency of alcohol intake.
	TRPA1	rs11988795			
Hinrichs (2006) (215)	TAS2R16	rs846664, rs978739, rs860170, rs1204014	262 families (2310 subjects) while 298 subjects from 35 pedigrees of African American, and 8 pedigrees of mixed ancestry.	Assessment of alcohol dependence was conducted based on DSM-IIIR, DSM-IV, Feighner definite alcoholism, alcohol dependence, and ICD-10 criteria.	Carriers of an ancestral allele of rs846664 tend to higher risk of being alcohol dependent, regardless of ethnicity while no association was found between rs978739, rs86017,0, rs1204014 and alcohol dependence.
Wang (2007) (179)	TAS2R38	rs713598, rs1726866, rs10246939	2309 subjects were from 262 families, while 219 families from European descent.	SSAGA was used to assess alcohol dependence, the largest number of drinks in a 24-hour period, age at first intoxication and onset of regular drinking.	Common taster haplotype had association with lower mean of largest number of drinks in a 24-hour period. Compared with the other haplotypes, but no association with alcohol dependence.
	TAS2R16	rs846664			Significant association between rs846664 and lower risk of alcohol dependence as well as risk lower mean of largest

					number of drinks in a 24-hour period.
Choi (2016) (181)	TAS2R38	rs713598, rs1726866, rs10246939	1524 Korean subjects (men 832, women 748) without diabetes mellitus, severe systemic or mental disease, any other cancer within the past five years or advanced gastric cancer, missing genotype, no dietary data, total energy intake was < 500 kcal or > 5,000 kcal).	Self-administered questionnaire (FFQ) was applied to assess alcohol intake.	No association with daily intake of alcohol.
Choi (2017) (216)	TAS2R38	rs713598, rs1726866, rs10246939	1829 subjects (997 men, 832 women) having no systemic or mental disorder, diabetes mellitus, cancers within the past five years and visited the Center for Cancer Prevention and Detection.	Questionnaire. Total daily alcohol consumption was estimated from the frequency of drinking, amount of alcohol consumed (ml) and the ethanol content drinks consumed.	Carriers of AVI haplotype of TAS2R38 were less likely to be a drinker while individuals with TT of TAS2R5 rs2227264 drank more alcohol compared to others. Significant association between TAS1R3 rs307355 CT and heavy
	TAS2R5	rs2227264			
	TAS2R4	rs2233998			
	TAS1R3	rs307355			
	TAS1R2	rs35874116			
	TAS2R50	rs1376251			
	TAS2R20	rs12226920			

				Drinkers were classified into heavy drinkers (>30 g/day), and light drinkers (<30 g/day)	drinking status. TAS2R4 rs2233998 and TAS2R5 rs2227264 linked with rice wine drinking while TAS1R2 rs35874116 exhibited significant association with wine consumption. Association between TAS2R50 rs1376251 and intake of rice wine and spirits. TAS2R20 rs12226920 was associated with spirits consumption.
Keller (2013) (162)	TAS2R38	rs713598, rs1726866, rs10246939	1007 participants from Eastern Germany (405 men, 602 women; average age 48) without type 2 diabetes.	Questionnaire.	Among the carriers of a minimum of one PAV haplotype vs. AVI/AVI homozygous, PAV groups showed lower weekly alcohol consumption.
Vinuthalakshmi (2019) (177)	TAS2R38	rs713598, rs1726866, rs10246939	296 healthy subjects of Koragas primitive of India who were free from sinus problems, food	Questionnaire.	AVI/AVI haplotype was significantly associated with alcoholics.

			allergies and not taking any medication.		
Dotson (2012) (161)	TAS2R38	rs713598 rs10246939 rs1726866	173 cancer patients (126 males and 47 females; average age 60.7) from clinics of University of Florida	First three questions of the AUDIT questionnaire: "How often do you have a drink containing alcohol?"; "How many drinks containing alcohol do you have on a typical day when you are drinking?"; "How often do you have six or more drinks on one occasion?	TAS2R38 associated with the first AUDIT question. Significant association exists between the C allele of rs713598 and decreased alcohol intake. TAS2R13 rs1015443 significantly associated with 2nd and 3rd AUDIT questions. Participants homozygous for the major allele (CC carriers) consumed alcoholic beverages less frequently compared to heterozygotes and minor allele homozygous. No association was found for the following variants: rs846672, TAS2R3 rs765007, TAS2R4 rs2234001, TAS2R5 rs2234012, TAS2R38 rs10246939, TAS2R38
	TAS2R13	rs1015443			
	TAS2R3	rs765007			
	TAS2R4	rs2234001			
	TAS2R5	rs2234012			
	TAS2R7	rs619381			
	TAS2R8	rs1548803			
	TAS2R10	rs10845219			
	TAS2R14	rs7138535 rs1376251			
	TAS2R19	rs10772420			
	TAS2R20	rs10845281			
	TAS2R39	rs4726600			
	TAS2R40	rs10260248			
	TAS2R41	rs1404635			
	TAS2R10 (161)	rs4763216			
	PRH1-	rs11612527			

	TAS2R14				rs1726866, TAS2R39 rs4726600, TAS2R40 rs10260248, N/A rs534126, EPHA1-AS1 rs12666496, TAS2R41 rs1404635, TAS2R7 rs619381, TAS2R8 rs1548803, TAS2R10 rs10845219, LOC107984459 rs4763216, TAS2R14 rs7138535, TAS2R14 rs1376251, TAS2R20 rs10845281, TAS2R19 rs10772420, PRH1-TAS2R14 rs11612527, PRR4 rs1047699, PRR4 rs1063193, PRH1 rs10492098
	EPHA1-AS1	rs12666496			
	PRH1	rs10492098			
	PRR4	rs1047699 rs1063193			
	TAS2R16 (84, 160, 161, 184)	rs1308724 rs846672			
	TAS2R40 (161, 217)	rs534126			

Choi (2019) (183)	TAS2R38	rs713598, rs1726866, rs10246939	3567 respondents of 40-89 years of age from Korea (men: 1338; women: 2229) who had no missing genotype and free from hypertension, hyperlipidemia, or diabetes mellitus, implausible total energy intake (5000 kcal/day).	Structured questionnaire. Subjects were categorized as never, past, or current drinkers. Daily alcohol intake was estimated based on types of alcoholic drinks, frequency of alcohol consumption, size of glass, and percentage of alcohol.	Not linked with alcohol consumption.
Choi (2017) (180)	TAS2R38	rs713598, rs1726866, rs10246939	2042 participants from Korea (men: 1390, women: 652, average 56.1 years).	Structured questionnaire.	Either individual or combined effect of TAS2R38 and CA6 genetic variants had no influence on alcohol intake.
	CA6	rs2274333			
Timpson (2005) (182)	TAS2R38	rs713598, rs1726866, rs10246939	3383 British women 60–79 years of age and had DNA available.	Questionnaire. Frequency of consumption was classified as consumption of alcohol	TAS2R38 PAV and AVI haplotypes not associated with the intake of alcohol.

				at any frequency and no alcohol consumption.	
Schembre (2013) (184)	TAS2R38	rs713598, rs1726866, rs10246939	914 colorectal adenoma cases (men 60.2%) and 1188 controls (men 62.7%) average age: 60.6) with available DNA.	Food Frequency Questionnaire.	No associations of theTAS2R38 PAV/PAV, TAS2R50 rs1376251 and TAS2R16 rs846672 with daily consumption of alcohol.
	TAS2R50	rs1376251			
	TAS2R16	rs846672			
Ong (2018) (203)	TAS2R38	rs1726866	438 870 subjects of England, Wales, and Scotland (men 45.8%; average age: 56.5).	Six-point frequency scale ranging from never to daily. The cut-off for light/non-drinkers (no consumption) and heavy drinkers (> 3-4 times weekly) are set at 20th and 80th percentile of the consumption distribution respectively.	TAS2R38 rs1726866 exhibited inverse association with alcohol intake while TAS2R19 rs10772420 and PRH1-TAS2R14 rs2597979 showed an association.
	TAS2R19	rs10772420			
	PRH1-TAS2R14	rs2597979			

AUDIT: Alcohol Use Disorders Identification Test; *FFQ:* food frequency questionnaire; ***SSAGA:*** Semi-Structured Assessment for the Genetics of Alcoholism.

4.4.3 Effect of taste preference genetic variants on drinking behaviours

The systematic review focused on 43 single nucleotide polymorphisms (SNPs) of 27 different taste preference-related genes. The relationships between different dimensions of alcohol consumption behaviour and TAS2R38 rs713598 (n=10), rs1726866 (n=9), rs10246939 (n=8) followed by TAS2R16 rs846672 (n=4); TAS2R16 rs1308724 (n=3); TAS2R50 rs1376251 (n=3); TAS2R16 rs846664 (n=3); TAS2R19 rs10772420 (n=3); TAS2R20 rs12226920 (n=2); TAS2R8 rs1548803 (n=2); and CA6 (Carbonic Anhydrase 6) rs2274333 (n=2) were analysed by multiple studies. The effects of other included polymorphisms on alcohol intake patterns were examined only by single studies.

Effects of those SNPs, which were included in our genetic association study on various aspects of drinking behaviours are illustrated in **Table 14**. Effects of other SNPs are illustrated in supplementary Table S4 titled Summary of impact of taste preference genetic SNPs on different alcohol consumption behaviors.

Table 14. Summary of the impact of taste preference genetic SNPs included in our genetic association study on different alcohol consumption behaviors

Gene	SNP	Association	No association
TAS2R38	rs713598, rs1726866, rs10246939	AVI/AVI carriers consumed significantly higher alcohol and alcoholic beverages than other genotypes (84). Drinkers had a higher frequency of AVV homozygotes and demonstrated a significant association with a higher intake of alcohol than carriers of heterozygotes and PAI homozygotes (178). Carriers of AVI/AVI drank higher alcoholic beverages compared to other genotypes (176). Significantly related to the common taster haplotype (179). Dominant model analyses established that individuals with the AVI haplotype were less likely to be drinkers (216). AVI/AVI positively associated with alcoholism (177). Weekly reduce alcohol consumption was found with PAV haplotype compared to AVI/AVI (162). Significantly associated with alcohol consumption frequency (160).	PAV/PAV, PAV/AVI and AVI/AVI not related to variations in daily alcohol intake (181). No relationship between beer and alcohol intake (216). Not linked to drinker status of alcohol (183). Not linked to daily alcohol intake (180). Not associated with drinker status (182). Not linked with frequency and amount of alcohol intake (184).
TAS2R38	rs713598	P allele carriers drank fewer standard drinks daily than non-carriers (216).	Not associated with the consumption of beer and wine (216).

		Significantly associated with the frequency of alcohol intake (160).	Not associated with 2nd and 3rd AUDIT questions (161).
		Participants with the C allele revealed a strong significant association with decreased alcohol intake (161).	Not related with the weekly intake of alcohol (162).
TAS1R3	rs307355	Compared to wild types, individuals of heterozygous genotype tend to be more heavy drinkers. Demonstrated minimal association with the consumption of Soju (216).	Not associated with the intake of beer, wine, and spirit (216).
TAS2R19	rs10772420		Not associated with alcohol intake (160). Not associated with the first 3 questions of AUDIT questionnaire (161). Not associated with drinking behavior and drinker status (203).
CA6	rs2274333		Not related to daily alcohol intake (180). Not associated with alcohol intake frequency (160).

Italic gene names refer to the nearest genes as used by cited authors; AUDIT: Alcohol Use Disorder Identification Test

DISCUSSION

Globally, harmful alcohol intake is considered a major public health problem. Besides individuals and their families, alcohol addiction also affects the whole community altogether. Harmful use of alcohol is linked to the reduction of production, increase in accidents, violence, and injuries, which ultimately distress the health, social and economic conditions of the community as a whole (218). Globally, the WHO European Region is recognised as the area of the highest alcohol intake together with highest percentage of poor health and premature death attributable to alcohol intake (7).

In recent times, ethnicity-specific health inequalities are given a major emphasis for public health research, though not all countries of the European Region have comprehensive data regarding various aspects of drinking behaviours stratified by factors other than age and gender. The occurrence of alcohol-linked poor health and premature death was unequally distributed between countries and within counties among different ethnic groups (219). In Hungary, consumption of alcohol has declined in recent years, and it was estimated to decline in the future as well in the pre-pandemic era. Though the pre-pandemic decrease in alcohol consumption levels, the prevalence of alcohol use disorders and dependence in Hungary was one of the highest in the world and among the countries of OECD areas (7, 8), which presumably will be influenced by the COVID-19 pandemic influence on alcohol consumption levels. In Europe, numerous studies were conducted to compare patterns of alcohol consumption behaviour between Roma and majority populations. Findings of some relevant studies demonstrated that in the case of binge drinking the rate was higher in Roma females than non-Roma (46), Roma mothers had 11.7 times higher risk of alcohol intake than non–Roma mothers (60), compared to non-Roma, Roma families spent more on alcohol and tobacco (49), regular excessive alcohol intake was 2–6 times higher among Roma social worker than non-Roma (51), Roma women have had significantly higher consumption of alcohol compared to non-Roma women (52), young Roma men are likely to drink more alcohol compared to other young men, but among women, the frequency of alcohol consumption was less among Roma than in the general population (53). A study conducted in Hungary depicted that though the numbers of abstainers were higher among Roma than the mainstream general population (59), in the case of drinking behaviours of alcohol non-Roma children and adolescents were in much more favourable condition than Roma adolescents (55-57). The only study, which was conducted in Slovenia, where the AUDIT questionnaire

was applied to evaluate drinking patterns illustrated that a higher and lower percentage of Roma participants were abstainers and non-hazardous drinkers, respectively (45).

The findings of our study demonstrated that 4.25% and 25% of HG participants had problematic drinking (total AUDIT score ≥8 for men and ≥5 for women) and hazardous drinking, respectively, and the percentage was higher among males compared to females for both drinking patterns. A study using a similar methodology was conducted in Australia by O'Brien to examine hazardous alcohol intake among respondents of 14 years or above, where the AUDIT questionnaire was used to assess drinking at hazardous levels (total AUDIT score ≥8). Results of the study indicated that in 2016 around 29.60% of the respondents, irrespective of age and gender had drinking patterns at hazardous levels, while for men it was 14.99%. (220). In our study, only 7.39% of HG males had problematic drinking (total AUDIT score ≥8). In addition, the latest available data regarding alcohol intake exhibited that among the population of 15 years and above recorded alcohol intake was higher in Hungary than in Australia (8). This lower percentage of HG men with problematic drinking may have resulted from underreporting of drinking behaviours, as unhealthy alcohol drinking is a sensitive issue and in our study information on problematic drinking was collected by the practice nurses. The study of Australia also demonstrated that a higher percentage of males were identified as positive for hazardous drinking compared to females (220), which is consistent with our study findings depicting that male respondents had higher odds of having alcohol intake at hazardous levels. Another study was conducted in Sweden to compare alcohol consumption between 1997 and 2018, where the AUDIT questionnaire was applied to evaluate harmful alcohol habits and alcohol-related problems. The results of this research illustrated that males were rather characterized by higher drinking than females (221).

The present study also represented that 81% of HG participants never reported consuming 6 or more alcoholic drinks on one occasion, while 13.90% of them had 6 or more alcoholic drinks on one occasion less than monthly. Similar Hungarian research called "Population National Survey on Addiction Problems in Hungary (NSAPH 2015)" provided comparable information with our study regarding various aspects of alcohol intake of the HG population. This study was conducted among 2274 HG participants within the age group of 18-64 years, where the AUDIT screening tool was used to collect information regarding drinking frequency and quantity, heavy drinking, drunkenness, family history of regular alcohol use, as well as outpatient- inpatient care owing to alcohol use. Research findings indicated that

around 79% of participants never experienced ≥ 6 alcoholic drinks on one occasion, and 14.6% respondents consumed alcohol less than monthly (222), which is consistent with our study findings. Among HG participants of our study, higher abstinence rates may be due to higher health awareness of the study participants. During the study, data of HG respondents was collected in the GP's offices, thus, for collection of data an additional visit was required to GPs, which may have indicated high levels of consciousness, compliance, and understanding of various health-related issues. The contrary to NSAPH, our study questionnaire was administered by practice nurses in a face-to-face way, therefore we should note that certain aspects of alcohol intake could have been considered as a potentially sensitive issue by patients attending the GPs' offices. Furthermore, the present study was conducted in two counties of Northeast Hungary, which counties are a part of the Northern Great Plain, where abstinent rates were the highest in the country (223). Furthermore, NSAPH gathered information nationwide on alcohol consumption for three years before our research was conducted. Another European study was conducted within the framework of the GENACIS project among nine countries such as Switzerland, Spain, the U.K. Sweden, Finland, the Netherlands, the Czech Republic, Iceland, and Hungary applying the AUDIT tool for describing various aspects of alcohol intake. The study results showed that monthly or more often consumption of ≥ 6 drinks among men and women of Hungary were 35.2% and 9.2%, respectively, which were higher compared to or present study (HG men: 10.56%; HG women: 0.87%) (224).

It was also observed from our study that 12.75% of HG participants had 2 to 3 times alcoholic drinks in a week or more, while for HG men and HG women, it was 24.58% and 3.49%, respectively. Findings of the European study conducted in nine European countries illustrated that consuming 2 or more drinks a week was highest among males (79.4%) and females (55.6%) in Switzerland, while among Hungarian males and females, the percentages were 43.2% and 11.2%, respectively, which are much higher than the findings of the current study (224). The results of this study were hard to compare with our study findings as age category, time and process of interviews as well as analysis of alcohol-related harms were different between the studies. During this European study data collection was carried out more than one and half decades ago (between 2000-2001) when alcohol intake was higher in Hungary and continued to remain at higher levels till 2006. After 2006 a decreasing trend in alcohol intake was observed among the Hungarian population (225).

The current study also aimed to compare the alcohol consumption patterns of HG and HR participants. From the study findings, it is observed that there was a significant difference in the frequency of having alcoholic drinks between the respondents of HG and HR, even when analysing the two sexes separately. In comparison with HG, a lower proportion of HR participants had alcoholic drinks 2 to 4 times a month and 2 to 3 times a week or more, while a higher percentage of HR individuals had alcoholic drinks monthly or less compared to HG participants. Additionally, a higher percentage of HR males had alcoholic drinks monthly or less than HG males. On the contrary, compared to HR females, a higher proportion of HG females drank alcohol monthly 2-4 times. Findings obtained from one study of Slovakia revealed Roma women were identified to report less frequent recent drinking than non-Roma women (46). Additionally, Sudzinová et al. stated that Roma patients of coronary angiography consume alcohol less frequently than non-Roma patients undergoing the same procedure, though after adjustment for several covariates such as educational level, gender and age these differences became statistically insignificant (226). A study conducted in Slovenia among Roma and non-Roma participants of 18-65 years of age demonstrated that for abstainers (Roma: 39.0%; non-Roma:16.0%) and non-hazardous drinkers (Roma: 38.0 %; non-Roma: 64.0 %), there were significant differences between participants of Roma and non-Roma, where ethnicity was identified to significantly influence drinking behaviour (45). Ostrihoňová and Bérešová illustrated that among Roma respondents, alcohol consumption frequency was significantly lower than in the majority population and this finding is harmonized with our study findings (227).

The present study also depicted that the number of standard alcoholic drinks consumed varied significantly between females of HG and HR, where 7.0% and 12.1 % of the HG females and HR females consumed 3 to 4 standard alcoholic drinks, respectively. Furthermore, in the case of 5 or more drinks, it was 0.4% for HG females and 4.3% for HR females. For 6 or more alcoholic drinks on one occasion there was no significant difference between the participants of the study groups not even after stratification by gender. Similar findings were obtained from another study in Slovakia stating that there was no significant difference in alcohol drinking (the previous day of data collection) of ≥1 drink and ≥6 drinks ever or once a month between Roma and non-Roma men. While Roma women were identified to report less frequent recent drinking as well as binge alcohol drinking of 6 or more drinks on a single occasion compared to females of the mainstream population (46). Contrasting results derived

from the study of the Czech Republic represented that among Roma prevalence of binge drinking was relatively high, where 36.0% and 20.4% of the respondents drank excessively at least once a month and once a week, respectively (51). Additionally, findings from other studies on minority populations illustrated that the majority of them were either abstinent or lower-level drinkers; but those who were drinkers, had a greater risk of harmful alcohol intake (228, 229).

Our study also demonstrated that ethnicity had a statistically significant association with the experience of alcohol-related harms and evidence of past problems related to alcohol drinking. The odds of having both harms and past problems were higher for Roma respondents. Results from another study demonstrated that among different U.S. ethnic groups, whites and Asians had lower alcohol-related harm than Native Americans, Hispanics, and blacks (230). It is also observed from another study that in comparison with white, African American, and Hispanic drinkers reported significantly higher social consequences attributable to drinking and the racial gap in alcohol-related problems was the highest among drinkers with little or no heavy drinking. The study also presented that these ethnic-specific differences in alcohol- related problems may be due to racial or ethnic stigma (23). Additionally, another European study also demonstrated that alcohol-related problems varied differentially with different socioeconomic statuses, where higher harms existed among individuals of low socioeconomic status even though accompanied by lower alcohol consumption (219).

Results of the current study indicated that even though frequency of alcohol consumption was lower among Roma participants, they suffered from more alcohol-related harms and evidence of past problems, which findings are in line with the above-mentioned ethnic studies conducted in the US. Similar findings were also obtained by Zelko et al., where the AUDIT screening tool was used to assess various alcohol consumption patterns of the study participants (45). Harms linked to alcohol intake are also distributed disproportionally among ethnic groups, where individuals from underprivileged areas and ethnic minorities experienced more harm compared to the upper-class majority population even from equal amounts of alcohol consumption. This difference may be due to variations in socioeconomic factors (24), variances in cultural attitudes towards alcohol (24, 231), problems with access to health care facilities dealing with alcohol problems, poor knowledge of adverse manifestations of harmful alcohol intake, shame, and stigma resulting from alcohol-related problems as well as biological and genetic distinctions of alcohol metabolism (24).

It is also articulated from the present study that gender had a significant association with all the alcohol consumption behaviours considered during this study. The odds were lower among females compared to male participants for total AUDIT score, problematic drinking, hazardous alcohol intake, alcohol dependence, alcohol-related harms, and evidence of past alcohol problems. One explanation for these lower alcohol intake and subsequent alcohol problems by females may be gender-specific differences in alcohol metabolism. As females have lower body weight than males, they have less body water to dissolve alcohol which results in more concentrated alcohol in women's bodies compared to men. Additionally, women possess fifty percent less ADH than men and thus more unmetabolized alcohol is passed into their bloodstream, which ultimately decreases alcohol requirement of the females than men to produce equal alcohol concentration in the blood. Besides, women from different ethnic communities have to follow specific cultural norms and practices which may have an influence on their drinking habits (156). Results of the study conducted in 16 European countries revealed that males had significantly higher alcohol intake at hazardous levels compared to females which is in line with our study findings (232). Another study in the United States also showed that in comparison with women, men drank alcohol more often and more heavily (233).

Our study also illustrated that marital status showed a significant association with alcohol intake at hazardous level. The odds of having hazardous alcohol intake were 1.57 times (OR: 1.57; 95% CI:1.00-2.48) and 1.16 times (OR: 1.16; 95% CI:0.67-2.03) higher among single individuals compared to those who were married and widow, divorced, respectively. Opposite findings derived from another study revealed that for both males and females living with a partner is linked with higher and riskier alcohol intake, while participants who lived alone were more likely to be abstainers (234). Furthermore, Power et.al. demonstrated that divorced and married respondents had the highest and the lowest levels of heavy drinking (women: >20 units/week; men: >35 units/week; 1 unit equals 8 grams of alcohol), respectively, while single participants could be characterized by intermediate heavy drinking (235). Another study conducted in Australia depicted that unmarried, divorced/separated respondents drank more alcohol at levels likely to increase risk of long-term and short-term harm than respondents who were married (236). These diverse associations of alcohol consumption patterns may be due to the quality of the marriage/relationship life. Living in a well-functioning relationship contributes to more favourable mental and physical health and happiness (237-240), which

situation changes negatively if losing the partner. On the other hand, alcohol consumption could be a certain “coping strategy” for some individuals living in problematic relationships, and in these cases, alcohol consumption levels may decrease after divorce (241).

The present study also demonstrated that age category had a statistically significant association with hazardous level alcohol intake, where the odds of having hazardous alcohol intake was (237) lower among the respondents of the oldest age group. Similar findings were obtained from another two studies, where higher age groups had a lower risk of hazardous alcohol consumption (220) and lower age group respondents scored higher in the AUDIT test (221). Life experience, prevalence of long-term illness, and overall health condition may be the most important factors for lower hazardous alcohol consumption among the oldest age group respondents of our study. Additionally, an increase in social responsibility with increasing age and a decrease in the ability to metabolize alcohol may also contribute to lower intake at hazardous levels. One study illustrated that among Hungarian respondents of both males and females alcohol intake is influenced by chronic disease conditions (242). Another research conducted in the U.S. demonstrated that the majority of the participants of ≥ 65 years of age with chronic illness avoid alcohol (243). Our study finding is also justified by some earlier European studies presenting that among individuals, heavy drinking declines with increasing age and social responsibilities (244-246).

The decomposition analysis of the present study also demonstrated that in the case of alcohol-related harms gender and differences in marital status acted more intensively among respondents of Roma compared to Hungarian general participants. Single marital status and female gender were associated with differences in alcohol-related harm. After equalization of these differences, the alcohol-related harm frequency gaps could be expected to be reduced by 8% and 60% for HG and HR participants, respectively. These gaps in alcohol-related harms may be due to the cultural factors of Roma respondents because in Roma communities single status and being a female are considered as inferior status (43, 247).

Additionally, taste receptor proteins mediating the oral sensation of taste may also mediate alcohol intake. Differences in receptor function for bitter, sweet, salty, sour, umami, and fat tastes could be the basis for inter-individual variations in taste perception (193). Changes in the functional properties of these receptor proteins can result from alterations in their genomic sequences, which consequently leads to differences in responsiveness and preference for a

specific taste. Thus, genetic variability in the taste perception mechanism might contribute to differences in alcohol consumption (86). People with increased sensitivity towards bitter-tasting compounds like PTC and PROP have been found to drink less alcohol compared to those with less sensitivity (77, 176). Individuals with intense responsiveness (supertaster) towards PROP (248), also experience more irritation (249, 250) and higher bitterness from ethanol compared to less sensitive persons (supertaster) (250) which ultimately decreases alcohol consumption among supertasters (251). Supertasting towards PROP is mediated by the number of fungiform papillae tongue (252). There is a positive association between PROP bitterness and a number of fungiform papillae (253), where non-tasters have fewer taste papillae on the anterior tongue compared to supertasters and thus experience less bitterness and more sweetness sensations from alcohol (176). Additionally, allelic variation of the TAS2R38 bitter-tasting gene, which determines the presence of a functional receptor may also influence the responsiveness towards bitter-tasting compounds (252). Supertasters of sweet drink more alcohol as sweetness elicited by ethanol was found to stimulate neural fibres sensitive to sweetness in gustatory nerves (254). Furthermore, central mechanisms like opioidergic, serotonergic, and dopaminergic systems activated by ethanol and sweet solutions, potentially contribute to the reward linked to alcohol intake consistent with that of sugar intake (254, 255).

Results of our study presented that TAS1R3 rs307355, TAS2R19 rs10772420, and CA6 rs2274333 depicted no statistically significant relationships with any phenotypes of our interest. The T alleles of TAS1R3 rs307355 were previously found to decrease sucrose taste sensitivity (121). This polymorphism may introduce variation in the perception of sweet and alcohol (216) via alteration of gene transcription through a substitution of cytosine to thymine (158). Though this finding is in line with our study results, since no other research demonstrated associations with alcohol intake. TAS2R19 rs10772420, which was intensively investigated by the literature in relation to bitter taste phenotypes, exhibited no association with alcohol intake (160) and heavy drinker status (203) in previous research. The A allele of TAS2R19 rs10772420 was found to be linked to the more intense perception of quinine and grapefruit juice (91), which may be resulted from strong linkage disequilibrium (LD) between two polymorphisms such as TAS2R19 and TAS2R31 (256). In our study, we also did not find any association between TAS2R19 rs10772420 and the first three questions of the AUDIT questionnaire. Moreover, results of other studies postulated that individuals with A alleles of CA6 rs2274333 were linked to PROP super tasting (186, 188, 190, 204). The CA6 rs2274333

was not linked to frequency of alcohol intake (97) and daily intake of alcohol (180) in other studies which corresponds with our findings.

It is articulated from our study that TAS2R38 rs713598 showed a significant association with AUDIT 2 (typical quantity of alcohol drinking) and AUDIT 3 (frequency of heavy drinking) among respondents of HG and HR, respectively. In the haplotypes of TAS2R38 (defined by rs713598, rs1726866, rs10246939) rs713598 (P/A) is placed in the first location, while rs1726866 (A/V) and rs1024693 (V/I) are located in second and third positions, respectively (225). The dominant haplotype of these three SNPs (PAV; proline–alanine–valine) indicates the taster phenotype and AVI (alanine-valine-isoleucine) homozygotes characterize the non-taster phenotype, while heterozygotes are entitled by intermediary responsiveness towards PROP and PTC (121). For signal transduction of bitter taste modality, rs713598 and rs1726866 retain the highest and the weakest effects, respectively, while rs10246939 depicted no quantifiable impact (226).

Contradictory results were derived from other relevant studies. Some research established that carriers of taster genotypes drank less alcohol, though these studies varied extensively in study participants and way of phenotype evaluation, while numerous studies were unable to report the relationship between these SNPs and alcohol consumption behaviours. On the contrary, another study, where the first three AUDIT questions were used to assess alcohol intake demonstrated that the major "C" allele was linked to decreased alcohol intake among head and neck cancer participants (161). The minor allele-based recessive model analysis in our study indicated that the non-taster GG genotype was negatively correlated with number of standard drinks consumed and the frequency of having six or more drinks per occasion among HG and HR participants, respectively. Similar to our findings, another study presented that tasters consumed more alcohol. This study also proposed that other factors may be involved in stimulating alcohol intake among individuals with increased responsiveness to bitterness sensitivity (160), such as the consumption of wine, which may be linked to an enhanced perception of PROP bitterness (257, 258). Analogous factors may explain the findings of the present study.

The abovementioned results exhibited ethnicity-specific differences in alcohol intake in some respects. TAS2R38 rs713598 was significantly associated with the number of standard drinks consumed and having six or more drinks on one occasion among HG and HR participants,

respectively. This difference in alcohol consumption behaviours between the two study groups could be due to differences in the influence of taste perception and preference on alcohol consumption. Additionally, the taste profile of consumed alcohol may vary among participants of two study populations. Furthermore, ethnic-specific findings were also found in some genetic association studies (259-268), even when comprising taste preference genetic variants (269), which may be resulted from variations in ethnic-specific LD (263, 270). Thus, the impact of investigated genetic polymorphisms might be weakened or masked by other not yet studied genes being responsible for the occurrence of phenotypes of interest (261). It may also be assumed that certain alleles act differently in certain populations (265, 270) and research findings also suggest that various alcohol consumption-related phenotypes (frequency and quantity measures, AUD) encompass different genetic backgrounds.

Several limitations need to be considered during the interpretation of the study results. There is a high possibility of underreporting of alcohol intake, which is demonstrated by other studies (271) even with the standard structured AUDIT questionnaire (272). Moreover, the effectiveness of the AUDIT screening tool may vary between ethnic groups and minorities (150). Results of other studies indicated that compared to mainstream populations, Roma respondents may tend to please the field investigators, which may affect the quality of collected information (159, 160, 216). Additionally, during our study, AUDIT questions were interviewed in a face-to-face manner and Roma participants are already subject to negative stereotypes, which may manipulate their responses on alcohol in a way that will not be considered negatively by others. Furthermore, the AUDIT questionnaire provides no information on lifelong alcohol use and associated problems, as well as fundamental causes of abstinence (161).

During the present study the Roma population was recruited only from two counties of North-East Hungary, where the majority of Roma individuals inhabit, thus included Roma participants did not represent the whole country's Roma population. Besides, some Roma individuals, who were integrated into the Hungarian population may not be willing to declare themselves as Roma (273); consequently, the Hungarian reference sample may have also comprised some Roma individuals. It is also important to mention that the proportion of female participants was higher among HR compared to HG which is in line with the previous survey and study conducted on segregated Roma settlements in Hungary (274) and in Slovakia, respectively (275). The potential reason for the higher proportion of HR female

participants is that in our study data was collected during the daytime when the majority of the households' women were at home and males travelled for public work. From 2010 to 2015 the Hungarian government expanded the budget for public works in all municipalities. These works were particularly pertinent for the villages, where the majority of the Roma communities are settled and most of the workers involved in the program are males from Roma communities (276). Furthermore, the present study did not comprise individuals aged ≥ 65 years as from previous Roma studies it was suggested that people ≥ 65 years of age represent only 3–4% of the total population (58, 274, 277), which is low to derive reliable inference for this stratum of the population.

To our knowledge, this is the first study that analysed factors potentially influencing several aspects of alcohol consumption behaviours of HG and HR populations applying the AUDIT questionnaire. Although the systematic review on taste preference genetic polymorphisms influencing alcohol drinking behaviours indicated that TAS2R38 rs10246939, rs1726866, rs713598 were mostly investigated, additional research is still recommended to elucidate susceptible and protective genetic factors for alcohol consumption-related phenotypes due to inconclusive findings. Understanding the ethnic-specific differences of genetic and other factors expected to impact alcohol consumption behaviours may facilitate the development of efficient policy and related interventions to address harmful alcohol use.

SUMMARY

Background: Unhealthy alcohol use is considered a significant public health problem globally, while the burden of mortality and disability-related to alcohol intake varies disproportionately between certain populations and ethnic minority groups. Consumption of alcohol is a complex human trait, which is influenced by a wide variety of environmental factors and numerous genetic variants including taste preference genetic polymorphisms.

Objective: Our study aimed to characterize and compare alcohol consumption behaviours of HG and HR participants as well as to evaluate the impact of potential influencing factors on various alcohol consumption patterns. We also aimed to synthetize evidence of the effect of taste preference-related genetic variants on various drinking behaviours.

Methods: 410 HG and 387 HR respondents of 20-64 years of age were included in our study and AUDIT questionnaire was used to assess alcohol consumption patterns. Univariate and multivariate logistic regression analysis were performed to elucidate the associations between various socioeconomic variables and different alcohol consumption phenotypes. To identify the taste preference-related genetic polymorphisms associated with various alcohol consumption behaviours, a systematic review was prepared. Based on this review, four single nucleotide polymorphisms (SNPs), TAS1R3 rs307355, TAS2R38 rs713598, TAS2R19 rs10772420 and CA6 rs2274333 linked with bitter and sweet taste preferences, were selected for further analysis.

Results: Compared to HG, Roma participants experienced more alcohol related harms and evidence of past problems related to alcohol intake. When alcohol-related harms were considered, impacts of differences in gender and marital status are much higher among Roma compared to non-Roma. Additionally, TAS2R38 rs713598 had significant association with AUDIT 2- number of standard drinks on a typical day and AUDIT 3- frequency of having six or more drinks per occasion among HG and HR participants respectively.

Conclusion: Roma ethnicity was demonstrated to influence certain alcohol consumption behaviours, i.e., having experience of alcohol-related harm as well as evidence of past problems related to alcohol drinking. For alcohol-related harm, gender and differences in marital status act more strongly among Roma participants compared to non-Roma. We may also presume that genetics influencing bitter taste phenotypes may have an effect on alcohol consumption patterns in our study samples, though it is suggested to interpret the findings with caution.

KEY WORDS

Alcohol consumption, AUDIT, Hungarian general population, Hungarian Roma population, decomposition, taste preference, genetic polymorphisms

REFERENCES

1. Rehm J, Parry C. Alcohol consumption and infectious diseases in South Africa. Lancet. 2009;374(9707):2053. doi:10.1016/S0140-6736(09)62150-4.

2. Grønbæk M. The positive and negative health effects of alcohol-and the public health implications. J Intern Med. 2009;265(4):407-20. doi: 10.1111/j.1365-2796.2009.02082.x.

3. Boden-Albala B, Sacco RL. Lifestyle factors and stroke risk: exercise, alcohol, diet, obesity, smoking, drug use, and stress. Curr Atheroscler Rep. 2000;2(2):160-6. doi: 10.1007/s11883-000-0111-3.

4. Ferreira MP, Willoughby D, Nutrition, Metabolism. Alcohol consumption: the good, the bad, and the indifferent. Appl Physiol Nutr Metab. 2008;33(1):12-20. doi: 10.1139/H07-175.

5. World Health Organization. Global Status Report on Alcohol and Health 2014; WHO Press: Geneva, Switzerland, 2014; Available online: https://www.who.int/substance_abuse/publications/global_alcohol_report/msb_gsr_2014_1.pdf?ua=1.%20Accessed%201/18/17 (accessed on 10 January 2023).

6. White AM, Castle IJP, Powell PA, Hingson RW, Koob GF. Alcohol-related deaths during the COVID-19 pandemic. Jama. 2022;327(17):1704-6. doi:10.1001/jama.2022.4308.

7. World Health Organization. Global status report on alcohol and health 2018: World Health Organization; 2019. Available online: https://apps.who.int/iris/rest/bitstreams/1151838/retrieve (accessed on January 10 2023).

8. OECD. Health at a Glance 2021:OECD Indicators. Paris: OECD Publishing. 2021. doi:10.1787/ae3016b9-en.

9. World Health Organization. Status report on alcohol consumption, harm and policy responses in 30 European countries 2019. World Health Organization. Regional Office for Europe; 2019. Available online at: https://www.euro.who.int/__data/assets/pdf_file/0019/411418/Alcohol-consumption-harm-policy-responses-30-European-countries-2019.pdf (accessed on January 10, 2023).

10. World Health Organization. Regional Office for Europe. Alcohol and Inequities. Guidance for Addressing Inequities in Alcohol-Related Harm. World health Organization.

2014. Available online at: https://www.euro.who.int/__data/assets/pdf_file/0003/247629/Alcohol-and-Inequities.pdf (accessed January 10, 2023).

11. Burke GL, Savage PJ, Manolio TA, Sprafka JM, Wagenknecht LE, Sidney S, et al. Correlates of obesity in young black and white women: the CARDIA Study. Am J Public Health. 1992;82(12):1621-5. doi: 10.2105/ajph.82.12.1621.

12. DiPietro L, Williamson D, Caspersen C, Eaker E. The descriptive epidemiology of selected physical activities and body weight among adults trying to lose weight: the Behavioral Risk Factor Surveillance System survey, 1989. Int J Obes Relat Metab Disord. 1993;17(2):69-76.

13. Folsom AR, Cook TC, Sprafka JM, Burke GL, Norsted SW, Jacobs DR. Differences in leisure-time physical activity levels between blacks and whites in population-based samples: the Minnesota Heart Survey. J Behav Med. 1991;14:1-9. doi: 10.1007/BF00844764.

14. Balcazar H, Cobas JA. Overweight among Mexican Americans and its relationship to life style behavioral risk factors. J Community Health. 1993;18(1):55. doi: 10.1007/BF01321521.

15. Kuczmarski RJ, Flegal KM, Campbell SM, Johnson CL. Increasing prevalence of overweight among US adults: the National Health and Nutrition Examination Surveys, 1960 to 1991. Jama. 1994;272(3):205-11. doi: 10.1001/jama.272.3.205.

16. Diehl AK, Stern M. Special health problems of Mexican-Americans: obesity, gallbladder disease, diabetes mellitus, and cardiovascular disease. Adv Intern Med. 1988;34:73-96.

17. Winkleby MA, Cubbin C, Ahn DK, Kraemer HC. Pathways by which SES and ethnicity influence cardiovascular disease risk factors. Ann N Y Acad Sci. 1999;896(1):191-209. doi: 10.1111/j.1749-6632.1999.tb08116.x.

18. Substance Abuse and Mental Health Services Administration. Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration. 2013(NSDUH Series H-46, HHS Publication No. (SMA) 13-4795).

19. Dawson DA. Beyond black, white and Hispanic: race, ethnic origin and drinking patterns in the United States. J Subst Abuse. 1998;10(4):321-39. doi: 10.1016/s0899-3289(99)00009-7.

20. Chen CM YH, Williams GD, Faden VB,. Trends in Underage Drinking in the United States, 1991–2007. 2009.

21. Borrell LN, Roux AVD, Jacobs Jr DR, Shea S, Jackson SA, Shrager S, et al. Perceived racial/ethnic discrimination, smoking and alcohol consumption in the Multi-Ethnic Study of Atherosclerosis (MESA). Prev Med. 2010;51(3-4):307-12. doi: 10.1016/j.ypmed.2010.05.017.

22. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2007;64(7):830-42. doi: 10.1001/archpsyc.64.7.830.

23. Mulia N, Ye Y, Greenfield TK, Zemore SE. Disparities in alcohol-related problems among White, Black, and Hispanic Americans. Alcohol Clin Exp Res. 2009;33(4):654-62. doi: 10.1111/j.1530-0277.2008.00880.x.

24. Chartier K, Caetano R. Ethnicity and health disparities in alcohol research. Alcohol Res Health. 2010;33(1-2):152.

25. Fraser AM. Gypsies (The Peoples of Europe): Blackwell Pub; 1992.

26. Hancock I, Kenrick D, Acton TJS, struggle tG. The emergence of Romani as a koine outside of India. 2000:1-13.

27. Kalaydjieva L, Calafell F, Jobling MA, Angelicheva D, de Knijff P, Rosser Z, et al. Patterns of inter-and intra-group genetic diversity in the Vlax Roma as revealed by Y chromosome and mitochondrial DNA lineages. Eur J Hum Genet. 2001;9(2):97-104. doi: 10.1038/sj.ejhg.5200597.

28. Kalaydjieva L, Gresham D, Calafell F. Genetic studies of the Roma (Gypsies): a review. BMC Med Genet. 2001;2(1):1-13. doi: 10.1186/1471-2350-2-5.

29. Mendizabal I, Lao O, Marigorta UM, Wollstein A, Gusmão L, Ferak V, et al. Reconstructing the population history of European Romani from genome-wide data. Curr Biol. 2012;22(24):2342-9. doi: 10.1016/j.cub.2012.10.039.

30. Mendizabal I, Valente C, Gusmão A, Alves C, Gomes V, Goios A, et al. Reconstructing the Indian origin and dispersal of the European Roma: a maternal genetic perspective. PLoS One. 2011;6(1):e15988. doi: 10.1371/journal.pone.0015988.

31. Moorjani P, Patterson N, Loh P-R, Lipson M, Kisfali P, Melegh BI, et al. Reconstructing Roma history from genome-wide data. PLoS One. 2013;8(3):e58633. doi: 10.1371/journal.pone.0058633.

32. Morar B, Gresham D, Angelicheva D, Tournev I, Gooding R, Guergueltcheva V, et al. Mutation history of the roma/gypsies. Am J Hum Genet. 2004;75(4):596-609. doi: 10.1086/424759.

33. Masseria C, Mladovsky P, Hernández-Quevedo C. The socio-economic determinants of the health status of Roma in comparison with non-Roma in Bulgaria, Hungary and Romania. Eur J Public Health. 2010;20(5):549-54. doi: 10.1093/eurpub/ckq102.

34. Framework for national Roma integration strategies up to 2020. Communication from the Commission to the European Parliament, the Council the European Economic and Social Committee and the Committee of the Regions. 2011(173):2011. Available online at: https://www.europarl.europa.eu/RegData/etudes/STUD/2020/642827/EPRS_STU(2020)642827_EN.pdf (accessed on January 17, 2023).

35. Bernáth A. Roma in Eastern Europe. Roma in Central and Eastern Europe Berlin: GESIS Leibniz Institute for the Social Sciences, Service Agency Eastern Europe. 2009:12-6.

36. Pásztor IZ, Pénzes J, Tátrai P, Pálóczi Á. The number and spatial distribution of the Roma population in Hungary–in the light of different approaches. Folia Geographica. 2016;58(2):5.

37. Tomovska I. Poverty, discrimination and the Roma: a human security issue. Human Security Perspectives. 2010;7(1):63-82.

38. Special Eurobarometer 393: Discrimination in the EU in 2012. European Commission, Directorate-General for Communication. Available from: http://data.europa.eu/88u/dataset/S1043_77_4_EBS393. (accessed on January 17, 2023).

39. European Union Agency for Fundamental Rights. The Situation of Roma in 11 EU Member States: Survey Results at a Glance. 2012. Available online at: https://fra.europa.eu/sites/default/files/fra_uploads/2099-FRA-2012-Roma-ata-glance_EN.pdf (accessed on January 17, 2023).

40. European Union Agency for Fundamental Rights. Poverty and employment: the situation of Roma in 11 EU member States, Roma survey – data in focus. 2014. Available online at: https://fra.europa.eu/sites/default/files/fra_uploads/fra-2014-roma-survey-dif-employment-1_en.pdf (accessed on January 17, 2023).

41. European Union Agency for Fundamental Rights. Discrimination against and living conditions of Roma women in 11 EU Member States, Roma survey – data in focus. 2014. Available online at: https://fra.europa.eu/sites/default/files/fra_uploads/fra-2014-roma-survey-dif-women-2_en.pdf (accessed on January 17, 2023).

42. Bartoš V, Bauer M, Chytilová J, Matějka F. Attention discrimination: Theory and field experiments with monitoring information acquisition. Am Econ Rev. 2016;106(6):1437-75. doi: 10.1257/aer.20140571.

43. Ciaian P, Kancs dA. Causes of the Social and Economic Marginalisation: The Role of Social Mobility Barriers for Roma; EERI Research Paper Series; EERI RP 2016/03; Economics and Econometrics Research Institute (EERI): Brussels, Belgium, 2016.

44. Cook B, Wayne GF, Valentine A, Lessios A, Yeh E. Revisiting the evidence on health and health care disparities among the Roma: a systematic review 2003–2012. Int J Public Health. 2013;58(6):885-911. doi: 10.1007/s00038-013-0518-6.

45. Zelko E, Švab I, Kolšek M, Podojsteršek J, Sever M. Differences in alcohol consumption habits between Roma and non-Roma in Northeastern Slovenia. Sloven Nurs Rev. 2017;51(2):116–23-–23. doi: 10.14528/snr.2017.51.2.156.

46. Babinská I, Gecková AM, Jarcuska P, Pella D, Mareková M, Stefkova G, et al. Does the population living in Roma settlements differ in physical activity, smoking and alcohol consumption from the majority population in Slovakia. Cent Eur J Public Health. 2014;22(Supp. l):P22-7. doi: 10.21101/cejph.a3897.

47. Diabelková J, Rimárová K, Urdzík P, Dorko E, Bušová A. Risk factors of preterm birth and low birth weight neonates among Roma and non-Roma mothers. Central European journal of public health. 2018;26(Supplement):S25-S31. doi: 10.21101/cejph.a5273.

48. Bobakova D, Kolarcik P, Geckova AM, Klein D, Reijneveld SA, van Dijk JP. Does the influence of peers and parents on adolescents' drunkenness differ between Roma and non-Roma adolescents in Slovakia? Ethn Health. 2012;17(5):531-41. doi: 10.1080/13557858.2012.678305.

49. Cace S, Cantarji V, Sali N, Alla M. Roma in the Republic of Moldova: United Nations Development Programme Chisnau; 2007.

50. Kanapeckienė V, Valintėlienė R, Beržanskytė A, Kėvalas R, Supranowicz P. Health of Roma children in Vilnius and Ventspils. Medicina. 2009;45(2):153. doi:10.3390/medicina45020020.

51. Chomynová P, Kozák J, Mravčík V. Substance use in Roma population in contact with social workers in the Czech Republic: A cross-sectional questionnaire survey. J Ethn Subst Abuse. 2021;20(2):275-94. doi: 10.1080/15332640.2020.1717399.

52. Carrasco-Garrido P, López de Andrés A, Hernández Barrera V, Jiménez-Trujillo I, Jiménez-García R. Health status of Roma women in Spain. Eur J Public Health. 2011;21(6):793-8. doi: 10.1093/eurpub/ckq153.

53. La Parra D. Towards equity in health: Comparative study of National Health Surveys in the Roma population and the general population in Spain, 2006. Madrid: Ministerio de Sanidad y Consumo. 2009.

54. Ekuklu G, Deveci S, Eskiocak M, Berberoglu U, Saltik A. Alcoholism prevalence and some related factors in Edirne, Turkey. Yonsei Med J. 2004;45(2):207-14. doi: 10.3349/ymj.2004.45.2.207.

55. Sárváry A, Kósa Z, Javorne Erdei R. Telepszerü körülmények között élö gyermekek egészségmagatartás Északkelet-Magyarországon {Article in Hungarian: Health behaviour of children living in colonies in North-Eastern Hungary}. Népeü. 2012;90:230-44.

56. Gerevich J, Bacskai E, Czobor P, Szabo J. Substance use in Roma and non-Roma adolescents. J Nerv Ment Dis. 2010;198(6):432-6. doi: 10.1097/NMD.0b013e3181e07d51.

57. Sárváry A, Kósa Z, Jávorné RE, Gyulai A, Takács P, Sándor J, et al. Socioeconomic status, health related behaviour, and self-rated health of children living in Roma settlements in Hungary. Cent Eur J Public Health. 2019;27(1):24-31. doi: 10.21101/cejph.a4726.

58. Sándor J, Kósa Z, Boruzs K, Boros J, Tokaji I, McKee M, et al. The decade of Roma Inclusion: did it make a difference to health and use of health care services? Int J Public Health. 2017;62(7):803-15. doi: 10.1007/s00038-017-0954-9.

59. Kósa Z, Széles G, Kardos L, Kósa K, Németh R, Országh S, et al. A comparative health survey of the inhabitants of Roma settlements in Hungary. Am J Public Health. 2007;97(5):853-9. doi: 10.2105/AJPH.2005.072173.

60. Rehm J, Room R, Monteiro M, Gmel G, Graham K, Rehn N, et al. Alcohol use. In Comparative Quantification of Health Risks; Ezzati, M., Lopez, A.D., Rodgers, A., Murray, C.J.L., Eds.; World Health Organization: Geneva, Switzerland, 2004.

61. Rehm J, Room R, Graham K, Monteiro M, Gmel G, Sempos CT. The relationship of average volume of alcohol consumption and patterns of drinking to burden of disease: an overview. Addiction. 2003;98(9):1209-28. doi: 10.1046/j.1360-0443.2003.00467.x.

62. Cyders MA, VanderVeen JD, Plawecki M, Millward JB, Hays J, Kareken DA, et al. Gender-specific effects of mood on alcohol-seeking behaviors: Preliminary findings using intravenous alcohol self-administration. Alcohol Clin Exp Res. 2016;40(2):393-400. doi: 10.1111/acer.12955.

63. Yusuf F, Leeder SR. Making sense of alcohol consumption data in Australia. Med J Aust. 2015;203(3):128-30. doi: 10.5694/mja15.00151.

64. Thompson A, Pirmohamed M. Associations between occupation and heavy alcohol consumption in UK adults aged 40–69 years: a cross-sectional study using the UK Biobank. BMC Public Health. 2021;21(1):1-12. doi: 10.1186/s12889-021-10208-x.

65. Nolen-Hoeksema S. Gender differences in risk factors and consequences for alcohol use and problems. Clin Psychol Rev. 2004;24(8):981-1010. doi: 10.1016/j.cpr.2004.08.003.

66. DeWit DJ, Adlaf EM, Offord DR, Ogborne AC. Age at first alcohol use: a risk factor for the development of alcohol disorders. Am J Psychiatry. 2000;157(5):745-50. doi: 10.1176/appi.ajp.157.5.745.

67. Mossakowski KN, medicine. Is the duration of poverty and unemployment a risk factor for heavy drinking? Soc Sci Med. 2008;67(6):947-55. doi: 10.1016/j.socscimed.2008.05.019.

68. Poortinga W. The prevalence and clustering of four major lifestyle risk factors in an English adult population. Prev Med 2007;44(2):124-8. doi: 10.1016/j.ypmed.2006.10.006.

69. Arunachalam U, Chandrasekaran A. Genetic Polymorphism in Alcohol-dependent Genes: A Review. SBV Journal of Basic, Clinical and Applied Health Science. 2020;3(1):10-5. doi: 10.5005/jp-journals-10082-02260.

70. Edenberg HJ, Dick DM, Xuei X, Tian H, Almasy L, Bauer LO, et al. Variations in GABRA2, encoding the α2 subunit of the GABAA receptor, are associated with alcohol dependence and with brain oscillations. Am J Hum Genet. 2004;74(4):705-14. doi: 10.1086/383283.

71. Covault J, Gelernter J, Hesselbrock V, Nellissery M, Kranzler HR. Allelic and haplotypic association of GABRA2 with alcohol dependence. Am J Med Genet B Neuropsychiatr Genet. 2004;129(1):104-9. doi: 10.1002/ajmg.b.30091.

72. Fehr C, Sander T, Tadic A, Lenzen KP, Anghelescu I, Klawe C, et al. Confirmation of association of the GABRA2 gene with alcohol dependence by subtype-specific analysis. Psychiatr Genet. 2006;16(1):9-17. doi: 10.1097/01.ypg.0000185027.89816.d9.

73. Lappalainen J, Krupitsky E, Remizov M, Pchelina S, Taraskina A, Zvartau E, et al. Association between alcoholism and γ-amino butyric acid α2 receptor subtype in a Russian population. Alcohol Clin Exp Res. 2005;29(4):493-8. doi:10.1097/01.ALC.0000158938.97464.90.

74. Villafuerte S, Heitzeg MM, Foley S, Wendy Yau W, Majczenko K, Zubieta J-K, et al. Impulsiveness and insula activation during reward anticipation are associated with genetic variants in GABRA2 in a family sample enriched for alcoholism. Mol Psychiatry. 2012;17(5):511-9. doi: 10.1038/mp.2011.33.

75. Ittiwut C, Yang BZ, Kranzler HR, Anton RF, Hirunsatit R, Weiss RD, et al. GABRG1 and GABRA2 variation associated with alcohol dependence in African Americans. Alcohol Clin Exp Res. 2012;36(4):588-93. doi: 10.1111/j.1530-0277.2011.01637.x.

76. Morozova TV, Goldman D, Mackay TF, Anholt RR. The genetic basis of alcoholism: multiple phenotypes, many genes, complex networks. Genome Biol. 2012;13(2):1-11. doi: 10.1186/gb-2012-13-2-239.

77. Lanier SA, Hayes JE, Duffy VB. Sweet and bitter tastes of alcoholic beverages mediate alcohol intake in of-age undergraduates. Physiol Behav. 2005;83(5):821-31. doi: 10.1016/j.physbeh.2004.10.004.

78. Allen AL, McGeary JE, Hayes JE. Polymorphisms in TRPV 1 and TAS 2Rs associate with sensations from sampled ethanol. Alcohol Clin Exp Res. 2014;38(10):2550-60. doi: 10.1111/acer.12527.

79. Basson MD, Bartoshuk LM, DiChello SZ, Panzini L, Weiffenbach JM, Duffy VB. Association between 6-n-propylthiouracil (PROP) bitterness and colonic neoplasms. Dig Dis Sci. 2005;50(3):483-9. doi: 10.1007/s10620-005-2462-7.

80. Shigemura N, Ninomiya Y. Recent advances in molecular mechanisms of taste signaling and modifying. Int Rev Cell Mol Biol. 2016;323:71-106. doi: 10.1016/bs.ircmb.2015.12.004.

81. Roudnitzky N, Behrens M, Engel A, Kohl S, Thalmann S, Hübner S, et al. Receptor polymorphism and genomic structure interact to shape bitter taste perception. PLoS Genet. 2015;11(9):e1005530. doi: 10.1371/journal.pgen.1005530.

82. Kim U, Drayna D. Genetics of individual differences in bitter taste perception: lessons from the PTC gene. Clin Genet. 2005;67(4):275-80. doi: 10.1111/j.1399-0004.2004.00361.x.

83. Bufe B, Breslin PA, Kuhn C, Reed DR, Tharp CD, Slack JP, et al. The molecular basis of individual differences in phenylthiocarbamide and propylthiouracil bitterness perception. Curr Biol. 2005;15(4):322-7. doi: 10.1016/j.cub.2005.01.047.

84. Hayes JE, Wallace MR, Knopik VS, Herbstman DM, Bartoshuk LM, Duffy VB. Allelic variation in TAS2R bitter receptor genes associates with variation in sensations from and ingestive behaviors toward common bitter beverages in adults. Chem Senses. 2011;36(3):311-9. doi: 10.1093/chemse/bjq132.

85. Tepper BJ. Nutritional implications of genetic taste variation: the role of PROP sensitivity and other taste phenotypes. Annu Rev Nutr 2008;28(1):367-88. doi: 10.1146/annurev.nutr.28.061807.155458.

86. Dinehart M, Hayes J, Bartoshuk L, Lanier S, Duffy V. Bitter taste markers explain variability in vegetable sweetness, bitterness, and intake. Physiol Behav. 2006;87(2):304-13. doi: 10.1016/j.physbeh.2005.10.018.

87. Ullrich NV, Touger-Decker R, O'Sullivan-Maillet J, Tepper BJ. PROP taster status and self-perceived food adventurousness influence food preferences. J Am Diet Assoc. 2004;104(4):543-9. doi: 10.1016/j.jada.2004.01.011.

88. Hayes JE, Duffy VB. Oral sensory phenotype identifies level of sugar and fat required for maximal liking. Physiol Behav. 2008;95(1-2):77-87. doi: 10.1016/j.physbeh.2008.04.023.

89. Kim Uk, Jorgenson E, Coon H, Leppert M, Risch N, Drayna D. Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide. Science. 2003;299(5610):1221-5. doi: 10.1126/science.1080190.

90. Guo SW, Reed DR. The genetics of phenylthiocarbamide perception. Ann Hum Biol. 2001;28(2):111-42. doi: 10.1080/03014460151056310.

91. Diószegi J, Llanaj E, Ádány R. Genetic background of taste perception, taste preferences, and its nutritional implications: a systematic review. Front Genet. 2019;10:1272. doi: 10.3389/fgene.2019.01272.

92. Henkin RI, Martin BM, Agarwal RP. Efficacy of exogenous oral zinc in treatment of patients with carbonic anhydrase VI deficiency. Am J Med Sci. 1999;318(6):392-405. doi: 10.1097/00000441-199912000-00006.

93. Barbarossa IT, Melis M, Mattes MZ, Calò C, Muroni P, Crnjar R, et al. The gustin (CA6) gene polymorphism, rs2274333 (A/G), is associated with fungiform papilla density, whereas PROP bitterness is mostly due to TAS2R38 in an ethnically-mixed population. Physiol Behav. 2015;138:6-12. doi: 10.1016/j.physbeh.2014.09.011.

94. Li X, Staszewski L, Xu H, Durick K, Zoller M, Adler E. Human receptors for sweet and umami taste. Proc Natl Acad Sci U S A. 2002;99(7):4692-6. doi: 10.1073/pnas.072090199.

95. Behrens M, Briand L, de March CA, Matsunami H, Yamashita A, Meyerhof W, et al. Structure–function relationships of olfactory and taste receptors. Chem Senses. 2018;43(2):81-7. doi: 10.1093/chemse/bjx083.

96. Chamoun E, Mutch DM, Allen-Vercoe E, Buchholz AC, Duncan AM, Spriet LL, et al. A review of the associations between single nucleotide polymorphisms in taste receptors, eating behaviors, and health. Crit Rev Food Sci Nutr. 2018;58(2):194-207. doi: 10.1080/10408398.2016.1152229.

97. Huang L, Massa L, Karle J. The kernel energy method: Application to a tRNA. Proc Natl Acad Sci U S A. 2006;103(5):1233-7. doi: 10.1073/pnas.0510342103.

98. Ishimaru D, Gotoh M, Takayama S, Kosaki R, Matsumoto Y, Narimatsu H, et al. Large-scale mutational analysis in the EXT1 and EXT2 genes for Japanese patients with multiple osteochondromas. BMC Genet. 2016;17:1-7. doi: 10.1186/s12863-016-0359-4.

99. Castaldelli-Maia JM, Bhugra D. Investigating the interlinkages of alcohol use and misuse, spirituality and culture–Insights from a systematic review. Int Rev Psychiatry. 2014;26(3):352-67. doi: 10.3109/09540261.2014.899999.

100. Casswell S, Huckle T, Wall M, Parker K, Chaiyasong S, Parry CD, et al. Policy-relevant behaviours predict heavier drinking and mediate the relationship with age, gender and education status: Analysis from the International Alcohol Control Study. Drug Alcohol Rev. 2018;37:S86-S95. doi: 10.1111/dar.12669.

101. Yang P, Tao R, He C, Liu S, Wang Y, Zhang X. The risk factors of the alcohol use disorders—Through review of its comorbidities. Front Neurosci. 2018;12:303. doi: 10.3389/fnins.2018.00303.

102. Chartier KG, Hesselbrock MN, Hesselbrock VM. Development and vulnerability factors in adolescent alcohol use. Child Adolesc Psychiatr Clin N Am. 2010;19(3):493-504. doi: 10.1016/j.chc.2010.03.004.

103. Rosenström T, Torvik FA, Ystrom E, Czajkowski NO, Gillespie NA, Aggen SH, et al. Prediction of alcohol use disorder using personality disorder traits: a twin study. Addiction. 2018;113(1):15-24. doi: 10.1111/add.13951.

104. Yap MB, Cheong TW, Zaravinos-Tsakos F, Lubman DI, Jorm AF. Modifiable parenting factors associated with adolescent alcohol misuse: a systematic review and meta-analysis of longitudinal studies. Addiction. 2017;112(7):1142-62. doi: 10.1111/add.13785.

105. Edenberg HJ, McClintick JN. Alcohol dehydrogenases, aldehyde dehydrogenases, and alcohol use disorders: a critical review. Alcohol Clin Exp Res. 2018;42(12):2281-97. doi: 10.1111/acer.13904.

106. Gelernter J, Kranzler H, Sherva R, Almasy L, Koesterer R, Smith A, et al. Genome-wide association study of alcohol dependence: significant findings in African-and European-Americans including novel risk loci. Mol Psychiatry. 2014;19(1):41-9. doi: 10.1038/mp.2013.145.

107. Kranzler HR, Zhou H, Kember RL, Vickers Smith R, Justice AC, Damrauer S, et al. Genome-wide association study of alcohol consumption and use disorder in 274,424

individuals from multiple populations. Nat Commun. 2019;10(1):1-11. doi: 10.1038/s41467-019-11916-0.

108. Walters RK, Polimanti R, Johnson EC, McClintick JN, Adams MJ, Adkins AE, et al. Transancestral GWAS of alcohol dependence reveals common genetic underpinnings with psychiatric disorders. Nat Neurosci. 2018;21(12):1656-69. doi: 10.1038/s41593-018-0275-1.

109. Zhou H, Sealock JM, Sanchez-Roige S, Clarke T-K, Levey DF, Cheng Z, et al. Genome-wide meta-analysis of problematic alcohol use in 435,563 individuals yields insights into biology and relationships with other traits. Nat Neurosci. 2020;23(7):809-18. doi: 10.1038/s41593-020-0643-5.

110. Clarke TK, Adams MJ, Davies G, Howard DM, Hall LS, Padmanabhan S, et al. Genome-wide association study of alcohol consumption and genetic overlap with other health-related traits in UK Biobank (N= 112 117). Mol Psychiatry. 2017;22(10):1376-84. doi: 10.1038/mp.2017.153.

111. Gelernter J, Sun N, Polimanti R, Pietrzak RH, Levey DF, Lu Q, et al. Genome-wide association study of maximum habitual alcohol intake in> 140,000 US European and African American veterans yields novel risk loci. Biol Psychiatry. 2019;86(5):365-76. doi: 10.1016/j.biopsych.2019.03.984.

112. Liu M, Jiang Y, Wedow R, Li Y, Brazel DM, Chen F, et al. Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use. Nat Genet. 2019;51(2):237-44. doi: 10.1038/s41588-018-0307-5.

113. Sanchez-Roige S, Fontanillas P, Elson SL, Team aR, Gray JC, de Wit H, et al. Genome-wide association study of alcohol use disorder identification test (AUDIT) scores in 20 328 research participants of European ancestry. Addict Biol. 2019;24(1):121-31. doi: 10.1111/adb.12574.

114. Gelernter J, Zhou H, Nuñez YZ, Mutirangura A, Malison RT, Kalayasiri R. Genomewide association study of alcohol dependence and related traits in a Thai population. Alcohol Clin Exp Res. 2018;42(5):861-8. doi: 10.1111/acer.13614.

115. Li D, Zhao H, Gelernter J. Strong protective effect of the aldehyde dehydrogenase gene (ALDH2) 504lys (* 2) allele against alcoholism and alcohol-induced medical diseases in Asians. Human genetics. Hum Genet. 2012;131(5):725-37. doi: 10.1007/s00439-011-1116-4.

116. Quillen EE, Chen XD, Almasy L, Yang F, He H, Li X, et al. ALDH2 is associated to alcohol dependence and is the major genetic determinant of “daily maximum drinks” in a GWAS study of an isolated rural Chinese sample. Am J Med Genet B Neuropsychiatr Genet. 2014;165(2):103-10. doi: 10.1002/ajmg.b.32213.

117. Jorgenson E, Thai KK, Hoffmann TJ, Sakoda LC, Kvale MN, Banda Y, et al. Genetic contributors to variation in alcohol consumption vary by race/ethnicity in a large multi-ethnic genome-wide association study. Mol Psychiatry. 2017;22(9):1359-67. doi: 10.1038/mp.2017.101.

118. Hurley TD, Edenberg HJ. Genes encoding enzymes involved in ethanol metabolism. Alcohol research: current reviews. 2012;34(3):339.

119. Dick DM, Foroud T. Candidate genes for alcohol dependence: a review of genetic evidence from human studies. Alcohol Clin Exp Res. 2003;27(5):868-79. doi: 10.1097/01.ALC.0000065436.24221.63.

120. Kimura M, Higuchi S. Genetics of alcohol dependence. Psychiatry Clin Neurosci. 2011;65(3):213-25. doi: 10.1111/j.1440-1819.2011.02190.x.

121. Köhnke MD. Approach to the genetics of alcoholism: a review based on pathophysiology. Biochem Pharmacol. 2008;75(1):160-77. doi: 10.1016/j.bcp.2007.06.021.

122. Barnard E, Skolnick P, Olsen R, Mohler H, Sieghart W, Biggio G, et al. International Union of Pharmacology. XV. Subtypes of γ-aminobutyric acidA receptors: classification on the basis of subunit structure and receptor function. Pharmacol Rev. 1998;50(2):291-314.

123. Grobin AC, Matthews DB, Devaud LL, Morrow AL. The role of GABAA receptors in the acute and chronic effects of ethanol. Psychopharmacology. 1998;139:2-19. doi: 10.1007/s002130050685.

124. McBride W, Bodart B, Lumeng L, Li TK. Association between low contents of dopamine and serotonin in the nucleus accumbens and high alcohol preference. Alcohol Clin Exp Res. 1995;19(6):1420-2. doi: 10.1111/j.1530-0277.1995.tb01001.x.

125. Fujimoto A, Nagao T, Ebara T, Sato M, Otsuki S. Cerebrospinal fluid monoamine metabolites during alcohol withdrawal syndrome and recovered state. Biol Psychiatry. 1983.

126. Gessa GL, Muntoni F, Collu M, Vargiu L, Mereu G. Low doses of ethanol activate dopaminergic neurons in the ventral tegmental area. Brain Res. 1985;348(1):201-3. doi: 10.1016/0006-8993(85)90381-6.

127. Wise RA. The neurobiology of craving: implications for the understanding and treatment of addiction. J Abnorm Psychol. 1988;97(2):118. doi: 10.1037//0021-843x.97.2.118.

128. Heinz A, Schmidt K, Baum SS, Kuhn S, Dufeu P, Schmidt L, et al. Influence of dopaminergic transmission on severity of withdrawal syndrome in alcoholism. J Stud Alcohol. 1996;57(5):471-4. doi: 10.15288/jsa.1996.57.471.

129. Harris GC, Aston-Jones G. Involvement of D2 dopamine receptors in the nucleus accumbens in the opiate withdrawal syndrome. Nature. 1994;371(6493):155-7. doi: 10.1038/371155a0.

130. Giros B, Jaber M, Jones SR, Wightman RM, Caron MG. Hyperlocomotion and indifference to cocaine and amphetamine in mice lacking the dopamine transporter. Nature. 1996;379(6566):606-12. doi: 10.1038/379606a0.

131. Laine T, Ahonen A, Torniainen P, Heikkilä J, Pyhtinen J, Räsänen P, et al. Dopamine transporters increase in human brain after alcohol withdrawal. Mol Psychiatry. 1999;4(2):189-91. doi: 10.1038/sj.mp.4000514.

132. Westerink BH. Sequence and significance of dopamine metabolism in the rat brain. Neurochem Int. 1985;7(2):221-7. doi: 10.1016/0197-0186(85)90108-1.

133. Wood PL, Altar CA. Dopamine release in vivo from nigrostriatal, mesolimbic, and mesocortical neurons: utility of 3-methoxytyramine measurements. Pharmacol Rev. 1988;40(3):163-87.

134. Amin F, Davidson M, Davis KL. Homovanillic acid measurement in clinical research: a review of methodology. Schizophr Bull. 1992;18(1):123-48. doi: 10.1093/schbul/18.1.123.

135. Kranzler HR, Anton RF. Implications of recent neuropsychopharmacologic research for understanding the etiology and development of alcoholism. J Consult Clin Psychol. 1994;62(6):1116. doi: 10.1037//0022-006x.62.6.1116.

136. Gelernter J, Pakstis A, Kidd K. Linkage mapping of serotonin transporter protein gene SLC6A4 on chromosome 17. Hum Genet. 1995;95:677-80. doi: 10.1007/BF00209486.

137. Lesch KP, Bengel D, Heils A, Sabol SZ, Greenberg BD, Petri S, et al. Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region. Science. 1996;274(5292):1527-31. doi: 10.1126/science.274.5292.1527.

138. Cloninger CR. Neurogenetic adaptive mechanisms in alcoholism. Science. 1987;236(4800):410-6. doi: 10.1126/science.2882604.

139. . Xuei X, Dick D, Flury-Wetherill L, Tian H, Agrawal A, Bierut L, et al. Association of the κ-opioid system with alcohol dependence. Mol Psychiatry. 2006;11(11):1016-24. doi: 10.1038/sj.mp.4001882.

140. Wang JC, Hinrichs AL, Stock H, Budde J, Allen R, Bertelsen S, et al. Evidence of common and specific genetic effects: association of the muscarinic acetylcholine receptor M2 (CHRM2) gene with alcohol dependence and major depressive syndrome. Hum Mol Genet. 2004;13(17):1903-11. doi: 10.1093/hmg/ddh194.

141. Diószegi J, Fiatal S, Tóth R, Moravcsik-Kornyicki Á, Kósa Z, Sándor J, et al. Distribution characteristics and combined effect of polymorphisms affecting alcohol consumption behaviour in the Hungarian general and Roma populations. Alcohol Alcohol. 2017;52(1):104-11. doi: 10.1093/alcalc/agw052.

142. Toth R, Pocsai Z, Fiatal S, Szeles G, Kardos L, Petrovski B, et al. ADH1B* 2 allele is protective against alcoholism but not chronic liver disease in the Hungarian population. Addiction. 2010;105(5):891-6. doi: 10.1111/j.1360-0443.2009.02876.x.

143. Tóth R, Fiatal S, Petrovski B, McKee M, Ádány R. Combined effect of ADH1B RS1229984, RS2066702 and ADH1C RS1693482/RS698 alleles on alcoholism and chronic liver diseases. Dis Markers. 2011;31(5):267-77. doi: 10.3233/DMA-2011-0828.

144. Hubáček JA, Šedová L, Olišarová V, Adámková V, Adámek V, Tóthová V. Distribution of ADH1B genotypes predisposed to enhanced alcohol consumption in the Czech Roma/Gypsy population. Cent Eur J Public Health. 2018;26(4):284-8. doi: 10.21101/cejph.a5090.

145. Ádány R, Pikó P, Fiatal S, Kósa Z, Sándor J, Bíró É, et al. Prevalence of insulin resistance in the Hungarian general and Roma populations as defined by using data generated in a complex health (interview and examination) survey. Int J Environ Res Public Health. 2020;17(13):4833. doi: 10.3390/ijerph17134833.

146. Kósa K, Daragó L, Ádány R. Environmental survey of segregated habitats of Roma in Hungary: a way to be empowering and reliable in minority research. Eur J Public Health. 2011;21(4):463-8. doi: 10.1093/eurpub/ckp097.

147. Széles G, Vokó Z, Jenei T, Kardos L, Pocsai Z, Bajtay A, et al. A preliminary evaluation of a health monitoring programme in Hungary. Eur J Public Health. 2005;15(1):26-32. doi: 10.1093/eurpub/cki107.

148. . Szigethy E, Széles G, Horvath A, Hidvegi T, Jermendy G, Paragh G, et al. Epidemiology of the metabolic syndrome in Hungary. Public Health. 2012;126(2):143-9. doi: 10.1016/j.puhe.2011.11.003.

149. World Health Organization. AUDIT: The alcohol use disorders identification test: Guidelines for use in primary health care. World Health Organization; 2001.

150. Reinert DF, Allen JP. The alcohol use disorders identification test: an update of research findings. Alcohol Clin Exp Res. 2007;31(2):185-99. doi: 10.1111/j.1530-0277.2006.00295.x.

151. Aalto M, Tuunanen M, Sillanaukee P, Seppä K. Effectiveness of structured questionnaires for screening heavy drinking in middle-aged women. Alcohol Clin Exp Res. 2006;30(11):1884-8. doi: 10.1111/j.1530-0277.2006.00233.x.

152. Aertgeerts B, Buntinx F, Ansoms S, Fevery J. Screening properties of questionnaires and laboratory tests for the detection of alcohol abuse or dependence in a general practice population. Br J Gen Pract . 2001;51(464):206-17.

153. Bradley KA, Bush KR, Epler AJ, Dobie DJ, Davis TM, Sporleder JL, et al. Two brief alcohol-screening tests From the Alcohol Use Disorders Identification Test (AUDIT): validation in a female Veterans Affairs patient population. Arch Intern Med. 2003;163(7):821-9. doi: 10.1001/archinte.163.7.821.

154. Gual A, Segura L, Contel M, Heather N, Colom J. Audit-3 and audit-4: effectiveness of two short forms of the alcohol use disorders identification test. Alcohol Alcoholism. 2002;37(6):591-6. doi: 10.1093/alcalc/37.6.591.

155. Aalto M, Hannu A, Halme JT, Seppä K. AUDIT and its abbreviated versions in detecting heavy and binge drinking in a general population survey. Drug Alcohol Depend. 2009;103(1-2):25-9. doi: 10.1016/j.drugalcdep.2009.02.013.

156. Collins RL, McNair LD. Minority women and alcohol use. Alcohol Research & Health. 2002;26(4):251.

157. Choi JH, Lee J, Yang S, Kim J. Genetic variations in taste perception modify alcohol drinking behavior in Koreans. Appetite. 2017;113:178-86. doi: 10.1016/j.appet.2017.02.022.

158. Fushan AA, Simons CT, Slack JP, Manichaikul A, Drayna D. Allelic polymorphism within the TAS1R3 promoter is associated with human taste sensitivity to sucrose. Curr Biol. 2009;19(15):1288-93. doi: 10.1016/j.cub.2009.06.015.

159. Beckett E, Duesing, K, Boyd, L, Yates Z, Veysey M, Lucock M. A potential sex dimorphism in the relationship between bitter taste and alcohol consumption. Food Funct. 2017;8(3):1116-23. doi: 10.1039/C6FO01759B.

160. Fu D, Riordan S, Kieran S, Andrews RA, Ring HZ, Ring BZ. Complex relationship between TAS2 receptor variations, bitterness perception, and alcohol consumption observed in a population of wine consumers. Food Funct. 2019;10(3):1643-52. doi: 10.1039/C8FO01578C.

161. Dotson CD, Wallace MR, Bartoshuk LM, Logan HL. Variation in the gene TAS2R13 is associated with differences in alcohol consumption in patients with head and neck cancer. Chem Senses. 2012;37(8):737-44. doi: 10.1093/chemse/bjs063.

162. Keller M, Liu X, Wohland T, Rohde K, Gast MT, Stumvoll M, et al. TAS2R38 and its influence on smoking behavior and glucose homeostasis in the German Sorbs. PLoS One. 2013;8(12):e80512. doi: 10.1371/journal.pone.0080512.

163. Colares-Bento FCJ, Souza VC, Toledo JO, Moraes CF, Alho CS, Lima RM, et al. Implication of the G145C polymorphism (rs713598) of the TAS2r38 gene on food consumption by Brazilian older women. Arch Gerontol Geriatr. 2012;54(2):e13-e8. doi: 10.1016/j.archger.2011.05.019.

164. Lucock M, Ng X, Boyd L, Skinner V, Wai R, Tang S, et al. TAS2R38 bitter taste genetics, dietary vitamin C, and both natural and synthetic dietary folic acid predict folate status, a key micronutrient in the pathoaetiology of adenomatous polyps. Food Funct. 2011;2(8):457-65. doi: 10.1039/c1fo10054h.

165. Bering AB, Pickering G, Liang PJCP. TAS2R38 single nucleotide polymorphisms are associated with prop—but not thermal—tasting: a pilot study. Chem Percept. 2014;7(1):23-30. doi: 10.1007/s12078-013-9160-1.

166. Wooding S, Gunn H, Ramos P, Thalmann S, Xing C, Meyerhof W. Genetics and bitter taste responses to goitrin, a plant toxin found in vegetables. Chem Senses. 2010;35(8):685-92. doi: 10.1093/chemse/bjq061.

167. Carrai M, Campa D, Vodicka P, Flamini R, Martelli I, Slyskova J, et al. Association between taste receptor (TAS) genes and the perception of wine characteristics. Sci Rep. 2017;7(1):1-7. doi: 10.1038/s41598-017-08946-3.

168. Keller KL, Olsen A, Cravener TL, Bloom R, Chung WK, Deng L, et al. Bitter taste phenotype and body weight predict children's selection of sweet and savory foods at a palatable test-meal. Appetite. 2014;77:115-23. doi: 10.1016/j.appet.2014.02.019.

169. . Mennella JA, Reed DR, Roberts KM, Mathew PS, Mansfield CJ. Age-related differences in bitter taste and efficacy of bitter blockers. PloS One. 2014;9(7):e103107. doi: 10.1371/journal.pone.0103107.

170. Risso DS, Giuliani C, Antinucci M, Morini G, Garagnani P, Tofanelli S, et al. A bio-cultural approach to the study of food choice: The contribution of taste genetics, population and culture. Appetite. 2017;114:240-7. doi: 10.1016/j.appet.2017.03.046.

171. Ooi SX, Lee PL, Law HY, Say YH. Bitter receptor gene (TAS2R38) P49A genotypes and their associations with aversion to vegetables and sweet/fat foods in Malaysian subjects. Asia Pac J Clin Nutr. 2010;19(4):491-8.

172. Behrens M, Gunn HC, Ramos PC, Meyerhof W, Wooding SP. Genetic, functional, and phenotypic diversity in TAS2R38-mediated bitter taste perception. Chem Senses. 2013;38(6):475-84. doi: 10.1093/chemse/bjt016.

173. Lipchock SV, Reed DR, Mennella JA. Relationship between bitter-taste receptor genotype and solid medication formulation usage among young children: a retrospective analysis. Clin Ther. 2012;34(3):728-33. doi: 10.1016/j.clinthera.2012.02.006.

174. Perna S, Riva A, Nicosanti G, Carrai M, Barale R, Vigo B, et al. Association of the bitter taste receptor gene TAS2R38 (polymorphism RS713598) with sensory responsiveness, food preferences, biochemical parameters and body-composition markers. A cross-sectional study in Italy. Int J Food Sci Nutr. 2018;69(2):245-52. doi: 10.1080/09637486.2017.1353954.

175. Joseph PV, Reed DR, Mennella JA. Individual Differences Among Children in Sucrose Detection Thresholds: Relationship With Age, Gender, and Bitter Taste Genotype. Nurs Res. 2016:3-12. doi: 10.1097/NNR.0000000000000138.

176. Duffy VB, Davidson AC, Kidd JR, Kidd KK, Speed WC, Pakstis AJ, et al. Bitter receptor gene (TAS2R38), 6-n-propylthiouracil (PROP) bitterness and alcohol intake. Alcohol Clin Exp Res. 2004;28(11):1629-37. doi: 10.1097/01.ALC.0000145789.55183.D4.

177. Vinuthalakshmi K, Sheik N, Mustak M S. TAS2R38 gene polymorphism and its association with taste perception, alcoholism and tobacco chewing among the Koraga-a primitive tribal population of Southwest coast of India. Meta Gene. 2019;20:100549. doi :10.1016/J.MGENE.2019.100549.

178. Ramos-Lopez O, Roman S, Martinez-Lopez E, Gonzalez-Aldaco K, Ojeda-Granados C, Sepulveda-Villegas M, et al. Association of a novel TAS2R38 haplotype with alcohol intake among Mexican-Mestizo population. Ann Hepatol. 2015;14(5):729-34. doi: 10.1016/S1665-2681(19)30768-9.

179. Wang JC, Hinrichs AL, Bertelsen S, Stock H, Budde JP, Dick DM, et al. Functional variants in TAS2R38 and TAS2R16 influence alcohol consumption in high-risk families of

African-American origin. Alcohol Clin Exp Res. 2007;31(2):209-15. doi: 10.1111/j.1530-0277.2006.00297.x.

180. Choi J-HL, J.; Oh, J. H.; Chang, H. J.; Sohn, D. K.; Shin, A.; Kim, J. Variations in the bitterness perception-related genes TAS2R38 and CA6 modify the risk for colorectal cancer in Koreans. Oncotarget. 2017;8(13):21253. doi: 10.18632/oncotarget.15512.

181. Choi JH, Lee J, Choi IJ, Kim YW, Ryu KW, Kim J. Genetic variation in the TAS2R38 bitter taste receptor and gastric cancer risk in Koreans. Sci Rep. 2016 Jun 1;6(1):1-8. doi: 10.1038/srep26904.

182. Timpson NJ, Christensen M, Lawlor DA, Gaunt TR, Day IN, Ebrahim S, et al. TAS2R38 (phenylthiocarbamide) haplotypes, coronary heart disease traits, and eating behavior in the British Women's Heart and Health Study. Am J Clin Nutr. 2005;81(5):1005-11. doi: 10.1093/ajcn/81.5.1005.

183. Choi J-H. Variation in the TAS2R38 bitterness receptor gene was associated with food consumption and obesity risk in Koreans. Nutrients. 2019;11(9):1973. doi: 10.3390/nu11091973.

184. Schembre SM, Cheng I, Wilkens LR, Albright CL, Marchand le L. Variations in bitter-taste receptor genes, dietary intake, and colorectal adenoma risk. Nutr Cancer. 2013;65(7):982-90. doi: 10.1080/01635581.2013.807934.

185. Timpson NJ, Heron J, Day IN, Ring SM, Bartoshuk LM, Horwood J, et al. Refining associations between TAS2R38 diplotypes and the 6-n-propylthiouracil (PROP) taste test: findings from the Avon Longitudinal Study of Parents and Children. BMC Genet. 2007;8(1):1-9. doi: 10.1186/1471-2156-8-51.

186. Cabras T, Melis M, Castagnola M, Padiglia A, Tepper BJ, Messana I, et al. Responsiveness to 6-n-propylthiouracil (PROP) is associated with salivary levels of two specific basic proline-rich proteins in humans. PLoS One. 2012;7(2). doi: 10.1371/journal.pone.0030962.

187. Hayes JE, Bartoshuk LM, Kidd JR, Duffy VB. Supertasting and PROP bitterness depends on more than the TAS2R38 gene. Chem Senses. 2008;33(3):255-65. doi: 10.1093/chemse/bjm084.

188. Calò C, Padiglia A, Zonza A, Corrias L, Contu P, Tepper BJ, et al. Polymorphisms in TAS2R38 and the taste bud trophic factor, gustin gene co-operate in modulating PROP taste phenotype. Physiol Behav. 2011;104(5):1065-71. doi: 10.1016/j.physbeh.2011.06.013.

189. Negri R, Di Feola M, Di Domenico S, Scala MG, Artesi G, Valente S, et al. Taste perception and food choices. J Pediatr Gastroenterol Nutr. 2012;54(5):624-9. doi: 10.1097/MPG.0b013e3182473308.

190. Melis M, Atzori E, Cabras S, Zonza A, Calò C, Muroni P, et al. The gustin (CA6) gene polymorphism, rs2274333 (A/G), as a mechanistic link between PROP tasting and fungiform taste papilla density and maintenance. PLoS One. 2013;8(9):e74151. doi: 10.1371/journal.pone.0074151.

191. Campbell MC, Ranciaro A, Froment A, Hirbo J, Omar S, Bodo J-M, et al. Evolution of functionally diverse alleles associated with PTC bitter taste sensitivity in Africa. Mol Biol Evol. 2012;29(4):1141-53. doi: 10.1093/molbev/msr293.

192. Deshaware S, Singhal R. Genetic variation in bitter taste receptor gene TAS2R38, PROP taster status and their association with body mass index and food preferences in Indian population. Gene. 2017;627:363-8. doi: 10.1016/j.gene.2017.06.047.

193. Mennella JA, Pepino MY, Reed DR. Genetic and environmental determinants of bitter perception and sweet preferences. Pediatrics. 2005;115(2):e216-e22. doi: 10.1542/peds.2004-1582.

194. Melis M, Sollai G, Muroni P, Crnjar R, Tomassini Barbarossa IJN. Associations between orosensory perception of oleic acid, the common single nucleotide polymorphisms (rs1761667 and rs1527483) in the CD36 gene, and 6-n-propylthiouracil (PROP) tasting. Nutrients. 2015;7(3):2068-84. doi: 10.3390/nu7032068.

195. Duffy VB. Associations between oral sensation, dietary behaviors and risk of cardiovascular disease (CVD). Appetite. 2004;43(1):5-9. doi: 10.1016/j.appet.2004.02.007.

196. Garneau NL, Nuessle TM, Sloan MM, Santorico SA, Coughlin BC, Hayes JE. Crowdsourcing taste research: genetic and phenotypic predictors of bitter taste perception as a model. Front Integr Neurosci. 2014;8:33. doi: 10.3389/fnint.2014.00033.

197. Robino A, Mezzavilla M, Pirastu N, Dognini M, Tepper BJ, Gasparini P. A population-based approach to study the impact of PROP perception on food liking in populations along the Silk Road. PLoS One. 2014;9(3):e91716. doi: 10.1371/journal.pone.0091716.

198. Sandell MA, Breslin PA. Variability in a taste-receptor gene determines whether we taste toxins in food. Curr Biol. 2006;16(18):R792-R4. doi: 10.1016/j.cub.2006.08.049.

199. Nolden AA, McGeary JE, Hayes JE. Differential bitterness in capsaicin, piperine, and ethanol associates with polymorphisms in multiple bitter taste receptor genes. Physiol Behav. 2016;156:117-27. doi: 10.1016/j.physbeh.2016.01.017.

200. Bell L, Methven L, Wagstaff C. The influence of phytochemical composition and resulting sensory attributes on preference for salad rocket (Eruca sativa) accessions by consumers of varying TAS2R38 diplotype. Food Chem. 2017;222:6-17. doi: 10.1016/j.foodchem.2016.11.153.

201. Suomela JP, Vaarno J, Sandell M, Lehtonen HM, Tahvonen R, Viikari J, et al. Children's hedonic response to berry products: Effect of chemical composition of berries and hTAS2R38 genotype on liking. Food Chem. 2012;135(3):1210-9. doi: 10.1016/j.foodchem.2012.05.079.

202. Sandell M HU, Mikkilä V, Mononen N, Kähönen M, Männistö S, et.al. Genetic variation in the hTAS2R38 taste receptor and food consumption among Finnish adults. Genes Nutr. 2014;9(6):433. doi: 10.1007/s12263-014-0433-3.

203. Ong JS, Hwang LD, Zhong VW, An J, Gharahkhani P, Breslin PA, et.al. Understanding the role of bitter taste perception in coffee, tea and alcohol consumption through Mendelian randomization. Sci Rep. 2018;8(1):1-8. doi: 10.1038/s41598-018-34713-z.

204. Padiglia A, Zonza A, Atzori E, Chillotti C, Calo C, Tepper BJ, et al. Sensitivity to 6-n-propylthiouracil is associated with gustin (carbonic anhydrase VI) gene polymorphism, salivary zinc, and body mass index in humans. Am J Clin Nutr. 2010;92(3):539-45. doi: 10.3945/ajcn.2010.29418.

205. Gabriel S, Ziaugra L, Tabbaa D. SNP genotyping using the Sequenom MassARRAY iPLEX platform. Curr Protoc Hum Genet. 2009;60(1):2-12. doi: 10.1002/0471142905.hg0212s60.

206. Oaxaca R. Male-Female Wage Differentials in Urban Labor Markets. Int Econ Rev. 1973;14(3):693-709. doi: 10.2307/2525981.

207. Blinder A. Wage Discrimination: Reduced Form and Structural Estimates. J Hum Resour. 1973;8(4):436-55. doi:10.2307/144855.

208. Powers D, Yoshioka H, Yun MS. Mvdcmp: Multivariate Decomposition for Nonlinear Response Models. Stata Journal. 2012;11(4):556-76. doi:10.1177/1536867X1201100404.

209. Cleves MA. Exploratory analysis of single nucleotide polymorphism (SNP) for quantitative traits. The Stata Journal. 2005;5(2):141-53. doi:10.1177/1536867X0500500201.

210. Cleves M. Hardy-Weinberg equilibrium test and allele frequency estimation. STATA Technical Bulletin. 1999;8(48).

211. Rohlfs R, Weir B. Distributions of Hardy–Weinberg equilibrium test statistics. Genetics. 2008;180(3):1609-16. doi: 10.1534/genetics.108.088005.

212. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097. doi: 10.1371/journal.pmed.1000097.

213. Sohani ZN, Meyre D, de Souza RJ, Joseph PG, Gandhi M, Dennis BB, et al. Assessing the quality of published genetic association studies in meta-analyses: the quality of genetic studies (Q-Genie) tool. BMC Genet. 2015;16(1):1-8. doi: 10.1186/s12863-015-0211-2.

214. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906. doi: 10.1016/j.ijsu.2021.105906.

215. Hinrichs AL, Wang JC, Bufe B, Kwon JM, Budde J, Allen R, et al. Functional variant in a bitter-taste receptor (hTAS2R16) influences risk of alcohol dependence. Am J Hum Genet. 2006;78(1):103-11. doi: 10.1086/499253.

216. Choi J-H, Lee J, Yang S, Kim J. Genetic variations in taste perception modify alcohol drinking behavior in Koreans. Appetite. 2017;113:178-86. doi: 10.1016/j.appet.2017.02.022.

217. Dotson CD, Shaw HL, Mitchell BD, Munger SD, Steinle NI. Variation in the gene TAS2R38 is associated with the eating behavior disinhibition in Old Order Amish women. Appetite. 2010;54(1):93-9. doi: 10.1016/j.appet.2009.09.011.

218. Popova S, Rehm J, Patra J, Zatonski W. Comparing alcohol consumption in central and eastern Europe to other European countries. Alcohol Alcohol. 2007;42(5):465-73. doi: 10.1093/alcalc/agl124.

219. Loring B. Alcohol and inequities: guidance for addressing inequities in alcohol-related harm: World Health Organization. Regional Office for Europe; 2014.

220. O'Brien H, Callinan S, Livingston M, Doyle JS, Dietze PM. Population patterns in alcohol use disorders identification test (AUDIT) scores in the Australian population; 2007–2016. Aust N Z J Public Health. 2020;44(6):462-7. doi: 10.1111/1753-6405.13043.

221. Källmén H, Berman AH, Elgan TH, Wennberg P. Alcohol habits in Sweden during 1997–2018: a repeated cross-sectional study. Nord J Psychiatry. 2019;73(8):522-6. doi: 10.1080/08039488.2019.1660912.

222. Paksi B, Demetrovics Z, Magi A, Felvinczi K. The methodology and sample description of the National Survey on Addiction Problems in Hungary 2015 (NSAPH 2015). Neuropsychopharmacol Hung. 2017;19(2):55-85.

223. Hungarian Central Statistical Office. STADAT Table 4.1.1.38. Distribution of population by alcohol consumption patterns. Available online: https://www.ksh.hu/stadat_files/ege/en/ege0038.html. Accessed on February 10, 2023.

224. Knibbe RA, Derickx M, Kuntsche S, Grittner U, Bloomfield K. A comparison of the Alcohol Use Disorder Identification Test (AUDIT) in general population surveys in nine European countries. Alcohol Alcohol Suppl. 2006;41(suppl_1):i19-i25. doi: 10.1093/alcalc/agl072.

225. World Health Organiztion. Health for All Database, Pure Alcohol Consumption, Age 15+ (Litres Per Capita). Available online: https://gateway.euro.who.int/en/indicators/hfa_426-3050-pure-alcohol-consumption-litres-per-capita-age-15plus/.

226. Sudzinova A, Nagyova I, Studencan M, Rosenberger J, Skodova Z, Vargova H, et al. Roma coronary heart disease patients have more medical risk factors and greater severity of coronary heart disease than non-Roma. Int J Public Health. 2013;58(3):409-15. doi: 10.1007/s00038-013-0462-5.

227. Ostrihoňová T, Bérešová J. Occurrence of metabolic syndrome and its risk factors amongst a selected group of Roma inhabitants. Hygiena. 2010;55(1):7-14.

228. Kell K, Judd S, Pearson K, Shikany J, Fernández J. Associations between socio-economic status and dietary patterns in US black and white adults. Br J Nutr. 2015;113(11):1792-9. doi: 10.1017/S0007114515000938.

229. Noble N, Paul C, Conigrave K, Lee K, Blunden S, Turon H, et al. Does a retrospective seven-day alcohol diary reflect usual alcohol intake for a predominantly disadvantaged Australian Aboriginal population? Subst Use Misuse. 2015;50(3):308-19. doi: 10.3109/10826084.2014.980951.

230. Chartier KG, Vaeth PA, Caetano R. Focus on: ethnicity and the social and health harms from drinking. Alcohol Res. 2013.

231. Petek D, Rotar Pavlič D, Švab I, Lolić D. Attitudes of Roma toward smoking: qualitative study in Slovenia. Croat Med J. 2006;47(2):344-7.

232. Bosque-Prous M, Espelt A, Borrell C, Bartroli M, Guitart AM, Villalbí JR, et al. Gender differences in hazardous drinking among middle-aged in Europe: the role of social context and women's empowerment. Eur J Public Health. 2015;25(4):698-705. doi: 10.1093/eurpub/cku234.

233. White A, Castle IJP, Chen CM, Shirley M, Roach D, Hingson R. Converging patterns of alcohol use and related outcomes among females and males in the United States, 2002 to 2012. Alcohol Clin Exp Res. 2015;39(9):1712-26. doi: 10.1111/acer.12815.

234. Svačinová K, Pechholdová M, Vrabcová J. Alcohol consumption and marital status in the Czech Republic. Quantitative Methods in Demography: Methods and Related Applications in the Covid-19 Era. 2022:277-90. doi: 10.1007/978-3-030-93005-9_18.

235. Power C, Rodgers B, Hope S. Heavy alcohol consumption and marital status: disentangling the relationship in a national study of young adults. Addiction. 1999;94(10):1477-87. doi: 10.1046/j.1360-0443.1999.941014774.x.

236. Liang W, Chikritzhs T. Brief report: marital status and alcohol consumption behaviours. J Subst Use. 2012;17(1):84-90. doi: 10.3109/14659891.2010.538463.

237. Stack S, Eshleman JR. Marital status and happiness: A 17-nation study. J Marriage Fam. 1998:527-36. doi: 10.2307/353867.

238. Lindström M. Marital status, social capital, material conditions and self-rated health: a population-based study. Health Policy. 2009;93(2-3):172-9. doi: 10.1016/j.healthpol.2009.05.010.

239. Scott KM, Wells JE, Angermeyer M, Brugha TS, Bromet E, Demyttenaere K, et al. Gender and the relationship between marital status and first onset of mood, anxiety and substance use disorders. Psychol Med. 2010;40(9):1495-505. doi: 10.1017/S0033291709991942.

240. Kendler KS, Lönn SL, Salvatore J, Sundquist J, Sundquist K. Effect of marriage on risk for onset of alcohol use disorder: a longitudinal and co-relative analysis in a Swedish national sample. Am J Psychiatry. 2016;173(9):911-8. doi: 10.1176/appi.ajp.2016.15111373.

241. Liew H. The effects of marital status transitions on alcohol use trajectories. Longit Life Course Stud. 2012;3(3):332-45. doi: 10.14301/llcs.v3i3.187.

242. Mihailovic N, Szőllősi GJ, Rancic N, János S, Boruzs K, Nagy AC, et al. Alcohol consumption among the elderly citizens in Hungary and Serbia—comparative assessment. Int J Environ Res Public Health. 2020;17(4):1289. doi: 10.3390/ijerph17041289.

243. Ryan M, Merrick EL, Hodgkin D, Horgan CM, Garnick DW, Panas L, et al. Drinking patterns of older adults with chronic medical conditions. J Gen Intern Med. 2013;28:1326-32. doi: 10.1007/s11606-013-2409-1.

244. Hajema KJ, Knibbe RA, Drop MJ. Changes in alcohol consumption in a general population in The Netherlands: a 9-year follow-up study. Addiction. 1997;92(1):49-60. doi:10.1111/j.1360-0443.1997.tb03637.x.

245. Kemm J. An analysis by birth cohort of alcohol consumption by adults in Great Britain 1978–1998. Alcohol Alcohol. 2003;38(2):142-7. doi: 10.1093/alcalc/agg039.

246. Ramstedt M, Hope A. The Irish drinking habits of 2002—Drinking and drinking-related harm in a European comparative perspective. J Subst Use. 2005;10(5):273-83. doi:10.1080/14659890412331319443.

247. Afanasieva L, Bukrieieva I, Glyns' ka L, Hlebova NI, Semikin M. Family Roles of Roma and Ways to Overcome its Socio-Cultural Isolation. Journal of History Culture and Art Research. 2020;9(3):288-96. doi:10.7596/taksad.v9i3.2716.

248. Bartoshuk LM, Duffy VB, Miller IJ. PTC/PROP tasting: anatomy, psychophysics, and sex effects. Physiol Behav. 1994;56(6):1165-71. doi: 10.1016/0031-9384(94)90361-1.

249. Prescott J, Swain-Campbell N. Responses to repeated oral irritation by capsaicin, cinnamaldehyde and ethanol in PROP tasters and non-tasters. Chem Senses. 2000;25(3):239-46. doi: 10.1093/chemse/25.3.239.

250. Bartoshuk LM. The biological basis of food perception and acceptance. Food Qual Prefer. 1993;4(1-2):21-32. doi :10.1016/0950-3293(93)90310-3.

251. Guinard J-X, Zoumas-Morse C, Dietz J, Goldberg S, Holz M, Heck E, et al. Does consumption of beer, alcohol, and bitter substances affect bitterness perception? Physiol Behav. 1996;59(4-5):625-31. doi: 10.1016/0031-9384(95)02124-8.

252. Bartoshuk L, Duffy V, Fast K, Kveton J, Lucchina L, Phillips M, et al. What makes a supertaster. Chem Senses. 2001;26(8):1074.

253. Delwiche JF, Buletic Z, Breslin PA. Relationship of papillae number to bitter intensity of quinine and PROP within and between individuals. Physiol Behav. 2001;74(3):329-37. doi: 10.1016/s0031-9384(01)00568-6.

254. Bachmanov AA, Bosak NP, Floriano WB, Inoue M, Li X, Lin C, et al. Genetics of sweet taste preferences. Flavour Fragr J. 2011;26(4):286-94. doi: 10.1002/ffj.2074.

255. Levine AS, Kotz CM, Gosnell BA. Sugars: hedonic aspects, neuroregulation, and energy balance. Am J Clin Nutr. 2003;78(4):834S-42S. doi: 10.1093/ajcn/78.4.834S.

256. Hayes JE, Feeney EL, Nolden AA, McGeary JE. Quinine bitterness and grapefruit liking associate with allelic variants in TAS2R31. Chem Senses. 2015;40(6):437-43. doi: 10.1093/chemse/bjv027.

257. Pickering GJ, Hayes JE. Influence of biological, experiential and psychological factors in wine preference segmentation. Aust J Grape Wine Res. 2017;23(2):154-61. doi: 10.1111/ajgw.12266.

258. Hayes JE, Pickering GJ. Wine expertise predicts taste phenotype. Am J Enol Vitic. 2012;63(1):80-4. doi: 10.5344/ajev.2011.11050.

259. Xiao QY, Fang XC, Li XQ, Fei GJ. Ethnic differences in genetic polymorphism associated with irritable bowel syndrome. World J Gastroenterol. 2020;26(17):2049. doi: 10.3748/wjg.v26.i17.2049.

260. . Harishankar M, Selvaraj P, Bethunaickan R. Influence of genetic polymorphism towards pulmonary tuberculosis susceptibility. Front Med. 2018;5:213. doi: 10.3389/fmed.2018.00213.

261. Han C, Han XK, Liu FC, Huang JF. Ethnic differences in the association between angiotensin-converting enzyme gene insertion/deletion polymorphism and peripheral vascular disease: a meta-analysis. Chronic Dis Transl Med. 2017;3(4):230-41. doi: 10.1016/j.cdtm.2017.07.002.

262. Chen D, Liu L, Xiao Y, Peng Y, Yang C, Wang Z. Ethnic-specific meta-analyses of association between the OPRM1 A118G polymorphism and alcohol dependence among Asians and Caucasians. Drug Alcohol Depend. 2012;123(1-3):1-6. doi: 10.1016/j.drugalcdep.2011.10.012.

263. Jia Y, Xie X, Shi X, Li S. Associations of common IL-4 gene polymorphisms with cancer risk: A meta-analysis. Mol Med Rep. 2017;16(2):1927-45. doi: 10.3892/mmr.2017.6822.

264. Castaño-Rodríguez N, Kaakoush NO, Goh K-L, Fock KM, Mitchell HM. The role of TLR2, TLR4 and CD14 genetic polymorphisms in gastric carcinogenesis: a case-control study and meta-analysis. PLoS One. 2013;8(4):e60327. doi: 10.1371/journal.pone.0060327.

265. Jing L, Su L, Ring BZ. Ethnic background and genetic variation in the evaluation of cancer risk: a systematic review. PloS One. 2014;9(6):e97522. doi: 10.1371/journal.pone.0097522.

266. Swinney RM, Beuten J, Collier III AB, Chen TT-L, Winick NJ, Pollock BH, et al. Polymorphisms in CYP1A1 and ethnic-specific susceptibility to acute lymphoblastic leukemia in children. Cancer Epidemiol Biomarkers Prev. 2011;20(7):1537-42. doi: 10.1158/1055-9965.EPI-10-1265.

267. Goldenberg I, Moss AJ, Ryan D, McNitt S, Eberly SW, Zareba W. Polymorphism in the angiotensinogen gene, hypertension, and ethnic differences in the risk of recurrent coronary events. Hypertension. 2006;48(4):693-9. doi: 10.1161/01.HYP.0000239204.41079.6b.

268. Radha V, Vimaleswaran KS, Babu HNS, Abate N, Chandalia M, Satija P, et al. Role of genetic polymorphism peroxisome proliferator–activated receptor-γ2 Pro12Ala on ethnic susceptibility to diabetes in South-Asian and Caucasian subjects: evidence for heterogeneity. Diabetes Care. 2006;29(5):1046-51. doi: 10.2337/diacare.2951046.

269. Burgess B, Melis M, Scoular K, Driver M, Schaich KM, Keller KL, et al. Effects of CD36 genotype on oral perception of oleic acid supplemented safflower oil emulsions in two ethnic groups: a preliminary study. J Food Sci. 2018;83(5):1373-80. doi: 10.1111/1750-3841.14115.

270. Garte S. The role of ethnicity in cancer susceptibility gene polymorphisms: the example of CYP1A1. Carcinogenesis. 1998;19(8):1329-32. doi: 10.1093/carcin/19.8.1329.

271. Gilligan C, Anderson KG, Ladd BO, Yong YM, David M. Inaccuracies in survey reporting of alcohol consumption. BMC Public Health. 2019;19(1):1-11. doi: 10.1186/s12889-019-7987-3.

272. Hoonpongsimanont W, Ghanem G, Chen Y, Sahota PK, Carroll C, Barrios C, et al. Underreporting of alcohol use in trauma patients: A retrospective analysis. Substance Abus. 2021;42(2):192-6. doi: 10.1080/08897077.2019.1671936.

273. Islam S, Small, N., Bryant, M., Yang, T., Cronin de Chavez, A., Saville, F. and Dickerson, J. Addressing obesity in Roma communities: a community readiness approach. Int J Hum Rights Healthc. 2019;12(2):79-90. doi: 10.1108/IJHRH-06-2018-0038.

274. Kósa Z, Moravcsik-Kornyicki Á, Diószegi J, Roberts B, Szabó Z, Sándor J, Ádány R. Prevalence of metabolic syndrome among Roma: A comparative health examination survey in Hungary. Eur J Public Health. 2015 1;25(2):299-304. doi: 10.1093/eurpub/cku157.

275. Macejova Z, Kristian P, Janicko M, Halanova M, Drazilova S, Antolova D, et al. The Roma Population Living in Segregated Settlements in Eastern Slovakia Has a Higher Prevalence of Metabolic Syndrome, Kidney Disease, Viral Hepatitis B and E, and Some Parasitic Diseases Compared to the Majority Population. Int J Environ Res Public Health. 2020;17(9):3112. doi: 10.3390/ijerph17093112.

276. Ádány R, Pikó P, Fiatal S, Kósa Z, Sándor J, Bíró É, et.al. Prevalence of insulin resistance in the Hungarian general and Roma populations as defined by using data generated in a complex health (interview and examination) survey. Int J Environ Res Public Health. 2020 Jul;17(13):4833. doi: 10.3390/ijerph17134833.

277. Kósa Z, Széles G, Kardos L, Kósa K, Németh R, Országh S, et.al. A comparative health survey of the inhabitants of Roma settlements in Hungary. Am J Public Health. 2007;97(5):853-9. doi: 10.2105/AJPH.2005.072173.

278. Smith JL, Estus S, Lennie TA, Moser DK, Chung ML, Mudd-Martin GJBrfn. TAS2R38 PAV haplotype predicts vegetable consumption in community-dwelling caucasian adults at risk for cardiovascular disease. Biol Res Nurs. 2020;22(3):326-33. doi: 10.1177/1099800420913935.

279. Feeney EL, Hayes JEJP, behavior. Exploring associations between taste perception, oral anatomy and polymorphisms in the carbonic anhydrase (gustin) gene CA6. Physiol Behav. 2014;128:148-54. doi: 10.1016/j.physbeh.2014.02.013.

280. Risso D. Genetic Epidemiology of Taste Perception and Cigarette Use. 2017.

281. Allen AL, McGeary JE, Hayes JEJ. Rebaudioside A and Rebaudioside D Bitterness do not Covary with Acesulfame-K Bitterness or Polymorphisms in TAS2R9 and TAS2R31. Chemosens Percept. 2013;6(3):109-17. doi: 10.1007/s12078-013-9149-9.

282. Knaapila A, Hwang L-D, Lysenko A, Duke FF, Fesi B, Khoshnevisan A, et al. Genetic analysis of chemosensory traits in human twins. Chem Senses. 2012;37(9):869-81. doi: 10.1093/chemse/bjs070.

283. Pirastu N, Kooyman M, Traglia M, Robino A, Willems SM, Pistis G, et al. Association analysis of bitter receptor genes in five isolated populations identifies a significant correlation between TAS2R43 variants and coffee liking. PLoS One. 2014;9(3):e92065. doi: 10.1371/journal.pone.0092065.

284. Ledda M, Kutalik Z, Souza Destito MC, Souza MM, Cirillo CA, Zamboni A, et al. GWAS of human bitter taste perception identifies new loci and reveals additional complexity of bitter taste genetics. Hum Mol Genet. 2014;23(1):259-67. doi: 10.1093/hmg/ddt404.

285. Risso D, Morini G, Pagani L, Quagliariello A, Giuliani C, De Fanti S, et al. Genetic signature of differential sensitivity to stevioside in the Italian population. Genes Nutr. 2014;9(3):1-9. doi: 10.1007/s12263-014-0401-y.

286. Dotson CD, Zhang L, Xu H, Shin YK, Vigues S, Ott SH, et al. Bitter taste receptors influence glucose homeostasis. PloS One. 2008;3(12):e3974. doi: 10.1371/journal.pone.0003974.

287. Fushan AA, Simons CT, Slack JP, Drayna DJCs. Association between common variation in genes encoding sweet taste signaling components and human sucrose perception. Chem Senses. 2010;35(7):579-92. doi: 10.1093/chemse/bjq063.

288. STRING Database (Available from: https://string-db.org) Accessed on December 3,2022.

289. Schütz M, Oertel BG, Heimann D, Doehring A, Walter C, Dimova V, et al. Consequences of a human TRPA1 genetic variant on the perception of nociceptive and olfactory stimuli. PLoS One. 2014;9(4):e95592. doi: 10.1371/journal.pone.0095592.

ACKNOWLEDGMENT

At first, I would like to convey my sincere gratitude and appreciation to Professor Dr. Róza Ádány to provide the opportunity to work on my PhD research. I am grateful to the professor for her continuous support and guidance in every aspect of my study and research during the whole PhD study period.

I would like to express my earnest gratefulness to my supervisor Dr. Judit Diószegi for her constant reliable supervision. My heartiest thankfulness to her for providing me sincere guidance, valuable advice and encouragement throughout my PhD research works and writing of manuscripts as well as preparation of dissertation report.

I am thankful to Professor Dr. János Sándor, Head of the Department of Public Health and Epidemiology of University of Debrecen, for permitting me to utilize the facilities available in the department.

I would like to thank Dr. Zsigmond Kósa, Dr. Péter Pikó and Dr. Ferenc Vincze for their supports, valuable advice and guidance which help me to complete my research work in time.

I am deeply grateful to all staff of the Department of Public Health and Epidemiology of University of Debrecen, for their kindness and endless support throughout my study in this department.

I am also grateful to the authority of the Stipendium Hungaricum Scholarship provider for their enormous support to continue my PhD study.

FUNDING

This work was supported by the GINOP-2.3.2-15- 2016-00005 project. The project was co-financed by the European Union under the European Social Fund and European Regional Development Fund, as well as by the Hungarian Academy of Sciences (TK2016-78) and the Eötvös Loránd Research Network (TKCS-2021/32). Project no. 135784 has also been implemented with the support provided by the National Research, Development, and Innovation Fund of Hungary, financed under the K_20 funding scheme.

APPENDIX

Table S1. The prevalence hazardous and harmful alcohol use among Hungarian general (HG) and Roma (HR) populations by gender (based on the WHO cut off "≥8").

		Prevalence hazardous alcohol use n(%)	p-value*
Male	HG	13 (7.39%)	0.054
	HR	14 (14.74%)	
Female	HG	1 (0.45%)	0.229
	HR	5 (1.84%)	
Total	HG	14 (3.50%)	0.253
	HR	19 (5.18%)	

*HG: Hungarian general population; HR: Hungarian Roma population; *Pearson chi-square and Fisher's exact test.*

Table S2. Factors influencing having AUDIT ≥8 based on binary logistic regression

Characteristics	Variable	OR (95% CI)
Ethnicity	HG	1.00
	HR*	1.37 (0.48-3.90)
Education	Primary or less	1.00
	Secondary	0.92 (0.31-2.70)
	High school	0.48 (0.11-2.15)
	Tertiary education	0.00 (0.00-0.00)
Economic activity	Worker	1.00
	Pension, other allowance, student	1.47 (0.48-4.49)
	Unemployed	1.62 (0.56-4.68)
Marital status	Married	1.00
	Single	1.36 (0.49-3.77)
	Widow, divorced	1.08 (0.37-3.22)
Financial status	Good	1.00
	Satisfactory	0.56 (0.20-1.55)
	Bad	1.21 (0.40-3.68)
Age category (years)	20-34	1.00
	35-49	10.58 (1.30-86.22)
	50+	**9.31 (1.09-79.31)**
Gender	Male	1.00
	Female	**0.09 (0.04-0.24)**

HG: Hungarian general population; HR: Hungarian Roma population. AUDIT: AUDIT total scores. OR: odds ratio, CI: confidence interval. Bold indicates statistical significance.

Table S3. Description of single nucleotide polymorphismsms included in the systematic review

Gene/*Nearest Gene*	Encoded protein	SNP ID	Alleles (dbSNP)	Effect on taste perception/preference (if available)
TAS2R38	taste 2 receptor member 38	rs713598, rs1726866, rs10246939	C>A, G, T G>A T>C	When haplotypes are considered rs713598 located first (P/A) followed by rs1726866 is the second location (A/V) and rs1024693 is the third location (V/I) (278). PAV (proline–alanine–valine) homozygotes, the dominant haplotype characterizes the taster phenotype while AVI (alanine-valine-isoleucine) homozygotes outline the non-taster phenotype and heterozygotes are designated by intermediate sensitivity to PROP and PTC (91). From the perspective of bitter taste signal transduction rs713598 possesses the highest effect and rs1726866 has weaker effects. On the other hand, rs10246939 showed no measurable effect (83).
TAS1R2	taste 1 receptor member 2	rs35874116	T>C	Influence in variation of sweet taste sensation and consumption of food and wine (216).
TAS1R3	taste 1 receptor member 3	rs307355	T>A, C	May affect gene transcription via cytosine to thymine substitution (158) and contribute to changes in perception for sweetness and alcohol (216). T alleles of this variant is also identified to reduce the taste sensitivity towards sucrose (91).
TAS2R10	taste 2 receptor member 10	rs10845219	T>C	-
TAS2R10 (161)	taste 2 receptor member 10	rs4763216	C>A, G	-

TAS2R13	taste 2 receptor member 13	rs1015443	T>A, C	Not associated with bitterness of capsaicin, piperine, ethanol, PROP (78, 165, 199, 279).
TAS2R14	taste 2 receptor member 14	rs7138535	T>A	Not associated with stevioside perception (280).
TAS2R16	taste 2 receptor member 16	rs846664	A>C, G	Not linked to bitterness of PROP (91) but leads to functional change in receptor (215) that may contribute in alteration of taste- linked signaling and sensitivity towards bitterness which ultimatey affect variations in alcohol intake.
TAS2R16	taste 2 receptor member 16	rs978739	T>C, G	No association with PROP bitterness (165).
TAS2R16	taste 2 receptor member 16	rs860170	C>T	A allele was linked with perception of salicin bitterness (165).
TAS2R16	taste 2 receptor member 16	rs1204014	C>G, T	-
TAS2R16 (84, 161)	taste 2 receptor member 16	rs1308724	G>A, C, T	Not associated with Acesulfame Potassium and quinine bitterness (281, 282).
TAS2R16 (84, 160, 184)	taste 2 receptor member 16	rs846672	A>C, T	Not related to bitterness of quinine (282).
TAS2R19	taste 2 receptor member 19	rs10772420	G>A	A allele was linked with more intense quinine and grapefruit juice perception (91), which may be resulted from the strong linkage disequilibrium (LD) between polymorphisms of TAS2R19 & TAS2R31 (256) .
TAS2R20	taste 2 receptor member 20	rs12226920	G>A, T	Correlated with intensities of bitter grosheimin (81) and quinine (282).
TAS2R20	taste 2 receptor	rs10845281	T>A, C, G	Correlated with intensities bitter grosheimin (81).

	member 20			
TAS2R3	taste 2 receptor member 3	rs765007	T>A, C	Not associated with bitterness of capsaicin, piperine and ethanol threshold (283).
TAS2R39	taste 2 receptor member 39	rs4726600	G>A, C	Not associated was quinine bitterness (282).
TAS2R4	taste 2 receptor member 4	rs2233998	T>C	Not linked with bitterness of PROP, capsaicin, piperine and ethanol (165, 199, 279).
TAS2R4	taste 2 receptor member 4	rs2234001	G>A, C, T	Not associated with intensity of sucrose, gentiobiose, aspartame, rebaudioside A and D (281).
TAS2R40	taste 2 receptor member 40	rs10260248	C>A	-
TAS2R40 (161, 217)	taste 2 receptor member 40	rs534126	C>G, T	-
TAS2R41	taste 2 receptor member 41	rs12666496	A>T	-
TAS2R41	taste 2 receptor member 41	rs1404635	G>A, C	-
TAS2R43	taste 2 receptor member 43	rs71443637	T>C	Linked with detection threshold & intensities of grosheimin (81) and coffee liking (283).
TAS2R46	taste 2 receptor member 46	rs2708377	C>A, G, T	Linked with perceived bitterness and detection threshold of caffeine (284).
TAS2R5	taste 2 receptor member 5	rs2227264	G>A, T	Predicted by SIFT algorithm to modify function (285).

TAS2R5	taste 2 receptor member 5	rs2234012	A>G	May regulate translation efficiency or stability of messenger RNA (84).
TAS2R50	taste 2 receptor member 50	rs1376251	C>T	Association between C allele and intake of dietary fiber & vegetable (184).
TAS2R50	taste 2 receptor member 50	rs10772397	C>A, G, T	Not associated with quinine bitterness (282).
TAS2R60	taste 2 receptor member 60	rs4595035	T>A, C, G	Not associated with quinine bitterness (282).
TAS2R7	taste 2 receptor member 7	rs619381	C>T	May impact TAS2R expression (286).
TAS2R8	taste 2 receptor member 8	rs1548803	C>T	Association with intensity of quinine (282).
CA6	carbonic anhydrase 6	rs2274333	A>G	A alleles linked with PROP supertasting (91).
GNAT3	g protein subunit alpha transducin 3	rs1524600	G>A	Association between C alleles and greater sucrose sensitivity (287).
PRH1*	proline rich protein haeiii subfamily 1	rs10492098	G>A, C	Modulate bitter taste perception (186).
PRH1-TAS2R14	proline rich protein haeiii subfamily 1 - taste 2 receptor member 14	rs2597979	G>A, C, T	Association between G allele and higher intensity rating of PROP (203).
PRH1-TAS2R14	proline rich protein haeiii	rs11612527	T>A	-

	subfamily 1 - taste 2 receptor member 14			
PRR4*	proline rich 4	rs1047699	T>A, C	Associated with Lipocalin-1 (LCN1) and thus may influence taste reception (288).
PRR4*	proline rich 4	rs1063193	C>A, G, T	Associated with Lipocalin-1 (LCN1) and thus may influence taste reception (288).
TRPA1	transient receptor potential cation channel subfamily a member 1	rs11988795	C>A, G, T	Not associated with quinine (282). Association was found between A allele and higher perception of odorous stimulants (289).

*Italic gene names indicate nearest genes as use by cite authors. * Potential role in taste perception based on STRING Database (https://string-db.org, accessed on 22 November 2022). – denoted no association or no explanation has yet been found/investigated for the potential effect of the variant.*

Table S4. Summary of impact of taste preference genetic SNPs on different alcohol consumption behaviors

Gene	SNP	Association	No association
TAS2R38	rs1726866	Reverse association with intake and drinker status of alcohol (203).	Not linked with first 3 questions of AUDIT questionnaire (161).
		Significant relationship with alcohol intake (160).	Not associated with weekly intake of alcohol (162).
TAS2R38	rs10246939	Significant relationship with frequency of alcohol intake (160).	Not associated with weekly alcohol consumption (162). Not linked with first 3 AUDIT questions (161).
TAS1R2	rs35874116	Carriers of C allele tend to drink less wine. Furthermore, Individuals with CC recessive drank wine higher than other genotypes (216).	Not associated with intake of Soju, beer and spirit (216).
TAS2R10	rs10845219		Not associated with the first three AUDIT questions (161).
TAS2R10 (161)	rs4763216		
TAS2R13	rs1015443	Exhibited a significant relationship with 2nd and 3rd questions of AUDIT. Carriers of CC alleles drank less alcoholic beverages than heterozygotes and homozygous of minor allele (161).	
TAS2R14	rs7138535		Not associated with the first three AUDIT questions (161).
TAS2R16	rs846664	Significant association between K172 allele and higher chance of alcohol dependence, regardless of ethnicity (215). Significant association with lower risk of alcohol dependence (184).	Not linked with intake of alcohol intake (160).
TAS2R16 (84, 161)	rs846672	Individuals with AA alleles drank alcoholic beverages double than heterozygotes or major allele homozygotes	No significant association with frequency as well as amount of alcohol

		(84).	consumption (184). Not associated alcohol intake (160). Not linked with first 3 questions of AUDIT (161).
TAS2R16 (84, 160, 184)	rs1308724	Carriers of CC drank alcohol less frequently compared to heterozygotes and GG homozygotes (84).	Not related to alcohol consumption (84). Not associated with first three AUDIT questions. (161).
TAS2R16	rs978739		Not associated with alcohol dependence (215).
	rs860170		
	rs1204014		
TAS2R20	rs12226920	Associated with spirits drinking (216).	Not associated with consumption of beer (160).
TAS2R20	rs10845281		Not associated with first 3 AUDIT questions (161).
TAS2R3	rs765007		
TAS2R39	rs4726600		
TAS2R4	rs2233998	Individuals of homo-recessive polymorphisms drank rice wine more than other genotypes (216).	Not significantly associated with intake of Soju, beer and spirit (216).
TAS2R4	rs2234001		Not associated with first 3 AUDIT questions (161). .
TAS2R40	rs10260248		
TAS2R40 (161, 217)	rs534126		
TAS2R41	rs12666496		
TAS2R41	rs1404635		
TAS2R43	rs71443637		Not related to alcohol intake (160).
TAS2R46	rs2708377		
TAS2R5	rs2227264	Carriers of TT drank higher alcohol and rice wine compared to carriers of other genotypes (216).	Not associated with intake of Soju, beer and spirit (216).
TAS2R5	rs2234012		Not associated with first 3 AUDIT

			questions (161).
TAS2R50	rs1376251	Associated with spirit drinker status while individuals with CC genotype drank more rice wine than others (216).	Not associated with daily alcohol intake (184). Not associated with intake of Soju, beer and wine (216). Not linked to first three AUDIT questions (161).
TAS2R50	rs10772397		Not associated with alcohol intake frequency (160).
TAS2R60	rs4595035		
TAS2R7	rs619381		Not associated with first three AUDIT questions (161).
TAS2R8	rs1548803		Not linked with first 3 questions of AUDIT tool (161). Not linked with frequency of alcohol intake (160).
TRPA1	rs11988795		Not associated with alcohol intake frequency (160).
GNAT3	rs1524600		Not associated with alcohol intake frequency (160).
PRH1	rs10492098		Not linked with first 3 AUDIT questions (161).
PRH1-TAS2R14	rs2597979		Not associated with drinking behavior and drinker status (203).
PRH1-TAS2R14	rs11612527		Not associated with first 3 questions of AUDIT questionnaire (161).
PRR4	rs1047699		
PRR4	rs1063193		

Italic gene names refer to nearest genes as used by cited authors; AUDIT: Alcohol Use Disorder Identification Test

List of Publications

UNIVERSITY of DEBRECEN

UNIVERSITY AND NATIONAL LIBRARY
UNIVERSITY OF DEBRECEN
H-4002 Egyetem tér 1, Debrecen
Phone: +3652/410-443, email: publikaciok@lib.unideb.hu

Registry number: DEENK/77/2023.PL
Subject: PhD Publication List

Candidate: Ali Abbas Mohammad Kurshed
Doctoral School: Doctoral School of Health Sciences

List of publications related to the dissertation

1. **Kurshed, A. A. M.**, Vincze, F., Pikó, P., Sándor, J., Kósa, Z., Ádány, R., Diószegi, J.: Alcohol consumption patterns of the Hungarian general and Roma populations.
   Front. Public Health. 10, 1-14, 2023.
   DOI: http://dx.doi.org/10.3389/fpubh.2022.1003129
   IF: 6.461 (2021)
2. **Kurshed, A. A. M.**, Vincze, F., Pikó, P., Kósa, Z., Sándor, J., Ádány, R., Diószegi, J.: Taste Preference-Related Genetic Polymorphisms Modify Alcohol Consumption Behavior of the Hungarian General and Roma Populations.
   Genes. 14 (66), 1-16, 2023.
   DOI: http://dx.doi.org/10.3390/genes14030666
   IF: 4.141 (2021)
3. **Kurshed, A. A. M.**, Ádány, R., Diószegi, J.: The Impact of Taste Preference-Related Gene Polymorphisms on Alcohol Consumption Behavior: a systematic review.
   Int. J. Mol. Sci. 23 (24), 1-22, 2022.
   DOI: https://doi.org/10.3390/ijms232415989
   IF: 6.208 (2021)

DEBRECENI EGYETEM Egyetemi és Nemzeti Könyvtár

UNIVERSITY AND NATIONAL LIBRARY
UNIVERSITY OF DEBRECEN
H-4002 Egyetem tér 1, Debrecen
Phone: +3652/410-443, email: publikaciok@lib.unideb.hu

List of other publications

4. Diószegi, J., **Kurshed, A. A. M.**, Pikó, P., Kósa, Z., Sándor, J., Ádány, R.: Association of single nucleotide polymorphisms with taste and food preferences of the Hungarian general and Roma populations.
Appetite. 164, 1-13, 2021.
DOI: http://dx.doi.org/10.1016/j.appet.2021.105270
IF: 5.016

Total IF of journals (all publications): 21,826
Total IF of journals (publications related to the dissertation): 16,81

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of the Journal Citation Report (Impact Factor) database.

10 March, 2023