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1. Introduction

Alcohol is the most commonly used and abused drug worldwide [1]. The highest level of alcohol consumption occurs in the developed world. This fact is not surprising since the history of alcoholic beverages is linked to the history of mankind. For centuries, alcohol consumption has been part of our culture and society. Drinking alcohol is a social activity, embedded today in traditional and sociocultural contexts. Probably, the main reason for alcohol consumption is its ability to produce positive moods and stress-relieving effects. In the last twenty years, worldwide per capita consumption of alcohol has remained stable. Currently, every person in the world aged 15 years or older drinks on average approximately 6 liters of pure alcohol per year. However, not all people in the world drink alcohol. Specifically, 61.7% of world population aged 15 years or older has not drunk alcohol in the past 12 months. This mean that those who drink alcohol consume on average 14.63 liters of pure alcohol annually. However, according to data from the Global Information System on Alcohol and Health [2], there are significant geographical variations in total per capita alcohol consumption. Thus, Chad (African WHO region) has the highest level of worldwide consumption at more than 33 liters per year. In comparison, alcohol consumption per capita in Pakistan (Eastern Mediterranean WHO region) averaged 1.2 liters per year (see Table 1).

Every year, a large amount of money is spent on alcohol worldwide. In fact, Europeans spend about 100 billion euros per year on alcoholic beverages. This is reflected in the region's high rate of alcohol consumption per capita: 15 liters of pure ethanol per year. Consuming and abusing these huge amounts of alcohol is clearly a problem, with enormous health and socioeconomic effects worldwide. Thus, harmful use of alcohol is a major public health problem. Drinking alcohol is socially acceptable and associated with relaxation and pleasure,
and some people drink alcohol without experiencing harmful effects. However, alcohol does cause a growing number of people to experience physical, social and psychological harmful effects. Alcohol has important effects on our body, even when consumed in small amounts. The effects of alcohol intoxication are greatly influenced by gender, drinking speed, type and amount of food consumed, etc. Physiological changes appear as a function of Blood Alcohol Concentration (BAC) (see Table 2). BAC refers to the milligrams of alcohol per 100 milliliters of blood, and is usually expressed as a percentage. For instance, having a BAC of 0.10 means that a person has 1 part alcohol per 1000 parts blood. As the amount of alcohol consumed in a single sitting increases, the BAC increases proportionately.

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Males (15+)</th>
<th>Females (15+)</th>
<th>Both sexes (15+)</th>
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<td>15.73</td>
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<tr>
<td>Western Pacific</td>
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<td>10.95</td>
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<td><strong>7.29</strong></td>
<td><strong>14.63</strong></td>
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Table 1. Total alcohol per capita consumption, drinkers only, 2010 (in liters of pure alcohol; aged 15+). Data from Global Status Report on Alcohol and Health (WHO, 2014)

As indicated in Table 2, excessive alcohol use has immediate physiological and psychological effects that increase the risk of many harmful health conditions. These effects vary from mood changes to alcohol poisoning and coma. Over time, excessive alcohol use can lead to chronic diseases (cardiovascular problems, liver diseases…), neurological impairment and social problems, including unemployment and family problems. Also, people who drink too much or too often, or are unable to control alcohol consumption, can develop an alcohol use disorder.
Alcohol dependence and harmful alcohol use are recognized as mental health disorders in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) [3] and the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) [4]. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines Alcohol Use Disorder (AUD) as the presence of at least 2 of 11 criteria within a 12-month period, defined by a cluster of behavioral and physical symptoms organized in four groups:

1. **Impaired control**: (1) alcohol is often taken in large amounts or over longer period than was intended, (2) unsuccessful efforts to stop or cut down alcohol use, (3) spending a great deal of time obtaining, using, or recovering from alcohol use, (4) craving for the substance.

2. **Social impairment**: (5) failure to fulfill major obligations due to use, (6) continued use despite problems caused or exacerbated by use, (7) important social, occupational or recreational activities given up or reduced because of alcohol use.

3. **Risky use**: (8) recurrent alcohol use in hazardous situations, (9) continued use despite physical or psychological problems caused or exacerbated by alcohol use.

4. **Pharmacological dependence**: (10) tolerance to substance effects, (11) withdrawal symptoms when not using or using less.

According to the DSM-5, the severity of the alcohol use disorder (mild, moderate and severe) is based on the number of criteria met. Anyone meeting 2 or 3 criteria would receive the mild AUD diagnosis. Anyone meeting 4 or 5 criteria would receive the moderate AUD diagnosis. Finally, anyone meeting 6 or more criteria would receive the severe AUD diagnosis.

Although a large proportion of the population consumes alcohol, not all of them become alcohol dependent. Research shows that people who drink moderately may be less likely to experience AUD. Thus, only 3.6% of alcohol users worldwide are alcohol dependent, a condition implying a degree of addiction that makes it difficult for them to abstain or reduce their drinking in spite of increasingly serious harm [2] (see Figure 1). When comparing different WHO regions, the following conclusion can be made. The highest lifetime prevalence of alcohol use disorder occurs in Europe (6.1%) and the Americas (5.4%). The lowest prevalence rates of alcohol use disorders occur in South-East Asia (2.1%) and Eastern Mediterranean countries (0.4%).

Specifically, alcohol use is ranked as the third leading risk factor for disease and disability in the world. It is the leading risk factor in the Western Pacific and the Americas, and the second largest in Europe. According to 2012 data from the Global Information System on Alcohol and Health [2], harmful use of alcohol kills 3.3 million people annually and represents 4.5% of the global disease burden. Also, alcohol has been shown to be causally related to more than 60 different types of diseases and injuries [5]. For example, 33.4% of all deaths caused by cardiovascular disease (i.e. hypertension, atrial fibrillation and hemorrhagic stroke [6] and diabetes mellitus [7] are causally related to ethanol consumption; also, alcohol has been related to gastrointestinal diseases such as liver cirrhosis and pancreatitis in 16.2% of cases [8]. Generally, the risk of suffering these disease is related to the volume of alcohol consumed: the higher the
volume, the larger the risk of these diseases. Recently, drinking alcohol has been related to the incidence of infectious diseases such as tuberculosis and HIV/AIDS [9].

The impact of harmful use of alcohol is not just personal, it may also impose significant social and economic costs on society. The economic cost of ethanol abuse is estimated at more than $235 billion every year [10]. More than 70 percent of the estimated cost of alcohol abuse is attributed to lost productivity. Other costs are largely the result of alcohol-related health care, motor vehicle accidents, and law enforcement and other criminal justice expenses.

Adolescents are a particularly vulnerable to the harmful effects of alcohol. In fact, ten years ago, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) formed an interdisciplinary working group on underage drinking in order to intensify research, evaluation and outreach efforts on the underage drinking problem. Alcohol is the most common drug of abuse in adolescence, more than tobacco and other illicit drugs. Misuse of alcohol among adolescent is an international problem. In fact, 320,000 young people aged 15 to 29 die each year from alcohol-related causes—9% of all deaths in that age group [11].

Bearing in mind all these data, in 2010 the World Health Assembly approved a resolution to urge countries to strengthen national responses to public health problems caused by the harmful use of alcohol.

2. Present situation

In general, adolescence can be defined as the transitional period between childhood and adult maturity characterized by behavioral, hormonal and neurochemical changes designed to prepare the body for independent survival. It is derived from the Latin *adolescere*- The present participle *adolescens* means growing up; the past participle *adultus* means grown up. The World Health Organization (WHO) defines adolescents as people between 10 and 19 years of age. However, different definitions of adolescence have been used in scientific literature. Thus,
whereas some clinical researchers define human adolescence as the age span from approximately 9 to 18 years of age [12], others consider the entire second decade of life as “adolescence” [13]. In spite of conceptual term differences, all studies agree with the idea that adolescence is a time of marked change, a time of transition into adulthood. Therefore, at this age, people experiment with adult aspects of life: they establish their own identities, make close relationship outside the family, and want to try out new things, some of which may be risky or even dangerous. Many teenagers experiment with alcohol and illegal drugs.

Epidemiological studies have detected the development of a new pattern of alcohol consumption in adolescents. This pattern is characterized by drinking large amounts of alcohol over a short period of time, especially in leisure time and weekends, with periods of abstinence between drinking episodes. In spite of the fact that young people drink less often than adults, on average they consume more drinks per drinking occasion than adult drinkers. Specifically, compared to adults, adolescents drink more than twice as much per drinking episode [14]. We can say that they show a pattern of binge drinking.

In 2004, the NIAAA defined binge drinking as a pattern of drinking that brings Blood Alcohol Concentration (BAC) to 0.08 grams percent or above. For adults, this pattern corresponds to drinking five or more drinks (male), or four or more drinks (female), in about two hours. For adolescents, an important debate has developed over the definition of binge and whether that definition must be different for adults and adolescents due to alcohol absorption differences. Thus, according to recent research estimates, reaching a given BAC level takes fewer drinks for young people.

Although it has declined in the last decade, underage drinking (ages 12-20) is still an important public health problem. Despite the fact that these teens are under the legal age for purchasing alcohol, many adolescents engage in underage drinking in general and binge drinking in particular. However, the levels and patterns of alcohol consumption vary widely between countries. According to the Global Status Report on Alcohol and Health [2] the prevalence of heavy episodic drinking in 15-19 year-olds ranged from 50.6% in Germany to zero in some Eastern Mediterranean countries, such as Afghanistan, Morocco or Tunisia. Particularly, in the African, Eastern Mediterranean and South-East Asia regions, young people (15 to 19) are less likely to engage in heavy episodic drinking (see Table 3). By contrast, adolescent alcohol use is common in many European and American countries. Thus, in a US study, 10% of 8th graders, 22% of 10th graders and 26% of 12th graders reported that they had consumed five or more drinks in a row within the previous 2 weeks [15]. Clearly, underage alcohol use increases with age. Specifically, the percentage of the population who drinks at least one whole drink rises steeply during adolescence. In Europe, the binge-drinking rates are even twice or three times higher than in United States [16]. Thus, 50–70% of 16-year olds have consumed alcohol once in their lives, and >35–70% of European adolescents who have ever drunk report at least one heavy drinking episode in the previous month [17].

Table 3 shows clear differences in alcohol use between genders. Underage males report more alcohol use than underage females, independently of WHO region. Similarly, previous studies in adults have shown that women drink less than men and also, that they have more alcohol-related problems than men [18]. Studies have shown that adolescent girls suffer more adverse
cognitive effect related to alcohol than adolescent boys, especially in working memory and visual-spatial functions. Multiple factors can contribute to gender differences in risk factors for alcohol use. For example, hormonal fluctuation, differences in alcohol metabolism, or gender-specific drinking patterns. In agreement with these data showing gender differences in alcohol use profile, alcohol prevention should take these sub-group differences into account.

<table>
<thead>
<tr>
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<th>Females</th>
<th>Both sexes</th>
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<tr>
<td>South-East Asia</td>
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<td>0.06</td>
<td>0.29</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>18.00</td>
<td>6.65</td>
<td>12.47</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>14.01</td>
<td>5.39</td>
<td>9.79</td>
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Table 3. Heavy episodic drinking prevalence* (% 15-19 year-olds), 2010. *Consumed at least 60 grams or more of pure alcohol on at least one occasion in the past

2.1. Binge drinking and short-and long-term outcomes

Binge drinking has many negative short-and long-term outcomes. In a 2004 global mortality patterns report, 3.2 million deaths were attributed to alcohol use among people aged 15 to 29. That is 19% of all deaths—the highest mortality risk factor in the age group. Binge drinking is associated with increased risk of:

- **unsafe sexual activity** [19,20]. Underage alcohol use has been associated to risky sexual behavior (unwanted, unintended and unprotected sexual activity) and multiple sex partners. For example, 32% of adolescent who started drinking at 13 reported having unplanned sex because of drinking, and 10% reported having unprotected sex because of drinking [21]. Such behavior increases the risk of unplanned pregnancy and sexually transmitted disease infection [19]. Also, young people who drink are more likely to carry out or be the victim of physical or sexual assault [21].

- **criminal and aggressive behavior** [22]. Hazardous alcohol use can reduced physical control and ability to recognize warning signs in potentially dangerous situation, therefore increasing the risk of becoming a victim of violence [22,23]. Similarly, reduced self-control and ability to process incoming information and assess risks can make some drinkers perpetrate acts of violence [24]. Recently, it has been proposed that a common risk factor (i.e. anti-social personality disorder) could explain the relationship between violence and heavy alcohol drinking [25, 26].

- **suicide ideation and suicide attempts** [27]. Thus, individuals with suicide ideation and attempts are more likely to engage in heavy episodic drinking and have greater alcohol problem [28].
Also, binge drinking has been associated with successful suicide [29]. Every year in the United States, about 300 young people under 21 commit suicide as result of underage drinking.

- **drunk driving or riding in a vehicle driven by a drunk driver** [30]. 24 percent of drivers aged 15 to 20 involved in fatal motor vehicle accidents had been drinking. Alcohol has a range of effects on reaction time, cognitive processing, coordination, alertness, vision, and hearing, all of which increase accident risk.

- **alcohol intoxication and accidental death.** Consuming alcohol can cause a range of physical consequences, from hangovers to death from alcohol poisoning. Alcohol intoxication is manifested by such signs as slurred speech, loss of coordination, unsteady gait, euphoria, confusion, impaired judgment or stupefaction. Also, it can lead to complications such as trauma, dehydration, delirium, heart attack or convulsions. In the most severe cases, alcohol poisoning can lead to coma and even death.

Finally, we know that the adolescent brain undergoes neurodevelopmental changes. These changes can be influenced by genetic, environmental and sexual hormone factors. Thus, drinking alcohol early in the adolescence has adverse effects on the brain [31].

### 2.2. The adolescent brain and substances of abuse

The transition to adolescence is characterized by a rapid biological transformation, including the hormonal and physiological changes of puberty. During this period, the body grows (height and weight), secondary sex characteristics emerge, and sex hormones reach adult levels. Adolescence is a time of substantial neuromaturation involving important changes in numerous brain regions, including the hippocampus, the prefrontal cortex, and limbic system structures. Although the human brain does reach approximately 90% if its adult weight by age 6 [32], structural changes continue throughout adolescence. Specifically, the prefrontal cortex, which plays an important role in executive control functions (i.e. planning, emotional regulation, decision making…) starts to develop early in life and continues after adolescence and into the early 20s. In contrast, the limbic system—the site that governs reward processing, appetite and pleasure seeking—develops earlier than the prefrontal cortex. This maturation disparity between limbic system and prefrontal cortex might explain the preponderance of behaviors driven by emotion and reward over more rational decision making in adolescents.

Changes observed in the adolescent brain are characterized not only by continued neural system maturation, but also by changes in the synaptic connection in these neural regions. During adolescence, the brain is highly plastic and shaped by experience. It has been shown that gray matter volume and density decrease during adolescence. Developmental declines in gray matter occur first in the sensory and motor regions of the cortex and then in the prefrontal cortex (PFC) and other cortical association areas [33, 34]. Such reduction in gray matter is largely due to the loss of weak or unused synapses via synaptic pruning. As the person matures into adulthood, this process makes these areas more efficient and promotes speed, overall efficiency, and enhanced information processing capacity. Conversely, white matter increases during the transition from childhood to young adulthood, first in the occipital regions and
then in the frontal, temporal and parietal association areas. Myelination has been related to increased cognitive efficiency. In general, this neural pruning may serve to refine the abundance of brain connections and increase brain efficiency during adolescence.

Similarly, throughout adolescence there are rapid changes in neurotransmission and plasticity. These changes have a particularly strong effect on dopamine (DA) and serotonin. Both neurotransmitters are dynamically changing in the adolescent brain. The dopaminergic system undergoes marked transitional changes during development. During adolescence, the brain shows elevated basal levels of extracellular DA in comparison with adulthood [35]. Also, dopamine D1 and D2 [36], but not dopamine D3 [37] receptor levels increase in the striatum during early adolescence. The activity levels of these dopaminergic receptors are 30-40% greater than in adults, measured as an increase in D1 and D2 receptor binding [38]. Moreover, the density of DA transporter (DAT), which removes DA from the synapses, is greater in adolescence than in adulthood [39, 40]. Bearing in mind the role of dopamine in reward and euphoria, these changes in the dopaminergic system could be related to the euphoric behaviors showed by adolescents.

Several studies have shown that the serotonergic system undergoes reorganization during postnatal development (from childhood through adolescence). Specifically, brain serotonin (5-hydroxytryptamine or 5-HT) concentration peaks early in life and then decreases to adult levels levels [41, 42]. 5-HT_{2A} subtype receptor levels behave similarly [43]. Moreover, the 5-HT turnover has been reported to be approximately 4 times lower in adolescents than in adults [44]. In addition, serotonin transporters—involved in neurotransmitter inactivation—steadily increase until adulthood [40, 45] and decrease synaptic 5-HT concentration. The low level of 5-HT has been associated with impaired impulse control, anxiety, and aggressive behavior. In summary, evidence indicates that during adolescence, there is relatively greater activity in the dopamine system than in the inhibitory serotonin (5-HT) system, potentially resulting in an imbalance in the reward (DA-mediated) and suppression (5-HT-mediated) mechanisms [38, 46].

Others neurotransmitters (acetylcholine, glutamate, GABA…) also undergo brain changes during development. Relative to adults, adolescents exhibit developmentally enhanced activity of the glutamatergic system in certain brain regions [47], while at the same time displaying developmentally immaturity of the gamma-aminobutyric acid (GABA) system [48,49]. On the other hand, the maturation of the central cholinergic system, which plays an important role in both memory/learning and anxiety, occurs in this critical period [50].

The neurochemical, cellular and structural organization of the adolescent brain makes it more vulnerable than the adult brain to disruption from activities such as binge drinking. The brains of adolescents that consume alcohol show a reduction on myelin fiber tracts with frontal connections as well as altered white matter integrity, events that might underlie dysfunctions in learning, memory and executive functions [51]. In addition, since alcohol interacts with some neurotransmitter systems that are essential for brain development, drug exposure during adolescence may be particularly harmful to the still developing brain. For example, binge drinking results in altered serotoninergic innervation and increased transporter density in several brain regions, including the forebrain [52]. Thus, underage drinking could contribute
to altered sleep patterns, impulsivity, satiation and other behaviors associated with serotonergic function. In the same way, given that acetylcholine is an important neurotrophic agent implicated in cholinergic target cell proliferation and differentiation [53, 54], ethanol consumption during adolescence could evoke neurodevelopmental abnormalities by disrupting the timing or intensity of neurotrophic actions. In addition, the alteration of cholinergic system could be mediating the learning and memory deficits shown by adolescent who consume alcohol.

Binge-drinking adolescents suffer volume reduction in several brain areas, such as the prefrontal cortex, the hippocampus and the left middle and inferior temporal gyrus [55-57]; this reduction is positively correlated with the duration of alcohol use. Several studies have shown cognitive impairments in adolescents with alcohol use disorder [58]. As such, neuropsychological studies have revealed that binge-drinking adolescents exhibit poor performance in tasks assessing verbal and nonverbal memory, problem solving, attention, working memory, and visual-spatial skills [58-61]. Furthermore, adolescent binge drinkers were faster in speed test response, confirming the hypothesis of increased impulsivity in this population [62]. Interestingly, a recent study has demonstrated that old people and young people who consume excessive alcohol show similar deterioration in executive function [63]. These data suggest that, as a consequence of alcohol consumption, the area of the brain undergoing deterioration is similar in both adolescents and old people. However, additional research could help clarify if alcoholism produces cognitive aging.

Finally, the changes in the adolescent brain have consequences not only at the time but also later in life. Recent studies have demonstrated that exposure to alcohol during adolescence has long-term effects on the brain that persist into adulthood. There is evidence that ethanol exposure during adolescence might also alter neuropeptide systems critically involved in voluntary ethanol intake. Thus, following binge-like ethanol exposure during adolescence, adult animals show increased mRNA expression of basal corticotrophin releasing factor (CRF) in the paraventricular nucleus of hypothalamus [64], decreased overall hippocampal neuropeptide Y (NPY) immunoreactivity in Wistar rats [65], and reduced α-MSH expression in the hypothalamus and the amygdala of adult rats [66]. Given the role of these neuropeptides in ethanol consumption and the fact binge-like ethanol exposure during adolescence increases the probability of ethanol consumption during adulthood, the changes observed in these studies might contribute to increased vulnerability to ethanol consumption during adulthood. However, additional studies are necessary to check this hypothesis.

3. Risk factors for alcohol consumption among adolescents

Alcohol consumption among adolescents has a multifaceted etiology. In this section, we will address the reasons why adolescents drink large amounts of alcohol, focusing on age-dependent alcohol sensitivity. Research literature has shown that, in general, adolescents are more sensitive than adults to the stimulating effects of alcohol, and less sensitive to some of the aversive effects of acute alcohol intoxication. Finally, and given that both environmental...
and genetic factors are found to affect levels of alcohol use from adolescence to adulthood [67], we will dedicate a subsection to this topic.

3.1. Adolescents and adults respond differently to the effects of alcohol

Ethanol use increases throughout adolescence and is often associated with relatively high consumption levels. Although the exact cause of the increase in ethanol consumption during adolescence is not known, age-dependent sensitivity differences to some ethanol effects may play a contributory role. Mainly, two complementary explanations are given as to why adolescents drink more alcohol than adults. First, they are more sensitive to the positive effects of alcohol, i.e. the social loss of inhibition effect of alcohol when compared with adults [68], which may serve to reinforce or promote excessive intake. In fact, on average and per occasion, adolescents consume more alcohol than adults. In agreement with these behavioral data, it has been demonstrated that in adolescence a single ethanol exposure causes a robust and pronounced increase in dopamine release in comparison with adults [69]. This enhancement in dopamine release is consistent with the greater rewarding effects of alcohol in adolescents [70]. Thus, the increased sensitivity to alcohol's rewarding effects could contribute to increased susceptibility to alcoholism in the adolescent population.

Secondly, numerous studies have demonstrated that adolescents are less sensitive to the negative effects of alcohol than adults, such as sedation, loss of coordination and hangover effect. This decreased sensitivity may allow adolescents to continue drinking longer than their adult counterparts, thereby increasing the risk of acute cognitive impairment and brain damage.

Because it is unethical and illegal to provide alcohol to minors for the purpose of research, the majority of research on this topic have been performed on laboratory animals, primarily rodents. Findings from several studies using animal adolescence models support the hypothesis that adolescents are less sensitive to the negative effects of alcohol than adults, including hypnotic [71], hypothermic [72,73], motor impairing [74,75] and anxiolytic effects [76].

For instance, adolescent rats are markedly less sensitive than adult rats to alcohol-induced sedation. Sedation refers to the calming or tranquilizing effect of a drug. In rats, sedation is measured by the loss of the righting reflex. After a large acute dose of ethanol, adolescent rats regained their righting reflex and woke up more quickly at higher blood alcohol levels (BAC) than adult animals [71]. These authors suggest that the same differences should exist in humans. Consequently, adolescents may experience minimal hypnotic effect from ethanol consumption, thus receiving less negative feedback as a result of drinking. In addition, adolescents appeared more sensitive to high doses of ethanol when examining ethanol's hypothermic effects [72]. In general, adolescent showed a greater magnitude of ethanol-induced hypothermia than adults; even though adults showed more rapid and sustained ethanol-induced hypothermia than adolescents [73].

It is well known that alcohol disrupts motor coordination. Numerous studies suggest that adolescent rats display age-related differences in the development of motor impairment [74,75], suggesting that the disruption is less pronounced in adolescents than in adults. Similarly,
human adolescents might drink more because of their relative insensitivity to motor cues signaling intoxication.

One important motivation for alcohol use is the fact that alcohol has anxiety-reducing properties. The evidence for the anxiolytic effect of ethanol in human [77] and animal models [78] has been demonstrated. Studies carried on adolescent rats have shown that they are less sensitive than adults to the anxiolytic effect of alcohol. Specifically, some investigators have found that, due to tolerance development, adolescent rats require greater quantities of alcohol than adults to reach anxiolytic effects [76].

Likewise, adolescent rats are less sensitive than adults to consequences associated with ethanol withdrawal. The signs of ethanol withdrawal include physiological (headache, fatigue, tremor, ...) and psychological (anxiety, guilt, depression, ...) symptoms. Adolescent rats show less anxiogenic signs of acute withdrawal as measured in the elevated plus maze [79], in the open field test [80] or in a social interaction test [81]. The results of these studies suggest that even when using different behavioral test to examine anxiety, adolescents fail to exhibit the withdrawal-induced anxiety seen in adults. Human studies have shown that, compared to adults, adolescents who commonly abuse alcohol, rarely report withdrawal symptoms upon drinking cessation [82].

In summary, findings derived from basic research indicate that adolescents and adults experience alcohol differently. In general, adolescents are less sensitive to the negative aspects of alcohol consumption (sedation, motor impairment, anxiety), but more sensitive to its positive and rewarding effects. Thus, adolescents are “resistant” to the negative effects of ethanol that limit consumption progression. In general, during adolescence, more drinks are necessary to elicit a signal that it is time to stop. Conversely, adolescents are more sensitive to the effects that facilitate the maintenance, progression and escalation of alcohol consumption. This pattern of response to alcohol would be a vulnerability factor for adolescents to engage in problematic drinking trajectories. However, there are environmental and genetic factors that may also contribute to alcohol consumption among adolescents.

3.2. Environment and heritability factors

The environment and heritability factors play a dramatic role in controlling individual predisposition to developing alcohol abuse [83, 84]. Knowing the characteristics that increase the risk of adolescent alcohol use disorder can be helpful in preventing or attenuating such risk.

The relationship between early use of alcohol during adolescence and the increased risk of excessive alcohol drinking and alcohol disorder in adulthood has been well documented. Several studies have reported that alcohol consumption before 14 years of age is associated with a fourfold increase in the risk of alcohol dependence in adulthood [85, 86]. Similarly, 10 years after alcohol initiation, 14% of adolescent who started to drink at early ages, versus 2% of those who delayed the drinking onset, met alcohol dependence criteria [87]. Also, early alcohol use is associated with more mental health and social negative effects [88] or even with increased later use and abuse of other substances (tobacco, marijuana or other illicit drugs) [89].
Another important risk factor associated with using alcohol for the first time at an earlier age is a family history of alcoholism [90-92]. Having a family history of alcohol drinking problems is associated with greater underage drinking [90, 91] and greater frequency of alcohol-use problems [92]. Several studies have reported that only the father’s drinking had a direct effect on adolescent drinking [93, 94] while the mother’s didn’t. Further research is needed to clarify the real impact of parental drinking on adolescent drinking. It is known that alcohol use disorder tends to be repeated within families. For example, 60% of people with alcohol dependence and a family history of alcohol (i.e., an alcoholic parent) initiated drinking at age 13. By contrast, when they did not have a family history of alcohol, only 28% initiated drinking at age 13 [95]. However, it is difficult to draw clear conclusions about this factor because this predisposition may be due to children inheriting certain genes that determine an underlying predisposition or because they learn certain behavioral patterns that lead to the development of alcoholism. Moreover, we should consider that other studies have shown no family history [96] and no offspring and/or parent gender dependence [94] on young adult problematic drinking. Given the non-conclusive data, additional research is needed to understand the relationship between family history of alcoholism and early use of alcohol during adolescence.

Other environmental factors recognized as important risk factors in excessive alcohol use among adolescents are: the influence of a stressful life event [97] and peer substance use on initiation and intensity of alcohol use. The exposure to stress is strongly associated with the initiation and prolongation of alcohol drinking which most often evolves into alcohol dependence. In other words, and given that adolescents are highly vulnerable to social influence and they tend to copy what their friends do to feel accepted, peer effects on risk-taking are strong in this age group. For example, having friends who drink increases the likelihood that an adolescent will drink too. According to the National Survey on Drug Abuse and Health (2012), the probability of ethanol consumption if a few friends have consumed alcohol within the past 30 days is 7.3%, 25% if most of them consumed alcohol and 41.4% if all of them consumed alcohol. Similarly, adolescents are also influenced by how much their friends drink [98].

It has been shown that intrapersonal risk factors predict alcohol-related problems among adolescents and young adults. Some of them are poor behavioral regulation and Attention Deficit Hyperactivity Disorder (ADHD) [99-101], delinquency and personality traits, like sensation seeking, impulsivity [102] and neuroticism [103]. All of them have been shown to be positively related to drug use among youth.

In addition, recent data have highlight the existence of protective factors, such as parental control and a supportive environment [104, 105]. Studies have consistently found that the parenting style significantly protects against adolescent drinking behavior. Specifically, both indulgent and authoritative parenting styles have been hypothesized to be a major source of influence on protection against adolescent substance use [106]. It seems that fostering an environment of acceptance, dialogue and affection is a good strategy to prevent adolescent alcohol consumption. For example, adolescents from authoritative households (i.e. harmonious, warm and responsive parents that exert concurrently firm control and maturity demands) use less illegal drugs [107]. As well as parental control, involvement in social activities is another protective factor in adolescent alcohol use [108]. Adolescents who
demonstrate a high involvement in social activities (sports, extracurricular and/or academic activities…), are less likely to consume alcohol or other drugs.

Studies have shown that alcohol use among adolescents could also be influenced by genetic factors. Behavioral genetic studies carried on twins have shown a significant genetic component in alcohol dependence (58%), regular alcohol use (43%) and alcohol-related problems (38.5%) [109, 110]. By analyzing the genetic makeup of adolescents who consume alcohol, researchers have found specific chromosome regions that correlate with this consumption pattern. One recent study found that a serotonin transporter polymorphism (5-HTTLPR) predicted adolescent increase in alcohol use over time [111]. In spite of having a similar initial level of alcohol consumption, adolescents with the 5-HTTLPR showed larger increases in alcohol consumption. Other genes associated with the risk of developing alcohol use disorder (AUD) during youth is μ-opioid receptor (OPRM1) polymorphism [112, 113]. Thus, adolescents who met criteria for an AUD diagnosis had a higher prevalence of this polymorphism. Finally, genes involved in gamma-aminobutyric (GABA) receptors have also been widely studied because of their role in alcohol use disorders in adolescence and young adulthood. The most frequently studied polymorphism included the GABA receptor subunits GABRA2 [114] and GABRG3 [115]. Further research is needed to identify the actual genes involved in the early alcohol consumption and their contribution to alcohol problems in adolescents.

In summary, studies have clearly shown that both genetic and environmental factors contribute to the risk of alcohol dependence in adolescence and later in adulthood, and it is likely that the interplay between these factors is critical in determining the risk of alcohol abuse and dependence. For example, twin studies have found that initiation on alcohol use is largely influenced by the environmental risk factor [116]. Once initiation has occurred, genetic factors explain a large amount of alcohol use frequency variations (34–72%) especially as adolescents get older [116]. Thus, studies that tested interactions between environmental factors and genes implicated in alcohol drinking in adolescence are necessary. We cannot forget that, in spite of the fact that certain genetic polymorphism may increase the probability to develop alcohol dependence, the manifestation of the disorder might depend on environmental factors.

4. Prevention programs

Alcohol dependence is a chronic disorder that causes high direct and indirect costs to public health and has important social and family implications. Moreover, it ranks among the first on the list of disorders that cause higher rates of death in the world. However, it has remained a relatively low priority in public policy, including in public health policy. Considering all these data, in 2010 the World Health Assembly approved a resolution to urge countries to strengthen national responses to public health problems caused by the harmful use of alcohol.

At 1.8 billion, adolescents and young adults represent more than a quarter of the world’s population. According to data from the WHO's Global Burden of Disease study, 7.4% of all disability and premature deaths in people aged 10-24 are alcohol-attributable, followed by unsafe sex (4%) or illicit drug use (2%) [117]. Also, it should be noted that most of the mental
disorders begin before age 25. This finding suggests that public health strategies should focus on child and adolescent health, paying special attention to adolescent drinking. Given that early initiation of alcohol use has been frequently associated with later alcohol-related problems [87], delaying the initiation of drinking from early adolescence to late adolescence or adulthood is an important prevention goal [118]. Understanding the precursors and etiology of drinking behavior is necessary to limit premature and excessive drinking among adolescents.

However, before we start to set up alcohol consumption prevention plans for adolescents, we must identify alcohol consumption determinants, i.e. why do young people drink? Numerous studies have demonstrated that both alcohol expectations and drinking motives are related to alcohol use [119, 120]. However, it seems that drinking motives are the most proximate factor preceding alcohol use. Adolescents appear to drink because of social motives being either positive (social camaraderie) or negative (peer pressure, not to feel left out). Thus, most adolescents drink alcohol to relax, to have fun or to belong to the group. In general, alcohol is used to gain social recognition [119]. Another factor that influences alcohol consumption among adolescents is alcohol expectations. Several studies have shown that high positive alcohol expectations predict alcohol consumption and alcohol problems among adolescents [121, 122]. In agreement with these data, alcohol use prevention programs may benefit from addressing adolescent perceptions about the positive consequences of alcohol use. In essence, knowing drinking motivations and alcohol expectations may lead to designing more effective preventive strategies.

Governments and other stakeholders can support and empower communities to use their local knowledge and cultural expertise to adopt effective approaches to prevent and reduce harmful use of alcohol [123]. Generally, government support for community action takes the form of training programs and policies for subgroups at particular risk, such as adolescents. There is a great variety of governmental initiatives to prevent alcohol use and abuse during adolescence from school-to-parents-based programs. Because early adolescence is a time when alcohol use experimentation often begins to occur, middle high school age student are most often targeted in this prevention programs. As well as school-based program, there are programs to teach parents effective ways to monitor and communicate with their children about the use of alcohol. Mainly, the majority of these programs focus on giving information about the negative health, social and behavioral outcomes of drinking alcohol during adolescence. These approaches considered that people make decisions about alcohol use and abuse based on their knowledge of the adverse consequences involved. However, it has been demonstrated that prevention programs based solely on providing information about the negative consequences of alcohol have little influence on alcohol consumption [124, 125]. Thus, the World Health Organization (WHO) suggested promoting prevention campaigns focused on affective and conative components of attitudes and not just cognitive components. In addition to the educational component, a section to induce changes in attitudes towards excessive alcohol consumption should be included in prevention programs. As is generally acknowledged, adolescent drinking behavior is strongly influenced by peers. For that, workshops where adolescents learn effective strategies of self-control based on the ability to say “no” in social
pressure situations are very effective to prevent alcohol consumption. Amongst the generic prevention programs, those based on psychosocial approaches demonstrated significantly greater reductions in alcohol use. Among the effective psychosocial and developmental alcohol misuse prevention programs currently used in schools, we would like to highlight the Like Skills Training Program, the Unplugged Program and the Good Behaviour Game. For example, the Unplugged Program is based on a social influence approach and addresses social and personal skills, knowledge, and normative beliefs about alcohol. Reviews of the literature dealing with school-based programs support the idea that this kind of programs based on a social influence model may prevent juvenile alcohol use through attitude modification, refusal skills and normative perceptions [126].

Community-based alcohol abuse prevention programs include some combination of school, family and public policy. Among public policies aimed at reducing alcohol consumption among adolescents, one of the measures proposed is the prohibition of selling alcohol to individuals under a certain age or the consumption of alcohol under this age. In 2012, most countries (69.27%) determined that the minimum legal drinking age (MLDA) is 18 years. However, some countries have no age limit or a 16-year age limit. Studies evaluating the minimum legal drinking ages showed a statistically significant inverse relationship with alcohol consumption. Thus, it seems that greater MLDA’s were associated with slight reductions in the prevalence of alcohol consumption [127]. Another policy to reduce adolescent alcohol consumption is increasing the price of alcohol. Several studies have shown that, as the price of alcohol increases, alcohol consumption and alcohol-related problems decline among the general population [128]. Specific studies to evaluate the real impact of the price of alcohol on adolescent populations is needed. Besides price, other controls on alcohol availability, such as restriction of the hours and days of alcohol purchasing or numbers and types of alcohol outlets, have been shown to affect levels of drinking.

Recent research has demonstrated that presenting a coordinated, comprehensive message across multiple delivery component is most effective in terms of changing behavior. We have mentioned some effective prevention programs in schools, families and communities. By implementing evidence-based strategies, governments can reduce excessive alcohol consumption and the many health and social costs related to it. Moreover, prevention programs for adolescent alcohol use could have a positive impact in preventing other common risks often associated to alcohol drinks, such as violent behavior or unprotected sex. At the same time, adolescent personal and social well-being will be promoted.

5. Conclusion

At 1.8 billion, adolescents and young adults represent more than a quarter of the world’s population. Many health-related behaviors usually starting in adolescence (i.e. alcohol use) contribute to disease in adulthood. Several studies have indicated that a considerable amount of adolescents drink alcohol, and this number is continually growing. Nevertheless, the increase in alcohol use and abuse among adolescents has been coupled with increasing social,
health and economic consequences. Adolescents who drink alcohol may experience a range of adverse short-and long-term consequences, including physical and mental health problems, violent and aggressive behavior, and adjustment problems in school and at home. Clearly, underage drinking and its consequences present a significant public health problem that must command our attention.

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