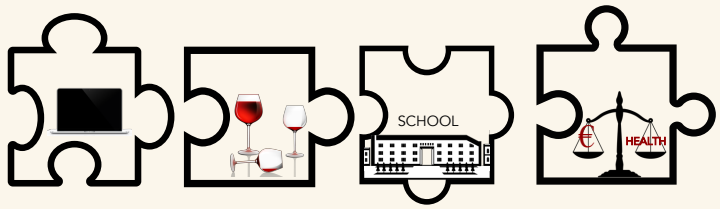
UNIVERSIDAD DE SEVILLA

COST-EFFECTIVENESS AND COST-UTILITY

ANALYSIS OF A WEB-BASED COMPUTER-TAILORED PROGRAMME FOR PREVENTION OF BINGE DRINKING IN ADOLESCENTS: ALERTA ALCOHOL PROJECT



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A thesis submitted for the degree of Doctor of Health Sciences

by

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Cost-effectiveness and cost-utility analysis of a web-based computer-tailored programme for prevention of binge drinking in adolescents: *Alerta Alcohol* project.

Abstract

Background: Alcohol abuse has been recognized as a global public health concern with high prevalence among adolescents, which has numerous health, social, and economic repercussions. In light of the need for prioritization and allocation of resources for public health interventions, the aim of this thesis is to assess the efficiency of *Alerta Alcohol*, a web-based computer-tailored intervention for the prevention of binge drinking (BD) among adolescents. To achieve this aim, the context surrounding adolescent drinking was examined and an analysis of the impact of binge drinking was carried out. The social, economic, and family factors associated with BD were explored, and a comparison was made between the health effects produced by the Alerta Alcohol programme as measured by health-related quality of life (HRQoL) and by reduction in excessive alcohol use.

Methods: The study population consisted of adolescents aged 15 to 19 years enrolled in public high schools in Andalusia, Spain. The sample was part of a two-arm cluster randomized controlled trial, with an intervention group who received the *Alerta Alcohol* programme and a control group who did not receive any active intervention. Longitudinal analyses were carried out to address the objectives proposed using econometric procedures (negative binomial, two-part model, finite mixture model, and generalized estimating equations approach). For the economic evaluation, a decision tree analysis was used to estimate costs and health outcomes, and incremental cost-effectiveness and cost-utility ratios were calculated from the Spanish National Health Service (NHS) and societal perspectives. Uncertainty was dealt through a multivariate deterministic sensitivity analysis of best/worst scenarios by subgroups.

Results: A total of 1,247 adolescents in the pre-intervention period and 612 in the four-month follow-up period formed the sample. In relation to socioeconomic and family factors associated with BD, being 17 years old or older and having more weekly pocket money and a higher family alcohol consumption frequency were associated with greater BD among adolescents. Additionally, higher adherence to the *Alerta Alcohol* programme was associated with a BD reduction at the four-month follow-up and with an increase in HRQoL, although this last effect was very small. Subjects who reduced their number of BD occasions reported

higher perceived HRQoL. Based on the economic evaluation, the intervention was shown to be dominant from the societal perspective using both cost per BD occasion per month averted and cost per QALY gained as outcome measures. It could also be cost-effective, depending on willingness to pay from the NHS perspective. In addition, subgroup analyses found a greater efficiency for girls and older adolescents (aged 17 years or older) of both sexes.

Conclusions: The findings in relation to social, family and economic factors associated with BD in adolescence could supplement prevention policies aimed at reducing the weekly pocket money or economic means available to adolescents, given the association between this variable and increased BD, and policies aimed at involving families in these interventions, given the influence of family alcohol consumption on this pattern of alcohol consumption. This type of programme based on computer-tailored feedback could be a cost-effective way to reduce and prevent BD and to increase QALYs in young people, but long-term follow-up would be needed to capture the full extent of the changes and effects of the programme, after introducing some improvements in the form of the intervention and the context in which it is carried out and after ensuring greater involvement of families.

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[1] The references included in Chapter 1 (Introduction) and Chapter 6 (Discussion) of this thesis have followed the structure proposed by the publication manual of the American Psychological Association (6th edition) (Viveros, 2010) and are included in the "References" section after Chapter 7 (Concluding remarks). The references included in Chapter 2, 3, 4 and 5 follow the structure required by the journal in which they have been published or submitted.

LIST OF ABBREVIATIONS

BAC	Blood Alcohol Concentration
BAIs	Brief Alcohol Interventions
BD	Binge Drinking
CBA	Cost-Benefit Analysis
CBR	Cost-Benefit Ratio
CCA	Cost-Consequence Analysis
CDIs	Computer-Delivered Interventions
CEA	Cost-Effectiveness Analysis (CEA)
CG	Control Group
CONSORT	Consolidated Standards of Reporting Trials
CUA	Cost-Utility Analysis
DALY	Disability-Adjusted Life Year
DCE	Discrete Choice Experiments
EDADES	Survey on Alcohol and other Drugs in Spain
	[Encuesta sobre alcohol y otras drogas en España]
ESPAD	European School Survey Project on Alcohol and Other Drugs
ESTUDES	Survey on drug use in Secondary Education in Spain
	[Encuesta sobre uso de drogas en Enseñanzas Secundarias en España]
GBD	Global Burden of Disease Study
GDP	Gross Domestic Product
GEE	Generalized Estimating Equations
GLMM	Generalized Linear Mixed Model
HBSC	Health Behaviour in School Aged-Children
HERG	Health Economists Research Group
HRQoL	Health-Related Quality of Life
ICER	Incremental Cost-Effectiveness Ratio
ICUR	Incremental Cost-Utility Ratio
IG	Intervention Group
INB	Incremental Net Profit
JCR	Journal Citation Reports
NHS	National Health Service
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NICE	National Institute for Clinical Health and Excellence

NPV	Net Present Value
QALY	Quality-Adjusted Life Year
QoL	Quality of Life
ROI	Return-on-Investment Analysis
SAMHSA	Substance Abuse and Mental Health Services Administration
SD	Standard Deviation
SES	Socioeconomic Status
TTO	Time TradeOff
USD	United States dollars
WHO	World Health Organization
WHOQOL	The World Health Organization Quality of Life

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Y llegó el momento…

Llegó el momento de dar GRACIAS en mayúsculas. Llegó el momento de pararme en el último capítulo de mi tesis, el cual es situado el primero estructuralmente. Y esta posición no es fruto de la casualidad. Dar las gracias y mencionar a todos aquellos que hicieron posible este trabajo es necesario y como expresa Alice Walker: *"Gracias' es la mejor plegaria que alguien puede decir. Yo la digo a menudo. Expresa humildad y entendimiento"*.

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[2] Respecto a las discriminaciones del lenguaje por género, los sustantivos masculinos empleados en plural se han utilizado para designar a personas de ambos sexo/género, a fin de favorecer la economía expresiva.

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DEDICATION

Dedicated to my parents, sister and life partner,

Manuel, María José, María and Juanma

Chapter 1
Introduction

CHAPTER 1 Introduction

1.1. Background

Among the multiple definitions of public health that exist is that established in 1988 by Sir Donald Acheson, who defined it as "the science and art of preventing disease, prolonging life and promoting, protecting and improving health through the organized efforts of society" (Acheson, 1988). Winslow (1920) had earlier proposed a broader definition:

> Public health is the science and art of preventing disease, prolonging life, and promoting physical health and efficiency through organized community efforts for the sanitation of the environment, the control of community infections, the education of the individual in principles of personal hygiene, the organization of medical and nursing services for the early diagnosis and preventive treatment of disease, and the development of the social machinery which will ensure to every individual in the community a standard of living adequate for the maintenance of health.

More recently, the International Union for Health Promotion and Education, in its 2007 document "Shaping the future of health promotion: Priorities for action", specifically defined health promotion as an objective:

> Health promotion aims to empower people to control their own health by gaining control over the underlying factors that influence health. The main determinants of health are people's cultural, social, economic and environmental living conditions, and the social and personal behaviours that are strongly influenced by those conditions.

It is based on this latter definition that the evidence in the literature regarding the determinants of a highly prevalent unhealthy behaviour among adolescents known as binge drinking – the focus of this study – has been included in the introduction of this thesis.

Many different models and frameworks are used to describe public health (Evans & Stoddart, 2003; Krieger, 2008; Solar & Irwin, 2007; Levine & The What Works Working Group with Kinder, 2004; Cockerham, 2007; Starfield, 2007). The conceptual framework defined by the National Institute for Health and Care Excellence (NICE) is based on a number of principles: first, that there are determinants of health and disease that are much

broader than biomedical causes; second, that these determinants operate in different ways, reflecting inequalities in society; third, that the determinants work through causal pathways to disease; fourth, that these causal pathways help to identify the best ways to prevent and alleviate disease; fifth, that there are causal avenues for health promotion; and sixth, that causal pathways include physical, biological, social, and psychological aspects (NICE, 2012). As noted in the fourth principle, the study of these determinants is key to identifying the best interventions to prevent or reduce binge drinking by the population group studied in this thesis.

In this conceptual framework, NICE, one of the leading centres explicitly evaluating public health interventions, points out that the available evidence on public health interventions and collated in its guidelines has a multidisciplinary basis (NICE, 2012). This institution uses economic evaluations to guide the prioritization and allocation of resources for public health interventions (NICE, 2012). Given the breadth of the public health field, it is important to map the areas of interest that it encompasses. These areas of interest are important owing to their connection to "vectors" of public health (population, environment, society, and organizations or institutions), social patterns in epidemiology, and gradients in related health outcomes (Cockerham, 2007; Bonnefoy, Morgan, Kelly, Butt, & Bergman, 2007). For this reason, data on the epidemiology, economic burden, and impact of binge drinking on the health and health-related quality of life (HRQoL) of adolescents have been included in the introduction of this thesis.

In its latest five-year strategic plan (2019–2023), the World Health Organization (WHO) established as a priority area the prevention of non-communicable diseases caused by, among other risk factors, the harmful use of alcohol (WHO, 2018a, 2019). Likewise, NICE compiled a list of the main public health areas of interest taking into account certain key general areas, some of which were related to disease, some to populations, others to behaviours and lifestyles, and still others to available technologies (NICE, 2012). The list includes alcohol, drugs, and smoking and tobacco use. It is therefore relevant to study this pattern of alcohol consumption – binge drinking – and the most appropriate interventions for preventing the associated health and non-health consequences, which are of great concern to the main international health institutions.

Economic evaluation is an integral part of the process of developing NICE public health guidance (NICE, 2009). The overall objective of such guidance is the achievement of the largest possible improvement in health, for which purpose the existence of a body of

knowledge identifying which interventions are the most cost-effective is essential. It is particularly important to evaluate public health interventions because they generate extensive costs and benefits and often target not only specific individuals but also populations or communities, something that presents methodological challenges (Weatherly et al., 2009; Drummond et al., 2007).

An overview of the epidemiology of alcohol consumption and, in particular, of binge drinking, is provided in this introductory chapter, starting from the health and non-health impacts (impact on health, economic burden, HRQoL) of this consumption pattern, its determinants, the most effective interventions identified in the literature for the prevention of binge drinking, and concluding with information on the need to evaluate the efficiency of these programmes, and the most prevalent types of economic evaluation of interventions for the prevention of alcohol consumption and binge drinking.

The main reason for including data on the epidemiology of binge drinking is its high prevalence, with figures of around 20% in the general population globally and exceeding 30% in Europe (Peacock et al., 2018). These figures are even higher among the youth population, especially in Spain, where they reach rates of 32.3% according to the latest data (ESTUDES, 2018).

As previously noted, this public health concern related to behaviours and lifestyles is one of NICE's areas of interest and also a priority area in the WHO strategic plan for 2019–2023. Its impact, in both health and non-health terms, is considered relevant due to the greater vulnerability observed among adolescents with regard to the effects of alcohol and this pattern of consumption on their health and to the social problems and the economic burden that it engenders for society. As we search for solutions to this public health concern, it seems important to study the determinants of binge drinking in order to enhance the effectiveness of interventions designed to prevent this unhealthy behaviour. Lastly, the inclusion of the evaluation of efficiency, which is developed later in this chapter, is driven by the need for resource management and decision-making support for political decision-makers.

At this point, it is important to highlight the concept of "opportunity cost". In the health field, the "opportunity cost" refers to the loss of potential benefits from other options when one option is chosen ("Health Affairs Blog", 2019). Money wasted on medicines, programmes, interventions, and health technologies cannot be spent to solve other health

problems. The inefficiency of health systems is sometimes revealed when money is spent on certain high-priced health technologies with little effectiveness in overall economic terms, as in the case of adjuvant pertuzumab and trastruzumab in early HER2-positive breast cancer (von Minckwitz et al., 2017). Other instances of this inefficiency can be seen in a 2018 report on new products, issued by Prescrire, a French non-profit organization that specializes in providing training and information on medicines for health professionals. In Prescrire's review of new pharmaceuticals and indications, it can be observed that around 65% of new drugs, dosages, pharmaceutical forms, or indications were classified as "Nothing new", "Not acceptable" or "Judgement reserved" (Prescrire, 2019).

1.2. Alcohol consumption: a global public health concern

Alcohol consumption has been recognized as a risk factor for mortality (Rehm & Shield, 2013). According to the most recent WHO report on the subject, around 3 million deaths were attributable to alcohol in 2016 (38.8 deaths per 100,000 population), accounting for 5.3% of all deaths worldwide (WHO, 2018b). A more recent report based on the 2017 Global Burden of Disease (GBD) study gave similar figures of around 2.8 million alcohol-attributable deaths and highlighted an increase of 11% in alcohol-related deaths since 2007 (Institute for Health Metrics and Evaluation, 2018). In Europe, alcohol was responsible for 62.8 deaths per 100,000 population in 2016, accounting for 10.1% of all deaths and making Europe the region with the highest proportion of alcohol-related deaths. In Spain, there were 11,475 alcohol-attributable deaths in the same year, amounting to 4.3% of all deaths (WHO, 2018b).

Regarding morbidity, the effect of alcohol consumption on disability-adjusted life years (DALYs) should be highlighted. The DALY is a measurement of health benefits that represents a time-based measure of overall burden of disease for a given population and combines mortality and morbidity into a single summary measure of health (Institute for Health Metrics and Evaluation, 2018; Rehm & Gmel, 2003). This measurement is calculated as the sum of years of life lost (YLLs) to premature mortality and years of life lived with disability (YLDs) (Peacock et al., 2018). Worldwide, alcohol accounted for 132.6 million DALYs in 2016 (1,758.8 per 100,000 population), representing 5.1% of all DALYs in that year (WHO, 2018b). In 2017, data reported by GBD researchers identified a total of 108 million DALYs, an increase of 5.5% with respect to 2007. In the WHO European Region, alcohol was responsible for 2,726.5 DALYs per 100,000 population, making it the region with the second highest proportion of total DALYs (10.8%). At the national level in Spain,

an analysis of the components of the Sustainable Development Goals, an initiative of the United Nations, indicated that alcohol consumption was one of the leading causes of health loss in Spain in 2016 and would continue to be in 2030. In addition, alcohol consumption was reported to be the fourth leading risk factor for DALYs (Soriano et al., 2018).

Given the repeated references to DALYs above, it is worth briefly clarifying the difference between this measure and the quality-adjusted life years, or QALYs, metric found in the literature. There seems to be no consensus regarding the health benefit measure of choice – QALYs or DALYs – for health economic evaluations (Augustovski et al., 2018; Gandjour, 2015). Globally, DALYs lost is the metric favoured by WHO for the evaluation and comparison of the burden of disease in different countries (Salomon et al., 2012), while in most economic evaluations of health technologies QALYs gained are the preferred option (Hjelmgren, Berggren & Andersson, 2001; Augustovski et al., 2010). The reason for this preference is basically that most health technologies try to improve the quality of life of patients and society in developed countries. In addition, QALY is a measure that is sufficiently widespread to be able to compare the health benefits of any intervention across different diseases. For this reason, the term QALY will be used more frequently below and both its conceptualization and its use will be further developed in this work.

As regards epidemiological data on the problem of binge drinking, which poses a health risk, it is remarkable that almost half of adults worldwide (43% of the global adult population) are classified as current drinkers, meaning that 2.348 billion people have consumed alcohol in the last 12 months. The proportion of current drinkers is highest in the European Region at 59.9% (WHO, 2018b). At the national level, the survey on alcohol and other drugs in Spain, known as EDADES (2019), found that three in four people (75.2%) in 2017 reported that they had consumed alcohol at some point during the previous year. In addition, the prevalence of inebriation was 18.6% in the 12 months prior to the study and 15.3% in the preceding 30 days.

With regard to alcohol-related mortality and morbidity among youths, according to WHO (2018b), the proportion of deaths attributable to alcohol consumption in the global adolescent population aged 15 to 19 years was around 8% in 2016. This percentage was highest in Europe, reaching approximately 16%.

In general, alcohol use in the youth population is associated with the leading causes of death and serious injury (motor vehicle accidents, homicides, and suicides) (Siqueira et al.,

2015). Moreover, this unhealthy behaviour ranks second among modifiable risk factors (after road traffic accidents) and fifth among all main causes of DALYs lost in the adolescent population aged 15 to 19, accounting for 3.4 million DALYs, or 4% of all DALYs. Globally, when it comes to gender in this same age subgroup, the Global Burden of Disease study noted 106 and 84 YLDs per 1,000 population and 47 and 53 YLLs per 1,000 population for girls and boys, respectively (Gore et al., 2011). In general, among young people aged 10 to 24, alcohol use is the sixth leading cause of DALYs, accounting for 7.1 million DALYs lost (3% of all DALYs) (Gore et al., 2011). As previously mentioned, data on QALYs lost have not been found in the literature regarding morbidity caused by alcohol use, with DALYs being a preferred measure in reports on the subject.

Worldwide, more than a quarter (26.5%) of all 15- to 19-year-olds are current drinkers (meaning that they have drunk alcohol in the previous 12 months); a figure representing 155 million adolescents in 2016 (WHO, 2018b). Prevalence rates for current drinkers are highest in the WHO European Region (43.8%) (WHO, 2018b). The 2015 report of the European School Survey Project on Alcohol and Other Drugs (ESPAD) found that 48% of 15- to 16-year-old European adolescents had consumed alcohol in the 30 days prior to the survey and that 13% had been intoxicated (excessive alcohol use) at least once in that time period. When the data were disaggregated by country, the study showed that 65% and 21% of Spanish adolescents had consumed alcohol or been intoxicated, respectively (ESPAD Group, 2016).

In Spain, the 2019 EDADES survey (2019), which presented data from 2017, noted that three in four young people aged 15 to 24 years (76%) said they had consumed alcohol sometime in the preceding year. In addition, it indicated a prevalence of drunkenness of 36% in the preceding year and 7.1% in the preceding month. More recent data from the 2018 report of the Health Behaviour in School Aged-Children (HBSC) study found that 13.2% of adolescents aged 13 to 18 consumed alcohol on a daily or weekly basis and 19.8% had experienced four or more drunken episodes in their lifetime (Leal-López et al., 2019). In 2018, the Spanish Survey on Drug Use in Secondary Schools, known as ESTUDES, which was carried out in Spain with a large sample of 38,010 participants, reported that alcohol was by far the most widespread psychoactive substance used by students aged 14 to 18 years. Additionally, 75.9% of the students said that they had consumed alcoholic beverages in the previous 12-month period, while approximately 60% had drunk alcohol in the 30 days prior to the study (ESTUDES, 2018).

In light of the above, it can be deduced that global alcohol consumption has a great impact on public health, given that it is one of the main causes of death and disease in adults and adolescents. According to the experts, alcohol is the drug that causes the most harm (more than other drugs, such as heroin or tobacco) (Nutt, King, Phillips & Independent Scientific Committee on Drugs, 2010), and is comparable to tobacco in terms of the increased risk of developing a disease and, therefore, the increased risk of death in the longer term. Not only does alcohol have long-term effects similar to tobacco, but experts say that it can also kill quickly, through poisoning or injuries attributable to alcohol consumption (Kypri & McCambridge, 2018). As a consequence, alcohol-related deaths are more prevalent among young people than those caused by tobacco (Kypri & McCambridge, 2018). The effects of alcohol on mortality and morbidity are also influenced by an individual's consumption volume and pattern of drinking. The most serious problems occur when large amounts of alcohol are drunk within a very short period of time.

1.3. What is binge drinking? A controversial definition

Commonly, binge drinking is defined as a frequency of alcohol consumption that exceeds a given number of drinks or units per occasion or episode. The definition of binge drinking (BD) may be controversial, however, as is reflected in the multiple definitions found in the literature.

In the United States, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) defines it as a pattern of drinking that brings blood alcohol concentration levels to 0.08 g/dL, which typically occurs after four drinks for women and five drinks for men in about two hours (NIAAA, 2004). Similarly, the US Substance Abuse and Mental Health Services Administration (SAMHSA) defines BD as the consumption of five or more alcoholic drinks for males or four or more alcoholic drinks for females on a single occasion (i.e., at the same time or within a couple of hours of each other) on at least one day in the past month (SAMHSA, 2016).

In Europe, the ESPAD Group (2016) defines BD as drinking five drinks on one occasion. According to the Spanish Survey on Drug Use in Secondary Schools (ESTUDES), BD is defined as the consumption of five or more alcoholic beverages on the same occasion or within a two-hour period (2018). Parada et al. (2011) defined BD among the Spanish population as the consumption of 60 or more grams of alcohol for boys and 40 or more grams for girls on a single occasion lasting between four and six hours, during which time a

blood alcohol concentration of 0.8 g/L (equal to the 0.08 g/dL defined by NIAAA) is maintained.

Moreover, there is a need to determine the quantity of alcohol consumed, the duration of a single occasion or episode (Foster, Held, Gmel & Mohler-Kuo, 2016), and the different definitions of a "standard drink", or alcohol unit, since the amount that constitutes one unit of alcohol in grams of pure alcohol differs by country. For instance, in the United Kingdom, one unit of alcohol is equal to 8 grams; in Spain and in the Netherlands, Ireland, New Zealand, Poland, Austria, and Australia, one unit of alcohol is equal to 10 grams; and in the United States, one standard drink is defined as containing 14 grams of pure alcohol. For these reasons, making comparisons between studies and countries is very difficult.

1.4. Binge drinking: a prevalent pattern among adolescents

Worldwide, Peacock et al. (2018) estimate that the prevalence of heavy episodic alcohol use (defined as drinking 60 grams or more of pure alcohol on one occasion, a definition that is similar to that of binge drinking) in the preceding 30-day period was 18.4% among the general population. Central, eastern, and western Europe registered some of the highest rates of heavy episodic drinking (33.1%, 24.3%, and 30.5%, respectively). These prevalence rates were exceeded only by those in Australasia (34.4%), central sub-Saharan Africa (32.8%), and the high-income countries of North America (25.7%) (Peacock et al., 2018). In Spain, the EDADES survey in 2017 found a prevalence of binge drinking of 15.1% in the previous 30 days among the general population (EDADES, 2019). The prevalence of this behaviour peaks between the ages of 25 and 29 years for men (30%) and 20 and 24 years for women (20.3%). After these ages, the rates begin to decline.

Regarding the adolescent population, according to the 2015 ESPAD report, the prevalence of "heavy episodic drinking" (defined as the consumption of five or more drinks on at least one occasion in the previous 30 days) in Europe was 35% among 15- and 16-year-olds (ESPAD Group, 2016). For Spain, the data were slightly lower, with a prevalence rate of 31%. The Spanish EDADES study, carried out in 2017 in the general population, found a prevalence of BD in the month prior to the study of 19.9% for boys and 13.7% for girls (EDADES, 2017). Lastly, the ESTUDES report, which specifically surveyed Spanish adolescents aged 14 to 18 years, found that the prevalence of BD in the month prior to the survey had increased by 0.5% compared with 2016, reaching 32.3% in 2018 (ESTUDES, 2018). This type of alcohol use is more widespread among 18-year-olds, where almost half

of girls (46.8%) and boys (47.4%) reported having engaged in BD. It can be concluded from the above-mentioned data that BD is one of the most prevalent alcohol consumption patterns among the adolescent population. This behavioural risk has been linked to numerous serious and diverse alcohol-related health harms and to adverse consequences that affect not only the adolescents but also others in their environment (families, peers, communities) (Chung, Creswell, Bachrach, Clark & Martin, 2018) as well as causing an economic burden.

1.5. Binge drinking in adolescence: Impact on health

Generally, certain levels of alcohol use that cause little or no damage in the adult population may be dangerous for adolescents. For instance, the effect of alcohol on brain development (brain volume reduction) (Squeglia et al., 2014) and the increased risk of developing a chronic alcohol use disorder during adolescence (Windle & Windle, 2017) have been studied. Siqueira et al. (2015) affirmed that the risks of suffering adverse outcomes associated with alcohol use are increased when adolescents engage in BD patterns.

In particular, BD is widely associated with a greater risk of numerous acute consequences (acute ethyl intoxication, motor-vehicle traffic crashes, homicide, suicide) (Stahre et al., 2014); long-term effects (alcohol use disorder, irreversible disabilities); and the direct consequences of an acute state of intoxication (hangovers, blackouts, memory loss) (Siqueira et al., 2015; Stephens et al., 2008). Recently, Charakida et al. (2019) showed that high-intensity alcohol consumption was associated with greater arterial stiffness in the short to medium term (a five-year period). Adolescent binge drinkers also have a higher risk of becoming involved in problematic behaviours, such as impaired driving, riding in a car with an impaired driver and using other drugs (Stolle et al., 2009). Additionally, BD is associated with lower school performance, earlier sexual activity, sexually transmitted diseases, infertility and a higher risk of becoming a victim of unwanted sexual activity (Stolle et al., 2009; Champion et al., 2004).

With regard to the effect on brain activity, López-Caneda et al. (2013) showed through a follow-up study that young university binge drinkers presented anomalous brain activity after two years of this pattern of alcohol consumption, which is associated with earlier onset of regular drinking and with a greater quantity and intensity of consumption. This behaviour leads to poorer performance in various neuropsychological tasks requiring decision-making, visuospatial memory, and sustained attention (Goudriaan et al., 2007; Squeglia et al., 2009).

In another study (López-Caneda et al., 2014), it was found that BD, together with starting to drink regularly at a younger age, increases susceptibility to experiencing anomalies in neural activity associated with response inhibition. Parada et al. (2012) showed that BD is associated with poorer performance of tasks that require executive skills, specifically executive control of working memory.

Among the acute consequences of BD, one is "blackout", which is defined as loss of memory of events that occurred during a drinking episode. BD interferes with the brain's ability to maintain long-term memories from short-term situations and experiences. Similarly, BD is related to an increased risk of suffering a hangover within 24 hours of an episode, which affects cognitive functioning (Stephens et al., 2008).

Traffic accidents, as mentioned above, are one of the numerous acute consequences of BD in young people. Road traffic accidents are the main cause of death among adolescents, and a third of all fatal road accidents are associated with drinking alcohol (Stolle, Sack & Thomasius, 2009). Stolle et al. (2009) also reported that teenagers who are binge drinkers more frequently ride a bike without a helmet and ride in motor vehicles with drivers who have been drinking.

The link between BD and suicide should also be highlighted. Windle (2004) found that girls who engaged in BD were twice as likely to attempt suicide as girls of the same age who did not drink. Another study, carried out by Miller et al. (2007), concluded that the risk of suicide among binge-drinking students aged 14 to 19 years was 4.3 times higher than among those who were not binge drinkers.

It is worth mentioning a strong association was found in several studies between binge drinking and the consumption of other substances (marijuana, cocaine, and inhalants) (Giacomozzi, Itokasu, Luzardo, Figuereido & Vierira, 2012; Raposo et al., 2017; Silva-Oliveira et al., 2014; Tucker, Pollard, Haye, Kennedy & Green, 2013). Other authors, such as McKetin, Chalmers, Sunderland, and Bright (2014), found a non-causal association (related to the cross-sectional nature of the study) between the use of stimulants, such as ecstasy, methamphetamines, amphetamines, or cocaine, and BD in young people. Another drug associated with binge drinking is tobacco. Gubner, Delucchi, and Ramo (2016) reported a high rate of smoking on binge-drinking days among young people and concluded that the extent of binge drinking influences the smoking characteristics of this population. In addition, Milicic and Leatherdale (2017), exploring whether the use of e-cigarettes is

associated with other health risk behaviours, found that adolescents aged 14 to 18 who binge drink are more likely to use e-cigarettes than non-binge drinkers.

Lastly, in relation to the association between BD and sexual activity among adolescents, Champion et al. (2004) reported that the risk to adolescent girls of becoming the victim of unwanted sexual activity increases by about threefold if they binge drink. More recent studies, such as that of Waterman, Lee, and Edwards (2019), reported that adolescents who engaged in binge drinking more often were more likely to commit sexual harassment and stalking, and were more likely to be victims of stalking and dating violence. These findings did not vary by gender.

1.6. Binge drinking in adolescence: Impact on Health-Related Quality of Life (HRQoL)

An understanding of the impact of BD on the HRQoL of adolescents could contribute to research and practice by providing data for economic evaluation studies and the design of policies to discourage excessive intake of alcohol. The connection between the HRQoL measurement and economic evaluation is evident, as HRQoL is used to calculate quality-adjusted life years (QALYs), an outcome measure recommended by academics and institutions, such as the National Institute for Health and Care Excellence (NICE), for carrying out cost-effectiveness analyses when evaluating health technologies (NICE, 2013).

A large European-wide study (Dormal et al., 2018) of young adults, specifically university students, explored the associations between binge drinking and quality of life. In general, BD in this population was associated with a decrease in quality of life, which had also been observed in French adults (Luquiens, Falissard, & Aubin, 2016), Irish (Mohamed & Ajmal, 2015) and in American adults (Okoro et al., 2004). The study concluded that the negative influence of alcohol consumption on quality of life is determined by the presence of BD habits rather than by the intensity of consumption. This study, however, used a specific tool to measure alcohol-related quality of life (Luquiens et al., 2014, 2015), which, unlike other tools described in this introduction, does not allow for the calculation of utilities in health and therefore cannot be used in economic evaluations.

The sociodemographic factors associated with adolescent HRQoL have been investigated in numerous populations in school-based cross-sectional studies, such as the European KIDSCREEN study and the international study on Health Behaviour in School-

aged Children (HBSC) (Moreno et al., 2016; Ravens-Sieberer et al., 2014). Nevertheless, there is currently a lack of literature on HRQoL among adolescents who are binge drinkers or on the association between, and the impact of, BD on HRQoL (Kruger et al., 2014; Lima-Serrano et al., 2016; Watson et al., 2017). A study carried out by Watson et al. (2017) assessed HRQoL through the five dimensions of the EuroQol Group EQ-5D-5L and EQ-VAS instruments – without calculating QALYs – in a small group of young people who were undergoing various treatments for substance misuse. In addition, using a specific quality of life (QoL) questionnaire (KIDSCREEN), Lima-Serrano et al. (2016) showed a lower QoL for those who consumed alcohol.

For these reasons, one of the aims of this thesis is to study or evaluate the effects on health, in terms of HRQoL, achieved through the Alerta Alcohol programme (Lima-Serrano et al., 2018), an intervention aimed at reducing BD among Spanish adolescents.

Before delving deeper into the definition of the different HRQoL instruments for adolescents, it would be useful to clarify and differentiate between QoL and HRQoL. The term QoL predates HRQoL. It was already being mentioned in the 1960s (Elkinson, 1966; Spitzer, 1987), and it became more important as medical treatment was able to prolong survival, sometimes at the expense of quality of life (Kaplan & Bush, 1982). WHO defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns" (WHOQOL Group, 1993). Other QoL definitions focus on the inclusion of objective factors, such as the one by Felce and Perry (1995), who defined quality of life as "an overall general well-being that includes objective descriptors and subjective evaluations of physical, material, social, and emotional well-being, together with the extent of personal development and purposeful activity, all weighted by a personal set of values".

HRQoL is a major part of QoL and is considered to be an important construct in describing general health status (Bullinger & Ravens-Sieberer, 1995; Fayer & Machin, 2000; KIDSCREEN Group Europe, 2006; von Rüden, 2007). There is consensus that the term includes the physical, emotional, and social aspects of health (Bisegger, Cloetta, von Rüden, Abel & Ravens-Sieberer, 2005; Varni, Limbers & Burwinkle, 2007; Anderson, Aaronson & Wilkin, 1993), in line with the WHO definition of health as a state of complete physical, mental, and social well-being and not merely the absence of disease (WHO, 1948). Von Rüden (2007) defined HRQoL, based on the commonly accepted definition by the WHO Quality of Life (WHOQOL) Group (1993), as "a multidimensional construct covering

physical, emotional, mental, social, and behavioural components of well-being and functioning as subjective perceived by a person depending on the cultural context and value system one is living in". Despite the differences, the two terms, QoL and HRQoL, are often used interchangeably (Karimi & Brazier, 2016). This thesis focuses on HRQoL because of its use in measuring utilities or preferences for different health conditions, which, when combined with length of life into a single index summary measure, yields QALYs. Additionally, HRQoL is used in economic evaluations of health technologies, including public health programmes like the intervention assessed in this thesis.

HRQoL is a broad concept and there are therefore many instruments for measuring it. These can be classified as generic or condition-specific instruments, the main difference being that generic HRQoL instruments are applicable to individuals with a wide range of conditions, including healthy individuals, whereas condition-specific HRQoL instruments are only applicable to individuals with one condition ((Morales, Edwards, Flores, Barr & Patrick, 2011). Although generic instruments have the advantage of being applicable to all persons, they may not be sensitive to the particular HRQoL impacts of a specific condition (Morales et al., 2011; Chen, Li & Kochen, 2005).

For children and adolescents, generic instruments include the Quality of Well-being (QWB) scale; the Health Utilities Index Mark 2 and Mark 3 (HUI2 and HUI3); the 16-dimensional and 17-dimensional measures of HRQoL (16D and 17D); the Assessment of Quality of Life 6-Dimension (AQoL-6D) Adolescent; the EuroQol Group 5-Dimensional Questionnaire, Youth Version (EQ-5D-Y); the Child Health Utility 9D (CHU9D); and the Adolescent Health Utility Measure (AHUM) (Chen et al., 2015) (see details in Appendix 1). Of these measures, the tools most widely used in economic evaluations (due to their usefulness for measuring utilities) that have been validated in Spain (García-Pérez et al., 2014) are described below: the HUI (Ruiz et al., 2003), the six-dimensional health state short form (SF-6D) (Abeñán-Perpiñán et al., 2012; Rebollo, Morís, Ortega, Valdés & Ortega, 2007), and the EQ-5D (Badía, Schiaffino, Alonso, & Herdman, 1998; Badía, Roset, Herdman, & Kind, 2001).

The HUI system is a generic preference-based measure of the state of health and is intended for use in the measurement of clinical results, in health surveys, in programme planning, and in resource allocation. The scores obtained through this tool provide a summary index of HRQoL on a scale of zero to 1.0, which can be used in cost-utility analyses by calculating the QALYs. The HUI comprises several aspects of health, which are termed

attributes rather than dimensions. Each attribute is measured by several levels of function, which allows for a large number of possible permutations of levels in the attributes. This generates a large number of health states. The task of estimating utilities for large numbers of health states can be simplified if the classifications of health states are chosen to be structurally independent. This means that if a person selects one level on one attribute, this selection does not limit their level on another, so that any combination of the attributes could be possible (Ruiz et al., 2003).

The HUI3 version achieved complete structural independence, while HUI2 has partial independence. The HUI2 evaluates seven attributes: sensation (vision, hearing and speech), mobility, emotion, cognition, self-care, pain, and fertility. Three to five levels of function were defined for each attribute. The most recent version – HUI3 – covers eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain, each with five or six levels (Feeny, Furlong, Boyle & Torrance, 1995; Torrance et al., 1996, Feeny et al., 2002). The HUI3 version was shown to be feasible and reliable for the Spanish population in a study carried out by Ruiz, Rejas, Soto, Pardo, and Rebollo (2003).

The SF-6D was derived from the SF-36 health survey, which is a standardized questionnaire for assessing a subject's health across eight dimensions (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health). The questionnaire consists of several items or questions for each dimension, with three response options: "limited a lot", "limited a little", or "not limited at all". However, the method of scoring the SF-36 is not based on preferences and assumes equal intervals between the response choices. It also assumes that the items are of equal importance. For instance, being limited in walking has the same importance as being limited in climbing flights of stairs. In the SF-6D version, the number of dimensions is reduced to six (physical functioning, role limitations, social functioning, pain, mental health, and vitality), each with between two and six levels. An SF-6D health state is defined by selecting one statement from each dimension, starting with physical functioning and ending with vitality. A total of 18,000 health states can be defined with this tool (Brazier, Roberts & Deverill, 2002). It is rarely used for the adolescent population (Gee, Abbott, Conway, Etherington & Webb, 2002; Jörngården, Wettergen & von Essen, 2006; Lins & Carvalho, 2016; Rankin et al., 2019).

The EQ-5D version for youth (EQ-5D-Y) has been validated for the population aged 8 to 15 years, but more studies are needed to inform the choice of instrument for valuing

HRQoL for the economic evaluation of adolescent healthcare treatments and services (Chen et al., 2015; Gusi, Perez-Sousa, Gozalo-Delgado & Olivares, 2014). Currently, there is no value set for the EQ-5D-Y and so its use in cost-utility analysis is limited (Kreimeier & Greiner, 2019), as the absence of a value set interferes with the calculation of QALYs (Kreimeier et al., 2018).

The EQ-5D-5L questionnaire was used in this thesis to calculate QALYs by means of the EQ Utility Index. This index was calculated by using the Spanish value set (García-Gordillo, Adsuar & Olivares, 2016; Martín-Fernández et al., 2017; Ramos-Goñi et al., 2018; Hernández et al., 2018). Nevertheless, the EQ-5D-Y questionnaire was not considered appropriate for measuring HRQoL in our sample because the questionnaire comprises values set for children and adolescents aged 8 to 15 years, as mentioned above, and our sample included adolescents between 15 and 19 years of age. The EQ-5D-5L (the adult version) was therefore considered to be the most appropriate version of the questionnaire, as it is indicated for use from the age of 15 years (Rowen, Rivero-Arias, Devlin & Ratcliffe, 2020). Additionally, this tool has been incorporated into the Spanish National Health Survey (ENSE) since 2011/12 (Ministerio de Sanidad, Servicios Sociales e Igualdad, 2014), and its language and number of dimensions are more suitable for teenagers aged 15 to 19 than other questionnaires, such as the SF-36 or the HUI.

1.7. Economic burden of the binge drinking

There is a lack of data on the economic burden of binge drinking. The most recent figures found in the literature are from 2010 and are detailed below.

At the international level, excessive drinking cost $249.0 billion in the United States in 2010, with the US government paying $100.7 billion (40.4%) of those costs (Sacks, Gonzales, Bouchery, Tomedi & Brewer, 2015). When disaggregated by consumption pattern, binge drinking accounted for $191.1 billion (76.7%) of those costs. Binge drinking also accounted for over 70% of the costs associated with excessive drinking in all US states, with more than 40% of binge-drinking-related costs being paid for by the state governments (Sacks et al., 2015).

In Europe, estimates of 1.3% of gross domestic product (GDP) (approximately €150 billion) were attributed to the social costs of alcohol misuse in 2010 (Rehm, Shield, Rehm, Gmel & Frick, 2012), although these data are not specifically for binge drinking. Previously,

Rehm, Mathers, Popova, Thavorncharoensap, Teerawattananon, and Patra (2009) had reported estimates of 1.4% of the GDP of France and of Scotland.

Regarding the social costs in Spain of alcohol misuse, although not specifically binge drinking, Ivano Scandurra, García-Altés, and Nebot (2011) estimated that the direct and indirect costs amounted to €2.7 billion in 2007. However, Rehm Rehm, Shield, Gmel, and Gual (2013) noted that this study had limitations, as major cost factors were not included. These authors estimated the real costs of alcohol misuse in Spain to be around 1% of GDP (Rehm, Rehm, Shield, Gmel & Gual, 2013). Previously, Baumberg (2006) had included data from Spain in his review, reporting that alcohol was found to account for 2.4% of total health spend in 2002.

In addition to the costs associated with binge drinking mentioned above, various studies have estimated costs associated with alcohol use, although not specifically binge drinking. Baumberg (2006) carried out a critical review of cost estimates of the global economic burden of alcohol, covering numerous studies from different countries. A global economic burden of between $210 billion and $650 billion in 2002 was estimated. These figures comprised $40–$105 billion in healthcare costs, $55–$210 billion in premature mortality, $30–$65 billion in absenteeism, $0–$80 billion in unemployment, $30–$85 billion in criminal justice systems, and $15–$50 billion in criminal matters, adding up to between 0.6% and 2.0% of GDP.

A study conducted by Rehm et al. (2009) also reported data on the total global economic costs of alcohol, differentiating between high- and middle-income countries. The total average cost in high-income countries (Canada, France, Scotland, United States) was $179.86 billion; in middle-income countries (Republic of Korea, Thailand), it was $15.1 billion. These total costs represent an average expenditure of 2.5% of GDP in high-income countries (with the highest expenditure, 2.7%, being in the United States) and 2.1% of GDP in middle-income countries (with the highest expenditure, 3.3%, being in South Korea). Indirect costs due to productivity losses were the predominant cost category of all the social costs attributable to alcohol in all countries and in both groups, ranging from 49% of the total cost in Canada to 95% in Thailand. In terms of direct costs in high-income countries, the "'other direct costs" category was the largest contributor in France and South Korea, while direct healthcare costs contributed the most to direct costs in Canada and the United States. In middle-income countries, direct healthcare costs accounted for the largest share of direct costs in Thailand.

At the European level, the average cost of alcohol-related crime and traffic accidents was estimated at €33 billion and €10 billion, respectively, in 2003 (Anderson & Baumberg, 2006).

Additional data on the costs associated with alcohol use in various countries were found in the literature. For instance, in the United Kingdom, data on the economic burden of alcohol were included in a report (Scarborough et al., 2011) updating the estimates of the economic burden for the National Health Service (NHS) of various behavioural risk factors for chronic diseases. The significant economic burden of these non-communicable diseases is noteworthy, as they represented 46% of the total costs of the NHS (more than £43 billion) in 2006 and 2007. In particular, alcohol-related health problems cost the NHS £3.3 billion. The UK Department for Transport (OECD, 2015) later reported on the specific costs associated with alcohol use. For example, in 2012, the economic loss to UK society of traffic accidents caused by alcohol abuse was estimated at £1.5 billion (€1.7 billion).

An economic evaluation using Markov processes and decision trees was recently carried out by Jyani, Prinja, Ambekar, Bahuguna, and Kumar (2019) in order to explore the potential health impact and economic burden of alcohol use on the population of India. The study estimated that the treatment of alcohol-related health conditions would result in a gross economic burden on the government of 5,421 billion Indian rupees (INR) (€66.12 billion) by 2050. When future costs are discounted at a rate of 3%, these costs would total INR 3,127 billion (€38.14 billion). The gross burden on society of alcohol-related health conditions, including health system costs, out-of-all expenditures, and productivity losses, would amount to INR 209,840 billion (€2,559.49 billion) and, after applying the discount, INR 121,364 billion (€1,480.32 billion). After all the analyses were carried out, the study concluded that if current patterns of alcohol consumption continue, the Indian economy would lose 1.45% of GDP per year due to alcohol consumption.

Another recent study (Ranaweera et al., 2018) found in the literature quantified the economic cost of alcohol-related conditions in Sri Lanka in 2015. The study reported a total economic cost of alcohol use of $885.85 million, of which $388.35 million (44%) were direct costs and $497.49 million (66%) were indirect costs. Regarding indirect costs, loss of productivity due to premature mortality was the highest cost category, representing 44% ($388.86 million) of the total costs. The next highest cost was a direct cost: the cost of hospital care, which, at $293.75 million, accounted for a third of the total costs.

In summary, costs related to alcohol consumption, and specifically to binge drinking, can be classified as direct costs and productivity losses. Among the direct costs, both healthcare-related and non-healthcare-related costs, such as the costs arising from traffic accidents and legal problems, were considered.

1.8. Binge drinking in adolescence: analysing socioeconomic determinants

Few studies have explored the socioeconomic determinants of alcohol consumption, and specifically of binge drinking, among adolescents. This could be due to the difficulty of carrying out longitudinal studies that can determine causality and the lack of a standardized measure of the drinking pattern known as binge drinking. Moreover, self-reporting by adolescents may increase the chances of erroneous data. Nevertheless, it is one of the few options currently available for studying the socioeconomic determinants of this behaviour in this population group.

Before describing the socioeconomic determinants of BD, particularly for adolescents, found in the literature, it is worth highlighting a recently published study by Beard, Brown, West, Kaner, Meier, and Michie (2019). The study analysed the relationship between different measures of social status, education, and income level and alcohol consumption among the adult population in England. They found that the lowest occupational categories, as measured by the British National Readership Survey Social Grade Classification Tool, such as semi-skilled and unskilled manual workers, the unemployed, pensioners, and casual workers, reported lower frequency of drinking than those who held professional or managerial jobs. Additionally, educational achievement was one of the strongest predictors. Those who reported having a lower educational level (for example, secondary education) drank substantially more and reported a higher frequency of binge drinking than those with a university education.

The socioeconomic determinants of BD in adolescence studied to date can be summarized as person-specific factors (personality, impulsivity, negative experiences, motives, expectancies, and academic achievement) and social (family, peers, environment) factors, according to the classification used by Kuntsche, Kuntsche, Thrul, and Gmel (2017). In addition, economic factors (parents' socioeconomic position, weekly pocket money availability) have been analysed in other studies.

Person-specific factors include biological factors, whose association with binge drinking is also being studied. As is already known, the pharmacokinetics of alcohol differ according to sex and age: higher blood alcohol concentrations (BACs) have been found in younger subjects when compared to adults with similar levels of alcohol consumption. Regarding sensitivity to alcohol, it is posited that hormonal changes can reduce adolescents' sensitivity to the effects of intoxication, such as sedation and loss of coordination. This lack of sensitivity to alcohol may also be related to immaturity of the neurotransmitter receptor system in adolescents (Siqueira et al., 2015). The ascending limb theory postulates that, in the initial phase of alcohol consumption, heavy drinkers are more sensitive than light drinkers to the subjective positive euphoric effects of alcohol but are less sensitive to the sedative effects. Therefore, young people, who are more sensitive to the subjective euphoric effects in the initial stages of alcohol consumption, are more likely to become heavy drinkers and also binge drinkers (Holdstock, King & de Wit, 2002).

Other person-specific factors are outcome expectancies and self-efficacy, which are key components of human behaviour in accordance with Bandura's social learning theory (1977). The expectancies that adolescents may have prior to consuming alcohol influence decision-making in this population group. In relation to binge drinking, boys are reported to have greater positive expectancies and are more frequently associated with this alcohol consumption pattern than girls (Blume, Schmaling & Marlatt, 2003). Among girls, it has been found that those with a history of child abuse see the reduction of continuous tension as a positive expectation of alcohol and therefore a justification for greater consumption.

As previously mentioned, Bandura's other important concept that influences health behaviour is self-efficacy. This may be related to the ability of young people to refuse alcohol, since those with low resistance skills have been found to have greater susceptibility to peer pressure to binge drink (Bandura, 1977; Connor, George, Gullo, Kelly & Young, 2011). With regard to alcohol outcome expectancies, Golpe, Gómez, Braña, Varela & Rial (2017) found that those who had engaged in BD in the previous year overrated the positive effects of alcohol ("positive" meaning "having fun", "feeling happy", and "feeling outgoing"). Likewise, they underrated the negative effects of alcohol, such as problems with the police, not being able to stop drinking, or causing harm to their health.

Other risk factors described in the literature relate to young people's motivations to drink excessively. One of the motivations associated with this pattern of alcohol consumption is the search for positive emotional states, which is related to personality

characteristics, such as sensation-seeking (Comeau, Stewart & Loba, 2001), low inhibitory control (Leeman, Patock-Peckham & Potenza, 2012), and impulsivity (Shin, Hong & Jeon, 2012). Regarding personality characteristics, Adan, Forero, and Navarro (2017), who conducted a systematic review of the findings on personality traits associated with binge drinking, found that the main personality characteristics are high impulsivity and high sensation-seeking, anxiety sensitivity, neuroticism (hopelessness), extraversion, and low conscientiousness.

Regarding parental influence, it has been shown that BD prevalence increases as the educational level of parents decreases (Golpe et al., 2017). This study also found statistically significant differences regarding the curfew set by parents: the later adolescents arrived home, the higher the BD rate. Having more weekly pocket money was also associated with higher BD percentages (Golpe et al., 2017). Sánchez et al. (2011) found that, among Brazilian students in private high schools, BD was significantly associated with not living with the mother, rarely talking to the parents or having meals with them, and having little trust in God, whereas the family's immigrant origin and the existence of parental control over curfew times at weekends tended to reduce the likelihood of binge drinking (Hernáez et al., 2012). Martínez-Hernáez, Marí-Klose, Julià, Escapa, and Marí-Klose (2012) found results similar to those of Sánchez et al. (2011) in relation to communication with parents, in particular that a higher degree of communication between girls and their fathers reduces the likelihood of BD. In addition, attending group prayer meetings at least once a week and not living with someone who gets drunk were inversely associated with BD. Living in a non-nuclear family increased the risk of harmful consumption among young people in rural areas (Llorens, Barrio, Sánchez, Suelves & Group, 2011).

A link between family alcohol consumption and BD among adolescents was also found in the study carried out by Golpe et al. (2017), which reported a higher prevalence of BD among adolescents whose family members drank alcohol regularly. The greatest differences noted were among adolescents whose siblings drank. This association is even stronger when an adolescent's peers drink alcohol, get drunk, smoke tobacco, or use other drugs.

Several authors have found that peers have a strong influence on both individual drinking volumes (Clapp & Shillington, 2001; Wechsler & Nelson, 2008; Larsen et al., 2009; Thrul & Kuntsche, 2015) and risky drinking patterns (Kuntsche et al., 2015). Sánchez et al. (2011) made the same finding with regard to Brazilian students who frequently went out with friends at night. No differences have been found between rural and urban environments with

respect to peer influence (Obradors-Rial, Ariza & Muntaner, 2014). In both environments, alcohol consumption among a young person's siblings and friends continues to be the most powerful explanatory factor for risky alcohol consumption (Llorens et al., 2011).

With regard to economic factors, a systematic review of the association between parental socioeconomic status (SES) and adolescent binge drinking concluded that most studies do not find any such relationship (Kwok & Yuan, 2016). Some differences were found depending on whether the studies were carried out in developed or developing countries. However, these results were largely explained by the variation in measurements used in the studies for both binge drinking and socioeconomic status (Kwok & Yuan, 2016). Bosque-Prous et al. (2017) found that parental socioeconomic position (SEP) (parental education and family affluence) was not associated with adolescent drinking, whereas high weekly student income and low academic achievement were associated with a greater likelihood of alcohol consumption (including weekly binge drinking and weekly alcohol consumption).

Although the relationship between SEP indicators and BD varied between different countries, in most countries adolescent SEP was associated with alcohol consumption (weekly binge drinking and weekly alcohol consumption), while parental SEP was not. Collins (2016) found that, although people with higher SES may consume similar or greater amounts of alcohol than people with lower SES, the latter group seems to be more negatively affected by alcohol-related consequences.

Other studies that analysed economic factors include the one carried out by Martínez-Hernáez, Marí-Klose, Julià, Escapa, and Marí-Klose (2012), who found that being enrolled in a school with a lower tuition rate was inversely associated with BD. When gender is taken into account, according to Martínez-Hernáez et al. (2012), women appear to be more susceptible to the influence of socioeconomic factors. The highest frequency of BD generally occurs among women from higher income groups. Differences between urban and rural areas have also been found. For instance, family factors seem to have a greater influence on young people in rural areas, who also tend to have a lower level of academic achievement (Stock et al., 2011). Education level also has an influence in rural areas, but not in urban areas, where socioeconomic status (Font-Ribera et al., 2013) is more important (Obradors-Rial, Ariza & Muntaner, 2014). In addition, Song, Smiler, Wagoner, and Wolfson (2012) report that greater availability of money exponentially increases the risk of harmful alcohol consumption among adolescents.

In summary, the variables that have been studied as factors associated with binge drinking are: biological factors, such as hormonal changes that can cause greater sensitivity to the effects of alcohol and the lack of maturity of the neurotransmitter receptor system in adolescents; alcohol expectancies and self-efficacy; sensation-seeking; loss of control and impulsivity; influence of the environment (parents, siblings, peers); parents' educational level; parental rules; communication at home; family composition; and family and peer alcohol consumption. It can be concluded that there is a consensus gap in relation to the economic factors associated with binge drinking, given the differences found in the various studies due to both the measures used and the characteristics of the population studied (origin, rural or urban residence, and gender).

This thesis sought to address some of the gaps noted in the literature through the study of these economic factors, together with other social and family factors that may contribute to binge drinking among adolescents. The findings in this regard are presented in paper 2, entitled *Social, economic and family factors associated with binge drinking in Spanish adolescents.*

1.9. Approaches for tackling binge drinking in adolescence: current preventive interventions

As previously discussed, the early initiation of alcohol consumption and the adoption of a binge drinking pattern increases the risk of developing alcohol dependence or abusing alcohol in the future (Caamaño-Isorna et al., 2017, DeWit et al., 2000; Grant & Dawson, 1997; Grant, Stinson, & Harford, 2001, Spoelder et al., 2015, Windle & Windle, 2017). Although interventions or programmes aimed at treating this dependence or disorder are needed, this section focuses on the implementation of prevention and early intervention programmes with a specific emphasis on preventing binge drinking among adolescents, as such programmes could prevent the progression towards an alcohol use disorder or dependence, thereby reducing the consequences of this unhealthy behaviour and its associated costs.

Although prevention and early intervention programmes to reduce adolescent substance abuse are common, very few are aimed specifically at preventing BD. Moreover, no systematic reviews were found that compared prevention programmes and early interventions to prevent or curb BD in the adolescent population. However, Das, Salam, Arshad, Finkelstein, and Bhutta (2016) recently published an overview of systematic reviews of interventions to prevent adolescent substance abuse, the majority of which were found to

be school-based interventions (Foxcroft & Tsertsvadze, 2012; Hennessy & Tanner-Smith, 2015; Scott-Sheldon et al., 2014; Strøm et al., 2014), family/community-based interventions (Foxcroft & Tsertsvadze, 2011a), digital platforms (Carey et al., 2009), policy interventions (Siegfried et al., 2014), or multi-component interventions (Foxcroft & Tsertsvadze, 2011b).

Das, Salam, Arshad, Finkelstein and Bhutta (2016) highlighted the lack of data about the differential effects of interventions by gender, socioeconomic status, and population density, and the lack of data on the sustainability and long-term effectiveness of programmes targeting adolescents. As a result, they consider it necessary to assess the relative effectiveness and cost-effectiveness of interventions. However, these authors found that school-based alcohol prevention interventions that included personalized feedback, moderation strategies, expectancy challenge, identification of risky situations, goal-setting, and brief alcohol interventions (BAIs) were associated with a reduction in alcohol-use frequency, while computer-delivered interventions (CDIs) were found to reduce not only the frequency of consumption but also the amount of alcohol consumed (Das et al., 2016).

In fact, a meta-analysis carried out by Krebs, Prochaska, and Rossi (2010) that examined computer-tailored interventions to facilitate health behavioural change demonstrated that this type of intervention has the potential to improve health behaviours. However, the study was focused on smoking cessation, physical activity, healthy eating, and regular mammography screening, rather than on reducing alcohol consumption or binge drinking.

Some examples of studies aimed specifically at preventing BD can be found in the literature. Hanewinkel, Tomczyk, Goecke, and Isensee (2017) tested a school-based prevention programme known as *Klar Bleiben* (Stay clear-headed), concluding that the intervention had an effect on the frequency and intensity of binge drinking among adolescents who had already consumed alcohol but not on those who had alcohol-related problems. On the other hand, Anderson-Carpenter, Watson-Thompson, Chaney, and Jones (2016) evaluated the Strategic Prevention Framework (SPF) aimed at reducing BD among adolescents in the US. The SPF is based on a model that supports the use of multi-component community-based approaches, and its implementation led to significant improvements in BD and enforcement outcomes, although there were no significant differences between the intervention and comparison groups. Anderson-Carpenter et al. (2016) therefore concluded that their findings would provide a basis for future research in implementing and evaluating the SPF.

The last study, by Jander, Crutzen, Mercken, Candel, and de Vries (2016), aimed to assess whether a web-based computer-tailored intervention known as *Alcohol Alert* was effective in reducing binge drinking among Dutch adolescents aged 15 to 19 years. The intervention proved effective in decreasing binge drinking among 15- and 16-year-olds. Additionally, the intervention's cost-effectiveness was analysed in terms of a reduction of one glass of alcohol per week or of one occasion of excessive drinking within a 30-day period (Drost et al., 2016). The study found positive incremental cost-effectiveness ratios (ICERs) from both societal and healthcare perspectives, meaning that the intervention was more expensive and more effective compared with receiving care as usual. The authors' subgroup analysis found that the intervention was cost-effective for older adolescents (17 to 19 years old) and those at a lower educational level from both the healthcare and societal perspectives.

1.10. Economic evaluation of alcohol prevention programmes in adolescence

The greatest effort and workload in public health is sometimes directed towards the design and implementation of policies, programmes, and projects, but insufficient attention is paid to the main objective of these measures, which is to impact positively on or to improve the health of populations (Sandín-Vázquez & Sarría-Santamera, 2008).

Health impact assessment (HIA) is a comprehensive methodology proposed by the WHO to determine the health impact of projects, policy proposals, and strategies that have health effects. HIA is a multidisciplinary process that combines qualitative and quantitative analyses in a decision-making framework. Its objective is to improve knowledge about the effect of policies or programmes on the health of populations, inform policymakers and affected populations, and facilitate changes in the evaluated policies to mitigate negative effects and maximize positive impacts (Parry & Kemm, 2005). For NICE (Health Development Authority, 2002), HIA is a procedure, method, or tool that predicts the consequences that a policy, strategy, programme, or project may have for the health of the population and its various groups. It influences policymakers by advising them to consider the implications and possible benefits of their decisions for public health (Sandín-Vázquez & Sarría-Santamera, 2008). Economic evaluation is a tool used for carrying out this assessment.

According to Foster, Dodge, and Jones (2003), economic evaluations are valued not only because of their usefulness in responding to statistically significant results of an intervention in terms of its impact on health, but also because they can help to ensure the

proper use of the intervention in line with the resources of the society. Moreover, economic evaluations have other benefits, such as enabling policymakers to compare different programmes on the basis of a common outcome metric (e.g., net benefits or quality of life), and to compare interventions that provide benefits that differ over time. This is because economic evaluations take into account the cost discount rate and future benefits (Foster et al., 2003).

1.10.1. Type of economic evaluations for alcohol prevention programmes

The most common analytical methods of economic evaluation that are used for alcohol programmes are cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). Cost-consequence analysis (CCA), cost-benefit analysis (CBA), and return-on-investment analysis (ROI) are also used, but less frequently (Hill, Vale, Hunter, Henderson & Oluboyede, 2017). In a CBA, if, after calculating the benefits of the intervention minus its costs, the net benefits are positive, then the intervention is desirable (Foster et al., 2003). Interventions with an estimated negative net present value should not be recommended, unless other factors, such as social value judgements, outweigh the costs.

The inclusion of the value of all non-health- and health-related effects in a CBA should be taken into account (NICE, 2014). Among the advantages of this type of analysis is the inclusion of the benefits achieved for people as a result of an intervention and the fact that the costs and benefits are expressed in monetary terms, thereby avoiding the difficulties of incorporating data from other analytical methods of economic evaluation, such as CCA (NICE, 2018). However, a CBA also has disadvantages, such as the difficulty in quantifying some outcomes in monetary terms and the requirement for surveys to sometimes be carried out in order to estimate all relevant costs and assess individuals' willingness to pay them (NICE, 2018).

Unlike CBA, a cost-effectiveness analysis (CEA) does not require the results to be measured in monetary terms. In contrast, the outcome measures remain in their natural metric (for example, a 1-point difference in a symptom checklist, a life-year saved, a death averted, a patient-year free of symptoms). The analyst then compares interventions or programmes in terms of their additional (or incremental) costs per aggregate unit of the outcome measure using different means (NICE, 2014; Zerbe & Dively, 1994). It should be pointed out that the outcome is not valued separately, but is only quantified; CEA compares the cost of different methods of achieving outcome units, but does not evaluate whether the

cost is worth incurring (NICE, 2014). When there is strong evidence that an intervention dominates the alternatives to which it has been compared – meaning that the intervention is more effective and less costly – that intervention should be recommended. However, when one intervention is more effective but also costlier than another, the incremental cost-effectiveness ratio (ICER) should be considered. For this purpose, an established ICER threshold must be used (NICE, 2014).

Cost-utility analysis is a form of cost-effectiveness analysis (NICE, 2014), but the outcome or measure of effectiveness is a measure of general well-being based on respondents' qualifications of various dimensions of well-being or quality of life. A commonly used measure of this type is the quality-adjusted life year (QALY) (Drummond et al., 1997). According to NICE (2014), CUA considers the gains in an individual's quality of life and length of life as a result of an intervention or programme. NICE recommends using QALYs as a measure of health effects and the EQ-5D questionnaire as a tool to measure HRQoL.

Another analytical method of economic evaluation that is used in alcohol programmes is the ROI analysis. This can be defined simply as a metric that allows the financial consequences (returns) of the actions (investments or costs) to be compared. It can be assumed that when returns exceed costs, a net profit is generated, which means that the investment is worth the costs incurred and a decision can therefore be made in favour of that investment (Pokhrel, Owen, Coyle & Coyle, 2017). NICE (2011) defines ROI as "a general term encompassing the techniques for comparing the costs and benefits generated by an investment" and suggests that several indicators can be used as ROI indicators: cost-benefit ratio (CBR), net present value (NPV) savings, incremental net profit (INB), and even the incremental cost-effectiveness ratio (ICER).

Certain aspects of the ROI analysis should be considered. As is known, the benefits of public health interventions are often observed or accumulated in the distant future. It is therefore critical in ROI analyses to consider what time horizon would be long enough to capture changes in health and broader benefits. In addition, since the concept of ROI comes from the business sector, it adopts an investment vision designed to compare and set priorities in the context of a "portfolio" of projects, which may comprise more than one action (investment). In relation to public health, this concept allows for the evaluation of a "package" of interventions in a specific area, such as a care pathway (for example, healthy

weight care pathways) or to mitigate an exposure (for example, control of alcohol consumption).

Given that the intervention studied in this thesis concerns the field of public health, it seems pertinent to include NICE's approach to the evaluation of interventions in this field. Although the inclusion of the CCA and CBA in the economic evaluation of these interventions is advised, NICE stresses that CEA and CUA will always be required, for various reasons (NICE, 2018). These reasons include the fact that, since CUA provides a single criterion or "currency" to measure impact on health, this type of analysis should be maintained whenever health is the predominant benefit of the intervention. Likewise, CUA allows interventions to be compared, thereby enabling the more efficient allocation of resources. NICE emphasizes the importance of ensuring that all programmes include a common cost-effectiveness analysis method that allows comparisons to be made between them. Lastly, given that in some circumstances, most of the benefits are health benefits, and in these cases, where there is a clear indication of cost-effectiveness, an intervention decision is unlikely to change, so no additional analysis (such as CCA or CBA) would be required.

1.10.2. Basic elements of economic evaluations for alcohol and binge drinking prevention programmes

Very few studies in the literature are focused on economic evaluations of interventions or programmes aimed at the prevention of binge drinking. To our knowledge, the study carried out by Ingels, Corso, Kogan, and Brody (2013), which is part of the systematic review carried out by Hill et al. (2017), was the only study in that review to examine the cost-effectiveness of an intervention specifically aimed at preventing binge drinking among adolescents. The study conducted an incremental cost-effectiveness analysis of the Strong African American Families-Teen (SAAF-T) programme. The programme is focused on reducing substance use among rural African American adolescents through family skills training, an approach that integrates individual adolescent skill-building, parenting skills training, and family interaction training (Ingels, Corso, Kogan & Brody, 2013). The other 26 studies covered in the Hill et al. review focused on economic evaluations of interventions aimed at preventing alcohol consumption, in general and in specific populations.

Subsequent to this review, several other studies involving economic evaluations of interventions for the prevention of binge drinking among adolescents have appeared in the literature (Crombie et al., 2018; Drost et al., 2016; Kruger et al.; 2014; Sumnall et al., 2017).

Regarding intervention coverage, the studies found focus more on evaluations of secondary/tertiary prevention interventions than on primary prevention interventions (Hill et al., 2017). The basic elements of the economic evaluations included in the studies mentioned above – namely, the analysis perspective, the time horizon and discount rate, the decision analysis or model used, and uncertainty – are summarized below.

Perspective

Regarding the perspective used, Drost et al. (2016), Ingels et al. (2013), and Sumnall et al. (2017) chose the societal perspective, although Drost et al. (2016) also used the healthcare perspective. Kruger et al. (2014) performed an economic evaluation from the perspective of the UK Department of Health, while Crombie et al. (2018) conducted their study from the perspective of the government (costs to the NHS and to social services). According to Hill et al. (2017), the perspective most often adopted in economic evaluations of alcohol programmes is that of the healthcare sector or a country's national health system. Nevertheless, economists emphasize the social perspective, which encompasses the perspective of all groups, including intervention participants and taxpayers (Foster et al., 2003).

The Washington Panel on Cost-effectiveness in Health and Medicine proposes the use of the social perspective in economic evaluations (Gold, Siegel, Russell & Weinstein, 1996; Neumann, Sanders, Russell, Siegel & Ganiats, 2016), while the National Institute for Health and Care Excellence in the United Kingdom (NICE, 2018) recommends a public sector or local government perspective as the most appropriate for conducting evaluations of public health interventions. One reason for not carrying out analyses from the social perspective is that there are often time and resource constraints that prevent the compilation of all the data necessary to truly reflect a social perspective (Byford & Raftery, 1998). Some costs and benefits can also be difficult to capture.

Limiting the analysis of a public health intervention to a health perspective can, however, lead to the intervention being either undervalued – if there are cost savings in other sectors – or overvalued – if costs are incurred in other sectors as a result of the intervention. Baal, van Berg, van Den, and Tariq (2008) point out that taking a medical care perspective means focusing only on the costs of medical care and ignoring the broader costs and consequences of alcohol abuse to society. However, this broader social impact is likely to be substantial. In addition, in accordance with Hoang et al. (2016), when assessing interventions

for alcohol and other drug problems, the selected perspective will be a key element in determining which costs and health benefits/effects are chosen and might have a strong impact on the assessment of the net benefits of treatments.

Time horizon and discount rate

With regard to time horizon, the authors who used a longer time horizon were Kruger et al. (2014) and Crombie et al. (2018), whose studies applied a lifetime horizon and a 29-month time horizon, respectively. The rest of the studies used time horizons that ranged from 4 to 18 months (Drost et al., 2016; Sumnall et al., 2017; Ingels et al., 2013). Most of the studies therefore adopted relatively short time horizons, limiting their analysis to a maximum of 12 months (short-term results) after the intervention (Hill et al., 2017). As a consequence, those studies cannot reflect the real impact of preventive interventions, since, for example, excessive alcohol consumption can lead to the development of chronic diseases in the longer term, over periods of no fewer than ten years (Rehm et al., 2010). Moreover, long-term economic evaluations should consider the possible decrease in the effect of interventions over time (Cowell, Brown, Mills, Bender & Wedehase, 2012; Havard, Shakeshaft, Conigrave & Doran, 2012; Barbosa, Cowell, Bray & Aldridge, 2015). Drost et al. (2016) and Ingels et al. (2013) did not apply a discount rate, while the other authors applied discount rates of 1.5% (Kruger et al., 2014) and 3.5% (Crombie et al., 2018; Sumnall et al., 2017) per annum. This latter figure is the one recommended in the NICE guidance (2013).

Modelling approaches

Given the difficulties associated with carrying out long-term studies, an alternative might be to use current modelling methods (Marsh, Phillips, Fordham, Bertranou & Hale, 2012), but to incorporate the results of the tests in a model along with the estimated data from the literature on external factors, thereby facilitating more informed decision-making.

With regard to available modelling approaches, the use of the Markov model was observed in a study by Kruger et al. (2014), and the mathematical model known as the Sheffield Alcohol Policy Model (Angus, Holmes, Robert, Meier & Brennan, 2016; Brennan et al., 2015; Purshouse et al., 2009) was used by Crombie et al. (2018). In a systematic review of modelling approaches in economic evaluations of health interventions for drug and alcohol problems, Hoang et al. (2016) concluded that decision trees and cohort-based

Markov models were the approaches most often used, followed by the system dynamics model and the individual-based model.

Costs

When carrying out an economic evaluation it is important to consider the four principles by which economists define and measure costs. The first principle is that the costs of a programme or intervention vary according to the perspective from which they are evaluated. The second principle is that economists measure costs in terms of opportunity costs, the value of a resource in its next best use (Gold, Russell, Siegel & Weinstein, 1996). The third principle is that some costs are indirect or are related to morbidity, and the fourth principle of an economist's view of costs is that marginal costs are the costs that matter (Warner & Luce, 1982). By "marginal", an economist means costs that change as a result of the activity involved.

For example, healthcare costs frequently include inpatient care, outpatient hospital care, primary care, pharmaceuticals, and ambulance services and often take into account both state and private systems. With regard to the social costs of alcohol, it is complicated to compare estimates of such costs internationally due to differences in data quality, definitions, and methodology across studies. Social costs often include: costs to individuals and households (crime and violence, personal health and care costs, informal care costs for families, lost income due to unemployment); "human values" costs (the pain and grief associated with illness, disability, and death); costs to public health and care services, costs to other public services (social care, criminal justice, and fire services); and costs to employers due to lost productivity, absenteeism, and accidents (Institute for Alcohol Studies, 2016).

Benefits

Along with the costs, the benefits obtained from an intervention – such as a medication, surgery, diagnostic test, or health programme – must be identified in order to carry out an economic evaluation. As pointed out by Pokhrel et al. (2017), the benefits of public health interventions are often seen only in the long term. It is therefore important to identify the short-term benefits of interventions in order to measure their effectiveness and be able to carry out an economic evaluation thereof, while also estimating the future benefits.

As noted by Hill et al. (2017), it is important to prioritize those benefits that are likely to have the greatest impact on the outcome of the evaluation. Some of the benefits reported

by Hill et al. (2017) were: health benefits, benefits to family members or carers who do not directly benefit from an intervention, positive productivity gains, increased employment, QALYs gained, DALYs averted, cost savings, number of alcohol use and binge drinking episodes prevented, and changes in the number of average drinks per drinking occasion and the number of heavy drinking occasions.

Uncertainty

Another basic element of economic evaluations is uncertainty, which was dealt with in the majority of the studies by using bootstrapping with 1,000–10,000 replications of the ICERs (Drost et al., 2016; Ingels, Corso, Kogan & Brody, 2013; Sumnall et al., 2017) and by using a probabilistic sensitivity analysis (Crombie et al., 2018; Kruger et al., 2014).

1.11. Justification of this study

In the course of this introduction, various needs have been identified, which highlighted the need to carry out the study on which this thesis is based and provided the structure for it.

First of all, harmful alcohol consumption, and, in particular, the unhealthy behaviour pattern known as "binge drinking", is recognized as a global public health issue of concern to various public organizations and institutions. This concern stems from the major impact that BD has in several spheres (economy, health, quality of life, society) and, in particular, its impact on the young or adolescent population. Despite the fact that BD is a prevalent health problem, and although advances have been made in the study of the determinants of this consumption pattern, there remains a gap in the literature regarding these associated socioeconomic factors, which is explained by both scarcity of studies on the topic and lack of consensus regarding the definition of BD and the socioeconomic factors associated with it.

Additionally, given the morbidity occasioned by this unhealthy behaviour in this population group and the lack of studies exploring the relationship between HRQoL and alcohol consumption and BD in adolescents, this would seem to be an important area for study. Such studies, which would make it possible to calculate the QALYs gained from interventions aimed at preventing or treating this public health problem, are, as noted below, rare. Moreover, very few of the interventions or programmes found in the literature have been aimed at the prevention and treatment of binge drinking in particular, nor have there

been many health impact assessments of such interventions aimed at determining their effectiveness and efficiency. In relation to the term "efficiency", few studies involving an economic evaluation of binge drinking prevention programmes were found, although such studies would be useful not only to assess the impact of interventions on health, but also to ensure their proper use, in line with the available resources of society. In addition, economic evaluation of these types of interventions/programmes would aid in decision-making by allowing their comparison in terms of health benefits and costs, including how these benefits differ over time.

During the development of this thesis, all these identified needs were studied in an attempt to address them, in particular by studying the social, economic, and family factors associated with binge drinking in adolescence; assessing the impacts of this consumption pattern on health and quality of life; and carrying out an economic evaluation, from both the societal perspective and the perspective of the Spanish National Health Service, of the web-based computer-tailored programme, Alerta Alcohol, which is aimed at preventing binge drinking and is used in schools.

1.12. Aim and objectives

The aim of this thesis is to assess the efficiency of *Alerta Alcohol*, a web-based computer-tailored intervention for the prevention of binge drinking among adolescents (see details of the *Alerta Alcohol* programme in Appendix 2).

In the context of assessing the efficiency of this intervention, the following four objectives were developed to better inform the economic evaluation conducted:

1) Examine the context surrounding adolescent drinking and analyse the impact of BD, including the health and social costs incurred at the international and national levels.
2) Explore the social, economic, and family factors associated specifically with binge drinking among adolescents aged 15 to 19 in Andalusia, Spain.
3) Compare the effects on health of the *Alerta Alcohol* programme – a web-based computer-tailored intervention for the prevention of binge drinking among adolescents aged 15 to 19 in Andalusia, Spain – as measured by HRQoL and by reduction in binge drinking.
4) Assess the cost-effectiveness and cost-utility of the *Alerta Alcohol* programme.

1.13. Outline of the dissertion

The thesis is structured in eight chapters. Chapters 2 to 5 comprise the papers that make up this thesis and address the objectives established. These papers have been published in journals indexed in Journal Citation Reports (Gustavii, 2012), apart from the paper in chapter 5, which has been submitted to the journal *BMC Public Health*.

The first of the objectives mentioned above was tackled in the first published paper, which contextualizes the current situation of BD in adolescence at the international and national levels; examines the economic, social, and health repercussions of BD in adolescence at the international and national levels; reviews international and national programmes and interventions designed to prevent alcohol use and BD among adolescents; and explores the current situation in relation to assessment of the efficiency of these programmes and interventions.

Given the information gap regarding factors associated with BD in adolescence specifically, the second objective was addressed in the second published paper, which explores alcohol use, binge drinking, and use of other substance among adolescents, their families, and their peers, and identifies the socioeconomic and family factors associated with BD among Spanish adolescents aged between 15 and 19 years.

The third objective, regarding health-related quality of life (HRQoL), was dealt with in the third published paper, which analyses the effects on HRQoL of reducing the number of BD occasions among adolescents; identifies the socioeconomic and family variables associated with HRQoL in adolescence; and compares the effects on health achieved through the Alerta Alcohol programme as measured by HRQoL and by reduction in binge drinking behaviour in terms of the number of BD episodes averted.

Lastly, after identifying the outcome measures to be used as parameters for populating the economic evaluation model, the fourth and final paper addresses the fourth objective of this thesis through an analysis of the effectiveness of the intervention on adolescents in terms of reducing the number of BD occasions by population subgroups (sex, age, and amount of weekly pocket money).; This paper determines the incremental costs and effects on health of the *Alerta Alcohol* programme in terms of the number of BD occasions averted and the number of QALYs gained in comparison with no active intervention; assesses the efficiency of the Alerta Alcohol programme through a cost-effectiveness and cost-utility analysis from both the Spanish National Health System (NHS) and societal perspectives for the entire sample and for subgroups (sex, age, and amount of weekly pocket money); and presents the

results of a multivariate deterministic sensitivity analysis of the best and worst scenarios for the whole sample and for the same subgroups.

Chapters 2 to 5 include the following subsections: main lessons learned, abstract, key findings, and main body of the paper. Chapter 6 consists of an in-depth discussion of the results obtained in the study described in each paper and a general discussion that covers the limitations and strengths of the study, as well as its contributions to the existing body of knowledge and suggestions for future research. Chapter 7 sets out the conclusions of this thesis.

Chapter 2

Paper 1. Impact of Binge Drinking (BD) in Adolescence. Are we doing it right?

2.1. Main messages learned

This chapter presents the first of the published papers forming the basis for this thesis. Its development was prompted by the need to carry out an initial literature review about the behaviour being studied in the thesis: binge drinking (BD) among adolescents. The paper's main aim was to analyse the available epidemiological data, as well as the socioeconomic and health impacts of binge drinking, and the approach currently being taken to the issue at the international and national levels. This paper was initiated during my internship at Brunel University, after collecting the study data and with the objective of cleaning and processing the database and learning about the use of STATA statistical software. This brief overview of the state of the art of the research on binge drinking as a public health problem was requested by my two mentors at the Health Economists Research Group (HERG) at Brunel University in order to understand the context for my database and analysis.

From the literature review I carried out, the key takeaway is the need for continued research in this field, due not only to the lack of literature regarding some aspects of BD in adolescence, but also to the question of whether the existing and evaluated interventions are really useful or widespread in a country. I tried to convey this message in the title of the paper, which asks: "Are we doing it right?" In the course of drafting this paper and throughout the doctoral thesis process, I have been developing my critical thinking skills and my competencies in terms of research and its implementation in clinical or health practice. This led to my interest in learning more about and deepening the evaluation of the efficiency of health technologies and, in particular, of preventive interventions in the field of public health, where health results are generally obtained in the long term. I have noted that the efforts of researchers to try to propose solutions to certain health problems or consequences resulting from unhealthy behaviours have not subsequently been applied in clinical practice. This points to an inefficient use of both human and material resources at a time of limited

budgets. The key questions I asked myself were: why are none of these research findings being applied to real practice, and are all these interventions needed? One of my main takeaways is that evaluating the effectiveness and efficiency of a particular intervention does not necessarily facilitate the transfer of knowledge about its societal impact from the research sphere to decision-making processes.

The editorial format of the paper was chosen because of the need to present the current situation regarding BD in adolescence within a short time frame and without really having the opportunity to carry out a full systematic literature review, which would have had its own particular methodological requirements.

Some of the positive lessons learned from this paper relate to the research-building process. This was my first experience of the publication process and the scientific dissemination of my work and the research that I thought relevant on the topic. It made me realize the importance of having access to reviews of the previous literature and to the contributions of experts and other persons with experience of the subject studied, before carrying out even simple technical activities, such as processing the database. Without this starting point, and without the technical knowledge provided by my HERG mentors regarding the cleaning and processing of the data, the statistical analyses subsequently carried out for the following papers would have been more difficult.

Additionally, my mentors, who showed clear interest in and understanding of the importance of the problem being studied, later worked with me on paper 3, "Measuring the effects on quality of life and alcohol consumption of a programme to reduce binge drinking in Spanish adolescents". Their experience and knowledge of economic evaluation of public health interventions aimed at promoting physical activity and tobacco cessation, and of studies of the relationship between HRQoL and these behaviours, contributed to the development of the subsequent papers. I also learned from them about the use of the EQ-5D-5L questionnaire mentioned in the introduction to this thesis, knowledge that proved useful in the economic evaluation presented in paper 4.

In addition to these lessons learned, it is worth mentioning that, after my experience with this paper, the need to delve into the theoretical framework and review the field studied became apparent. A rigorous systematic review of the literature would have provided a more solid basis for the objectives proposed in this thesis. In addition to all this, this paper guided me in the search for answers regarding the factors associated with binge drinking, its effect

on HRQoL, and the efficiency of the intervention evaluated in this thesis, subjects discussed in the subsequent papers.

Given the lack of literature on this topic, the journal *Adicciones*[3] (Q1) was interested in publishing this paper in an editorial format. The process of selecting which scientific journal to publish in started at that moment and has become, and will remain, part of my research life.

In conclusion, this paper reflects my efforts during a three-month internship in a health economics unit at a UK university, my first publishing experience, and my progress as a researcher in the field of health economics applied to public health. The paper gives an overview of the current reality with regard to the dimensions of the problem of alcohol consumption among the youth population, and it provided the starting point for exploring the data and building the knowledge needed to draft the papers in chapters 3, 4, and 5 of this thesis.

[3] This journal, edited by the Spanish Scientific Society for the Study of Alcohol, Alcoholism and Other Drug Addictions (SOCIDROGALCOHOL) and funded by the Ministry of Health, Social Services and Equality, is indexed in the Journal Citation Report (JCR). It has an impact factor of 3.167 and is positioned within the "Substance Abuse" category in Q1 (6/35) of the Social Science Citation Index (SCI) and Q2 (6/19) of the Science Citation index (SCI).

2.2. Abstract

Nowadays, one of the most prevalent patterns of alcohol consumption is called binge drinking (BD). In 2015, the European School Survey Project on Alcohol and Drugs (ESPAD) Group estimated that about 35% of adolescents of 15–16 years old have had at least one BD occasion in the past 30 days while at national level, the series of surveys on the use of drugs in adolescents of secondary education ESTUDES 2014-2015 determined that 32.2% of adolescents stated having performed BD in the last month. The aim of this editorial was to update the context of adolescence drinking and analyzing the impact of BD by ages, including health and social costs derived. Once the magnitude of the problem was set, some research and action lines have been established in order to guide future work for the prevention of alcohol misuse and for establishing future preventive policies on alcohol. Finally, the need for evaluating these interventions from the efficiency point of view was discussed and assessed.

Keywords: alcohol drinking; binge drinking; health and social costs; efficiency; health promotion; adolescence

2.3. Unique selling points

- There are no significant gender differences regarding high-risk alcohol consumption among adolescents.
- BD is mainly associated with acute effects in young people.
- All the adverse or acute consequences of acute alcohol intoxication can be associated with economic consequences.
- The various programmes for preventing alcohol use among adolescents currently include web-based computer-tailored prevention programmes, which are generally more widely used at the international level.
- Given current budget constraints, studies of the cost-effectiveness of interventions are needed in order to inform health decision-making.
- There are serious gaps in the estimation of the alcohol-related mortality and morbidity burden, the prevalence of alcohol use disorders, the social costs of alcohol consumption, and the efficiency of interventions or programmes aimed at preventing harmful alcohol consumption in Spain.

2.4. Main body of the paper

Based on:

Vargas-Martínez, A.M., Trapero-Bertran, M., Gil-García, E. & Lima-Serrano, M. (2018). **Impact of Binge Drinking (BD) in Adolescence. Are we doing it right?.** *Adicciones*, 30(2), 152-154. Doi: 10.20882/adicciones.1033

Dear Editor,

Excessive alcohol use and alcohol use disorders are major causes of death and disability worldwide (WHO, 2014). According to the World Health Organization, 10% of adolescent deaths (those aged 15 to 19 years) in the European Region were attributable to alcohol (Drost et al. 2016).

Nowadays, one of the most prevalent patterns of alcohol consumption is called binge drinking (BD). In 2015 it was estimated that about 35% of European adolescents of 15–16 years old have had at least one BD occasion in the past 30 days (ESPAD Group, 2016). Moreover, in Spain, the series of surveys on the use of drugs in adolescents of secondary education, ESTUDES 2014-2015, stated that 32.2% have performed at least one BD occasion in the last month (National Plan on Drugs, 2016) whereas a recent study by Golpe, Gómez, Braña, Varela & Rial (2017) concluded that 33.1% of Spanish adolescents were doing intensive consumption last year and 20% last month (3 or more alcoholic drinks per sitting and drunkenness). Moreover, 19.8% of adolescents were doing a risk alcohol consumption without significant differences by gender. Romo-Avilés, Marcos-Marcos, Tarragona-Camacho, Gil-García & Marquina-Márquez (2016) found small differences between the amount of alcohol consumed or in "botellón" participation between boys and girls. This suggests that intensive alcohol consumption and BD have increased in girls.

In the European Union, alcohol-attributable costs were estimated at €125 billion in 2003. In Spain, the total social costs of alcohol consumption can be around 1% of gross domestic product (more than 10.000 million euros) (Pulido, Indave-Ruiz, Ruiz-García, Bartroli & Barrio, 2014).

We did not find any study regarding costs associated with BD and underage drinking in Europe but previous works have shown youthful drinkers are at greater risk of: being victimized and perpetrating youth violence; low educational attainment; and low college expectations, putting a financial burden on the criminal justice system and educational sector (WHO, 2014).

Based on the evidence, BD is mainly related to acute effects in young people, such as acute intoxication, accidental and intentional injuries, road crashes, scholar problems due to lower cognitive performance and brain alterations as well as school absenteeism caused by

the symptoms caused by the hangover after acute alcohol intoxication, unprotected and unplanned sex, consumption of other drugs, legal problems due to the reduction of cognitive and verbal ability to resolve conflicts and developing an alcohol use disorder in adulthood (Pulido et al., 2014, Windle & Windle, 2017). In a research carried out by Windle & Windle in 2017 found that diagnostic accuracy of adolescent alcohol problems in predicting alcohol dependence 7 years later was 74%. In Spain, the annual prevalence self-informed about acute alcohol intoxication was higher than 30% in population between 15 and 34 years old in 2011, being higher in adolescents between 15 and 16 years old (Pulido et al., 2014).

However, all these adverse or acute events could be associated to economic consequences such as outpatient care, hospital stays, some of the direct costs associated with violence as emergency care, police services or criminal justice, traffic accidents with healthcare and scholar absenteeism (Pulido et al., 2014; WHO, 2014).

Given the high prevalence and health, social and economic consequences of alcohol use and BD, it seems clear that strategies aimed at the prevention must be carried out. Which measures are taken today for prevention of alcohol use? To date, different programs to prevent alcohol use in adolescents have been designed (Foxcroft y Tsertsvadze, 2012; Jander, Crutzen, Mercken, Candel & de Vries, 2016). Currently there are some web-based computer-tailored prevention programs but they are more extended usually at international level.

A meta-analysis of computer-tailored interventions for health behaviour change showed these interventions would have clinically significant impact on rates of behavioural risk factors (Krebs, Prochaska & Rossi, 2010). On the one hand, these interventions have the potential to reach many people from different social classes and ages. This is because a significant percentage of the population, today, has access to the internet. On the other hand, tailored information is perceived as more relevant than no tailored information (Schulz et al., 2014).

Despite of international and national interventions (Foxcroft y Tsertsvadze, 2012) aim to prevent the alcohol use, in very few occasions their cost-effectiveness and their efficiency has been assessed (Drost et al., 2016). In a limited budget situation studying the cost-effectiveness of interventions is a need to assess health decision making. Therefore, cost-effectiveness analysis is a useful tool to inform the interest of an intervention and influence policy and health planning.

In conclusion, there are important gaps in the information about social and health harms associated to alcohol consumption in Spain, especially in the estimation of mortality and morbidity burden, the prevalence of alcohol use disorders, the social costs of consumption and the efficiency of preventive interventions or programs. Therefore, there is a need to evaluate the economic burden and economic evaluation of interventions of BD.

Authorship contributions

AM Vargas-Martínez has prepared the first draft and coordinated the work. E Gil-García has reviewed the work and added the gender perspective. M Lima-Serrano and M Trapero-Bertran have contributed substantially to the text, have made critical revisions to its content. All the authors have approved the final version.

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Conflicts of interest

None.

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Chapter 3

Paper 2. Social, economic and family factors associated with binge drinking in Spanish adolescents

3.1. Main messages learned

This chapter presents the second paper of this thesis, the development of which was prompted by the lack of evidence detected in the literature review on the study of certain socioeconomic and family factors associated with binge drinking in the adolescent population.

I began working on this paper during an internship at the Universitat Internacional de Catalunya (UIC), under the supervision of my thesis director, Marta Trapero-Bertrán, during which time I had the opportunity to continue learning about statistics and, specifically, to discover the field of econometrics with Toni Mora, PhD, who made great methodological contributions to this paper. When I believed that the database was ready to start the statistical analyses, I had just begun to realize the importance of dedicating time to good prior data processing, so I continued learning about it. During the days I spent working with the database and the STATA software for this paper's analysis, I learned about the different types of regression analysis, which, until then, I had only encountered in recommended reading. I began to appreciate the value that econometrics brings to research and the importance of a multidisciplinary approach in health science research. I learned how certain analysis models improve on the shortcomings of others and saw the importance of adjusting to the best-suited model for the measures used, based on how the variables behave, their distribution, and so on. Another of the lessons I learned relates to bias control. From the available data, I introduced variables that controlled for these information biases and could influence the responses given by the study subjects. This learning area concerned the different types of risk of bias, and I have been deepening my knowledge on this throughout the doctoral process. I consider this issue to be of great importance in research, since it provides rigour in terms of the methodological quality of the studies.

Regarding the findings of this paper, the association between certain factors related to family influence, such as the frequency of BD in the family environment and weekly pocket

money, and BD in adolescence is shown. This finding demonstrates the importance of parental education and the influence of parenting styles on adolescent behaviour. Additionally, it suggests that the target population for public health interventions to prevent or change unhealthy behaviour should probably be the whole family unit instead of just a particular individual.

Given the aim of this paper, which is focused on identifying factors associated with BD in adolescence – a necessary first step before designing possible solutions and interventions – and the fact that this pattern of alcohol consumption represents a global public health concern, I sought to have the paper published in a journal focused on public health. The paper was submitted to and published in the journal *BMC Public Health*[4]. The process of reviewing this paper from submission to acceptance was one of my first experiences of peer review, which was carried out by a large team of experts whose contributions enriched this paper.

In conclusion, this paper reflects my efforts to acquire methodological competencies in statistics and econometrics, as well as my experience of teamwork in research and my first exposure to the review process for an international journal with a strong position in its category and a high impact factor. It addresses some of the gaps found in the literature review carried out for the previous paper and provides knowledge for use in the studies described in chapters 4 and 5 of this thesis.

[4] This journal is an open access, peer-reviewed journal and is indexed in the Journal Citation Report (JCR). It has an impact factor of 2.567 and is positioned within the "Public, Environmental and Occupational Health" category in Q2 (59/186) of the Science Citation Index (SCI).

3.2. Abstract

Background: The main aim of this study was to determine the socioeconomic and family factors associated with binge drinking (BD) in Spanish adolescents who participated in a web-based computer intervention for the prevention of binge drinking known as *Alerta Alcohol*.

Methods: Longitudinal analyses were carried out in a sample of Andalusian adolescents aged 15 to 19 enrolled in public schools, which was part of a two-arm cluster randomized controlled trial with an intervention group (IG) who received the *Alerta Alcohol* programme and a control group (CG) who did not receive any active intervention. Panel count data and the following econometric procedures were used: negative binomial, a two-part model and a finite mixture model. The endogenous variable in all models was the number of BD occasions in the last 30 days. A total of 1,247 subjects in the pre-intervention period, with an average age of 16.8 years, plus 612 adolescents in the follow-up period (four months later), were included in the analysis.

Results: In relation to findings, being older (≥ 17 years old), having more pocket money and higher family alcohol consumption were associated with greater BD. By contrast, subjects who completed the questionnaire on Wednesday, Thursday or Friday, further from the previous weekend, indicated a lower number of BD occasions.

Conclusions: Our results suggest the need to include families, especially parents and siblings, in interventions aimed at preventing alcohol use among adolescents, given the association shown between BD and both family alcohol consumption and weekly pocket money or availability of money to adolescents. Given the findings with regard to age, future research aimed at intervening in early adolescence to prevent BD would be justified.

Keywords: binge drinking, adolescence, socioeconomic factors, intervention.

3.3. Unique selling points

- A BD prevalence of 36.64% among adolescents was observed in the baseline period.
- An increase in age, weekly pocket money, and family alcohol consumption frequency were associated with an increase in the number of BD occasions.
- A decrease in the number of BD occasions was associated with a higher educational level of the mother and completion of the questionnaire later in the week following the previous weekend (i.e. on Wednesday, Thursday, or Friday, rather than on Monday or Tuesday).

3.4. Main body of the paper

Based on:

Vargas-Martínez, A.M., Trapero-Bertran, M., Mora, T., Lima-Serrano, M. **Social, economic and family factors associated with binge drinking in Spanish adolescents**. *BMC Public Health, 20,* 519. doi:10.1186/s12889-020-08605-9

Background

According the World Health Organization (WHO), alcohol was the seventh cause of disease and premature death among the world's population in 2016. Also, alcohol is the cause of more than 200 health conditions, in addition to diseases with a high mortality burden such as liver cirrhosis, cancer and cardiovascular diseases [1, 2]. In Europe, alcohol accounts for 10.1% of all deaths and 10.8% of all disability-adjusted life years (DALYs) [1, 2].

With regard to alcohol use in different life stages, it is known that alcohol abuse is a public health concern across all age groups. Nevertheless, it is important to highlight that alcohol is the most widely used substance among adolescents in both Europe and North America [3]. In Spain, the alcohol-related disease burden for the young population aged 15 to 29 years is estimated at the equivalent of 786,479 DALYs (16% of the total for the Spanish population) [4]. Specifically, for young people, alcohol has numerous consequences, mainly on morbidity, such as the effects on the brain [5], visuospatial memory deficits, and attention impairments [6]; alcohol use can also increase the risk of unprotected sex or of involvement in an aggressive incident or an activity with a high risk of injury [7].

As is known, the pattern of alcohol consumption differs according to the age of the population. It has been pointed out that binge drinking (BD) among young people is a particularly prevalent pattern of alcohol consumption, characterized by the intake of high amounts of alcohol (at least five standard drinks for men and four standard drinks for women) on a single occasion [8-11]. The definition of BD is controversial, and multiple definitions exist [12, 13]. Additionally, there are different definitions of "standard drink unit", as the amount that constitutes one unit of alcohol in grams of pure alcohol differs by country [13].

In Europe, the European School Survey Project on Alcohol and Drugs (ESPAD) estimated that about 35% of adolescents aged 15-16 years had engaged in at least one BD occasion in the past 30 days in 2015 [14]. The latest survey on drug use in secondary education in Spain, known as ESTUDES, reported that the prevalence of BD in the past month among students aged 14 to 18 was 31.7% (approximately one in three adolescents) in 2016. The highest rate of BD occurs between the ages of 17 and 18, reaching up to 58.9% among boys and 54% among girls [15].

In addition to the acute consequences associated with alcohol consumption mentioned above, Bockërman et al. [16] found that BD, in particular, is negatively associated with

employment months and therefore also with subsequent long-term adverse labour market outcomes. Furthermore, BD is associated with three of the main causes of death among young people, particularly among female adolescents: unintentional injury, homicide, and suicide [17, 18]. For that reason, it is necessary to know the determinants that lead adolescents to acquire these behaviours. The effects of certain social, economic and family factors on health-related behaviours can influence disease outcomes, manifesting themselves in later stages of life [19].

In the current literature regarding the factors associated with this alcohol consumption pattern, the study carried out by Jander et al. [20], through focus group interviews conducted with adolescents aged 16 to 18, found some factors that could influence propensity to engage in binge drinking, such as parental attitudes, being at a party or in a bar with friends on weekend days, peer influence, family affluence and policies concerning the availability of alcohol in the environment. One of the factors that has been shown to have an association with binge drinking is socioeconomic status, as measured by the mother's educational level, the parents' occupational status and the subjective perception of wealth [21]. However, the majority of studies analysed in a systematic review carried out by Kwok and Yuan [22] found no relationship between parental socioeconomic status and binge drinking in adolescents. This finding is mentioned due to the variation in measurements of binge drinking and parental socioeconomic status.

Educational aspirations of young people have also been associated with alcohol use. Liu et al. [23], in a study that looked at 15-year-old adolescents from the Finnish Health Behaviour in School-aged Children study from 1990 to 2014, noted that both boys and girls with low educational aspirations were more likely to report frequent drunkenness than those with high educational aspirations.

Regarding family factors, it has been found that the children of parents who engage in bouts of heavy drinking are more likely than children of abstainers to have heavy drinking occasions [24]. They are also more likely to have higher household income, suffer early-life stress and traumatic events, have a negative relationship with their fathers during childhood and adolescence, live in an environment where alcohol is easily accessible and begin using alcohol at an early age [25]. However, there is also literature that did not find a significant association between parental drinking and the different patterns of alcohol use in adolescence in terms of both quantity and frequency of alcohol use [26].

Although some studies analyse the association between different alcohol consumption patterns in adolescents, there is scarce updated knowledge about the influence of socioeconomic factors on binge drinking, which are needed to plan and implement strategies to prevent this particular and frequent pattern of alcohol use [27]. Moreover, Kendler et al. [28] have suggested that, given the complexity of the relationship between socioeconomic variables and alcohol-related behaviours during adolescence there is a need for future studies using longitudinal data for establishing causal relationships.

Hence, the main aim of this work was to explore the social, economic and family factors associated specifically with binge drinking among Spanish adolescents between 15 and 19 years old.

Methods

Design and sample

Data from a longitudinal study, a two-arm cluster randomized controlled trial with an intervention group (IG) and a control group (CG) randomized at the school level, for prevention of BD in adolescents known as *Alerta Alcohol were used in this work (more information about the design of the study can be obtained from the published study protocol; see Lima-Serrano et al., 2018)* [29]. Alerta Alcohol is a web-based computer-tailored programme consisting of six sessions, of which sessions 1 and 6 consist of assessment questionnaires and sessions 2 to 5 are aimed at providing feedback through preventive messages and personalized information to intervene on alcohol use. Results in the IG were compared with the absence of intervention. Hence, the CG only received sessions 1 and 6, whereas the IG participated in all the sessions.

A sample was selected from the overall population of Andalusian adolescents aged 15 to 19 years enrolled in public higher secondary schools, lower secondary schools and lower vocational training schools. Specifically, to be included, adolescents had to be enrolled in the fourth course of compulsory secondary education, the first course of higher secondary education or the first course of vocational training (equivalent to 10th and 11th grades in the United States of America). This sample was randomized at school level. For the recruitment of schools, collaboration was requested from the Educational Plans and Programs Service of the Department of Education, Culture and Sports of the Government of Andalusia. Schools were contacted by various means (telephone, email and through visits). A total of

16 schools were randomized into the control group or the intervention group. Of the schools randomized to the control group, one withdrew its participation before the baseline period.

The average number of adolescents per school was around 83 students. The school councils and the youths' parents were informed in advance of the study's objectives and methods. The sample was calculated using the online GRANMO tool, taking into account the prevalence of adolescent binge drinking in Spain (33.1%) [15] and estimating that the intervention would reduce consumption by 10%, accepting a p value of <0.05 and a statistical power of 0.80, for a two-sided test. Based on the study by Jander et al. [30], a dropout rate of about 50% was anticipated. The arc sine approximation was used.

The sample comprised 1,247 subjects in the baseline period (January-February 2017) and 612 (49.07%) subjects in the follow-up period (April-May 2017) (see Table 1).

Table 1. Characteristics of subjects at baseline period (n=1247) and at 4-month follow-up (n=612) by intervention and control group.

		Intervention group		Control group	
	Description of variable	**Baseline**	**Follow-up**	**Baseline[a]**	**Follow-up[b]**
		Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Socioeconomic					
	Age at the beginning of program[1]	16.866 (1.06)		16.681 (1.04)***	
	Family functionality: APGAR[1]	1.677 (0.57)		1.727 (0.53)	
	Mother's schooling years[1]	11.211 (3.33)		11.807 (3.28)**	
	Father's schooling years[1]	11.040 (3.37)		11.357 (3.58)	
	Pocket money (weekly)[1]	10.610 (9.08)		11.206 (9.61)	
	Female[2]	0.535 (0.50)		0.523 (0.50)	
	Spanish[2]	0.954 (0.21)		0.936 (0.24)	
	Catholic[2]	0.623 (0.49)		0.604 (0.49)	
	No religion[2]	0.317 (0.47)		0.337 (0.47)	
	Type of family composition: nuclear[2]	0.741 (0.44)		0.743 (0.44)	
	Current job situation of the mother[2]	0.634 (0.48)		0.691 (0.46)	
	Current job situation of the father[2]	0.798 (0.40)		0.727 (0.45)**	
	Good economic situation at home[2]	0.449 (0.50)		0.491 (0.50)	
	Economic difficulties at home[2]	0.364 (0.48)		0.291 (0.46)**	
Alcohol consumption					
	Number of BD occasions[1]	1.125 (1.90)	0.876 (1.74)	1.081 (1.91)	1.065 (2.15)
	Frequency of alcohol use in public outdoor places[1]	1.194 (2.28)	0.966 (2.24)	1.108 (2.20)	0.712 (1.55)
	(…) at parties or celebrations[1]	1.543 (2.57)	1.114 (2.22)	1.481 (2.38)	1.094 (2.02)
	(…) at home or someone else´s home[1]	0.960 (2.07)	0.615 (1.44)	1.104 (2.28)	0.727 (1.66)
	Glasses of alcohol consumed in outdoor public places[1]	1.640 (2.14)	1.26 (2.056)	1.478 (2.16)	1.273 (2.20)
	(…) at parties or celebrations[1]	2.492 82.68)	1.980 (2.33)	2.518 (2.61)	2.05 (2.61)

(…) at home or someone else´s home[1]	1.325 (1.98)	0.983 (1.83)	1.467 (2.11)	1.358 (2.22)**
Alcohol use on last weekend[2]	0.235 (0.42)	0.112 (0.32)	0.216 (0.41)	0.113 (0.32)
Mother consumes alcohol moderately/more frequently[2]	0.233 (0.42)	0.113 (0.32)	0.281 (0.45)*	0.121 (0.33)
Father (…)[2]	0.418 (0.49)	0.181 (0.39)	0.444 (0.50)	0.192 (0.39)
Siblings (…)[2]	0.225 (0.42)	0.082 (0.28)	0.240 (0.43)	0.115 (0.32)*
Partner (…)[2]	0.179 (0.38)	0.066 (0.25)	0.152 (0.36)	0.069 (0.25)
Friends (…)[2]	0.814 (0.39)	0.342 (0.48)	0.818 (0.39)	0.398 (0.49)**
Best friend (…)[2]	0.584 (0.49)	0.249 (0.43)	0.543 (0.50)	0.248 (0.43)
Mother binge drinks moderately/more frequently[2]	0.051 (0.22)	0.027 (0.16)	0.073 (0.26)	0.022 (0.15)
Father (…)[2]	0.156 (0.36)	0.067 (0.25)	0.160 (0.37)	0.044 (0.20)*
Siblings (…)[2]	0.128 (0.33)	0.053 (0.22)	0.150 (0.36)	0.053 (0.23)
Partner (…)[2]	0.119 (0.32)	0.044 (0.21)	0.111 (0.31)	0.057 (0.23)
Friends (…)[2]	0.683 (0.47)	0.272 (0.45)	0.640 (0.48)	0.309 (0.46)
Best friend (…)[2]	0.446 (0.50)	0.190 (0.39)	0.388 (0.49)**	0.196 (0.40)
Family alcohol consumption[3] (BD of the mother, father and/or siblings)	0.336 (0.63)	0.147 (0.47)	0.491 (0.66)	0.119 (0.39)
Consumption of other substances				
Number of cigarettes a week[1]	4.361 (13.92)	4.257 (16.35)	4.047 (15.07)	3.333 (12.37)
Number of shishas or hookahs a week[1]	0.821 (2.49)	0.652 (1.68)	1.050 (2.77)	1.053 (3.44)*
Smoker[2]	0.224 (0.42)	0.168 (0.38)	0.234 (0.42)	0.196 (0.40)
User of cannabis[2]	0.061 (0.24)	0.053 (0.22)	0.085 (0.28)*	0.079 (0.27)*
Prescribed tranquilizers, sedatives or sleeping pills[2]	0.019 (0.14)	0.026 (0.16)	0.032 (0.18)	0.028 (0.16)
Not prescribed tranquilizers, sedatives or sleeping pills[2]	0.012 (0.11)	0.019 (0.14)	0.028 (0.16)**	0.026 (0.16)

Note: [1] Continuous variable; [2] Dichotomous variable; [3] Categorical variable
In the context of engaging in binge drinking for family members, "occasionally or more frequently" is compared with "never or almost never". Initially, these items had four response options, from never to more frequently, and subsequently, were dichotomized.
[a]We show the average values and standard deviations in brackets. ***, ** and * represent statistically significant differences at 1%, 5% and 10% between values of variables in intervention and control group (2nd and 4th column) in pre-intervention or baseline period.
[b]We show the average values and standard deviations in brackets. ***, ** and * represent statistically significant differences at 1%, 5% and 10% between values of variables in intervention and control group (3rd and 5th column) in post-intervention or follow-up period.

Measures and procedures

The measurements included in this study were collected by means of an online questionnaire administered during school hours. Information was collected at two different points in time [baseline (January-February) and at the 4-month follow-up (May-June)]. The questionnaire was divided into the following sections: socioeconomic variables (age, sex, family composition, nationality, economic situation at home, parents' education level, weekly pocket money, etc.), alcohol use (binge drinking occasions in the last month, alcohol use in the last week, etc.), other substances use and social influences (parents, sibling, friend's alcohol use, etc.) [31]. Only the number of BD occasions in the last 30 days and variables related to alcohol use were assessed at two assessment points, pre- and post-intervention.

The rest of the variables were assessed only at baseline (also called the pre-intervention period). Definitions of these variables are explained below.

Within socioeconomic variables, age was calculated by dividing the difference between the date on which the subject completed the pre-intervention questionnaire and the subject's birth date by 365.25.

Family composition was determined by means of the question "What is the composition of your family?", with multiple answers being allowed from the following response options: mother, father, brother(s)/sister(s) who live(s) at home, brother(s) who do/do(es) not live at home, sister(s) who do/do(es) not live at home, other (nominal response). We created a new categorical variable called "family composition", which classified families as "nuclear", "extended nuclear", "divorced", "extended divorced", "reconstituted" and "other", but due to the large proportion of nuclear families in the sample, we dichotomized this into "nuclear" and "others".

Nationality was a dichotomous variable with two response options: 1 if the respondent was Spanish and 0 if the respondent had another nationality or nationalities. When adolescents answered "other(s)", they specified the additional nationality(ies). Given the proportion of responses for each other nationality, this variable was used in the analyses only as a dichotomous variable.

Religion was determined through a categorical variable with several answers, which were recoded in three response options: "Catholic", "other religion", "no religion".

Parents' educational level was calculated according to years of schooling. Initially, we collected data on the educational level with a categorical variable by asking "What is the highest level of education achieved by your father/mother?".

The economic situation at home was obtained using the question "Of the following situations, which one would you identify with the most?". The response options were: (a) We have many economic problems at home and we don't make it to the end of the month; (b) We manage economically at home, but we have trouble making it to the end of the month; (c) We are pretty well off economically and we make it to the end of the month; and (d) We are very well off economically. This variable was converted into a dummy variable, with a value of 1 indicating "good economic situation at home" [including options (c) and (d)], and

a value of 0 indicating "other economic situation" [including options (a) and (b)]. This question was developed ad hoc and used in another study carried out by Lima-Serrano et al. [32].

To measure weekly pocket money, we asked about the amount of money the subject had available to spend on his/her appearance weekly (not including money for clothing or his/her savings). Response options were: "0 euros", "up to 10 euros", "between 11 and 20 euros", "between 21 and 30 euros", "more than 30 euros". Due to the proportions of responses in each category, these amounts were recoded into three categories: €0, between €1 and €20, and more than €20. Similar recoding was used in a study carried out by Díaz-Geada et al. [33] This categorical variable was converted to a continuous variable using the mean number of euros for each option.

Family functionality was measured using the family APGAR questionnaire [34-37], which is a tool frequently utilized in primary care and general medicine settings to assess family function through a five-item questionnaire measuring five constructs (adaptability, partnership, growth, affection and resolve).

In relation to alcohol use, the model's endogenous variable was the number of BD occasions in the last 30 days, obtained directly from the answers given by the adolescents to the question: "During the last month, how many times did you drink 4 glasses or more of alcohol (if you are a girl) or 5 glasses or more of alcohol (if you are a boy) on one single occasion (e.g., in a bar, at a party, etc.)?". The word "glass" was used in the question to refer to a standard drink, and an image was provided in the questionnaire to help respondents understand the meaning of a standard beverage unit or glass of alcohol. The definition of binge drinking used in this study is consistent with ESTUDES [15], as well as with the definition used by Jander et al. [38], as Alerta Alcohol is an adaptation of the Dutch programme Alcohol Alert [30]. One alcoholic drink equivalent in the Dutch programme was defined as a drink containing 9.9 grams of pure alcohol, which is similar to the measure in Spain, where one standard unit of alcohol is equivalent to 10 grams of alcohol. This variable was self-reported in both pre-intervention and post-intervention periods. The units of this measure were event counts.

With regard to other substance use, tobacco use was a categorical variable (with nine response options from "never smoke" to "daily"), which was converted to a dummy variable, with a value of 1 for "smoker" and a value of 0 for "non-smoker". Those who reported

being smokers were asked about the number of cigarettes and shishas they consumed in terms of a numerical variable.

Regarding social influences, family alcohol consumption was calculated on the basis of binge drinking among family members, i.e., the mother, the father and siblings. Three items were taken from the questionnaire that asked about the frequency of those family members who consumed 4-5 glasses of alcohol or more on a single occasion (Response options: "never", "almost never", "occasionally", "more frequently"). Subsequently those items were dichotomized (1: mother/father or siblings occasionally or more frequently consumed 4-5 glasses of alcohol or more on a single occasion; 0: mother/father or siblings never or almost never consumed 4-5 glasses of alcohol or more on a single occasion). Then, the items were combined in a single ordinal variable with four response options (0: mother, father and siblings did not engage in binge drinking; 1: mother or father or siblings engaged in binge drinking; 2: two members of the family (mother, father or siblings) engaged in binge drinking; 3: mother, father and siblings engaged in binge drinking).

Additional variables were created in order to carry out the analysis. The latter included variables that indicated how close in time the subject was to the most popular local events in each city (there were a large number of events during the study period) and how much time had elapsed since the last weekend when the subject completed the questionnaire. The first variable was taken into account because binge drinking is a pattern of alcohol consumption that usually occurs during weekends and summer and spring vacations, on holidays (e.g., New Year's Eve) and at parties such as graduation events, and at sporting events [39]. To obtain the first variable, we codified the date on which the questionnaire was completed and the date of the closest local event for each city and then calculated the difference between the two codes. For the second variable, we recoded the date on which the subject completed the questionnaire as the corresponding day of the week. The variable was then dichotomized into subjects who completed the questionnaire on Monday or Tuesday and subjects who completed the questionnaire later in the week. In relation to the first session, all participants were asked to answer the initial questionnaire for the same event, which was Christmas.

Data analysis

We used panel count data for the empirical analysis. The analysis to determine the factors associated with binge drinking in the sample studied was conducted using three econometric procedures: a negative binomial, a finite mixture model and a two-part model. Given the nature of the endogenous variable (count data), we used a negative binomial specification, which would resolve the main drawback of the Poisson model in which the variance is equal to the mean. The data showed greater variance than average due to multiple causes, notably the high frequency of zeros.

The basic idea of these models (negative binomial regression models) is that the zeros (all or part of them) do not come from the same data-generating process as the rest of the values. For instance, in this study, for those who had engaged in binge drinking zero times, the reason might be because they are non-drinkers (they never drink alcohol) or are alcohol users (they usually drink alcohol) but are not binge drinkers, or it might also be because, even though they are binge drinkers, they had not engaged in binge drinking in the last month. In the baseline period, 33.28% of adolescents were non-drinkers and 66.72% were alcohol users. Of those who were alcohol users, 57.8% were binge drinkers. In the total sample (non-drinkers and alcohol users), 38.6% were binge drinkers.

The two-part model was used, along with the finite mixture model, to explain the probability of not reporting binge drinking and how often it happened, given that the two variables could be completely independent of each other. Finite mixture models have received increased attention in recent years due to their usefulness for modelling heterogeneous data with a finite number of unobserved sub-population and the probability of belonging to each unobserved group in order to estimate distinct parameters of a regression model or distribution in each group, to classify individuals into the groups and to draw inferences about how each group behaves [40].

The aim in using various models other than the Poisson model was to allow for greater flexibility, bearing in mind the main disadvantage of the Poisson model, which is the difficultly in capturing overdispersion – i.e., when the conditional variance exceeds the conditional average. Specifically, the first part of the two-part model is estimated using a logit regression model and the second part is specified as a generalized linear model panel regression. This model was used because of the presence of a large proportion of zero count observations [41]. In the dataset, the number of binge drinking occasions was zero for 60.95% pre-test and 67.32% post-test.

Additionally, the introducing interactions between socioeconomic variables and the intervention were estimated. However, none of these interactions turned out to be statistically significant, so we decided to use the entire sample for this analysis.

The analysis was conducted using Stata (version 16.0; StataCorp, College Station, TX, USA).

Ethics approval

The study received approval from the Bioethics Committee of Andalusia. Written informed consent was obtained from parents and students prior to participation in the study. The questionnaires were self-completed by the adolescents and confidentiality was ensured.

Results

Alcohol and other substance use

Regarding alcohol use, in the IG, 40.03% of adolescents had consumed 4 or 5 glasses of alcohol on a single occasion in the last month in pre-test period; in the CG, the proportion was 36.44%. Regarding other drug use, in the IG 22% smoked a mean of 4.36 cigarettes (SD = 13.9; 95% CI: 2.92-5.80) and a mean of 0.82 shishas per week, and 6% were cannabis users. In the CG, 23% of subjects smoked a mean of 4.04 cigarettes (SD = 15.06; 95%CI: 2.19-5.90) and a mean of 1.05 shishas per week; 8% were cannabis users.

Dealing with missing data

Due to the high desertion rate (>50%) in the post-intervention period, for the majority of variables in the follow-up questionnaire we decided not to use multiple imputation and instead carried out the analysis with pairwise deletion. In relation to the main differences between subjects who replied the post-questionnaire and those who did not replied it (missing subjects), we found that the missing subjects were older, their father's and mother's schooling years were lower, the current job situation of the mother was worse, they had a worse economic situation at home and they had higher weekly pocket money. Moreover, in relation to alcohol use, those who did not answer the post-intervention questionnaire had engaged in binge drinking more frequently and consumed more alcohol in last week; they also had friends/a best friend who consumed alcohol more frequently. In addition, a higher proportion of those who did not answer the questionnaire in the post-intervention period

were smokers. These differences were statistically significant. Despite the differences between the missing and not missing subjects, however, these differences did not affect the results of the analyses, so the entire sample was analysed.

Social, economic and family factors associated with binge drinking

Table 2 shows the variables associated with binge drinking among adolescents.

Table 2. Intervention marginal effects on BD: two-part model (logit+glm).

		Marginal effects
Intervention	Period	0.279 (0.20)
	Treated	0.201 (0.14)
Socioeconomic	Age	0.265 (0.05)***
	Female	0.068 (0.09)
	Spanish	0.226 (0.25)
	Nuclear family composition	-0.110 (0.08)
	Mother's schooling years	-0.002 (0.00)*
	Good economic situation at home	0.030 (0.09)
	Pocket money (weekly)	0.022 (0.01)***
	Completed questionnaire more days after last weekend	-0.330 (0.11)***
	Completed questionnaire near to local events	-0.001 (0.00)
Alcohol	Family alcohol consumption	0.502 (0.06)***
	N x T	1,638
	Wald χ^2	182.72 (0.00)
	Log likelihood	-1,432.04
	Pseudo-R2 1st part	0.0774

Note: we show the parameter estimates and standard deviations in brackets. ***, ** and * represent statistical significance at 1%, 5% and 10%; 1,000 replications were used for bootstrapping and standard errors were clustered at classroom level. In the negative binomial regression and the finite mixture model, regressions were also controlled by period of intervention, female sex, age, Spanish nationality, having a partner, years of schooling of the mother, nuclear family, pocket money, family pressure, answering the questionnaire late in the week and answering the questionnaire near the date of local events.

The two-part model showed the highest performance level by far regarding statistical measures according to the value of the log-likelihood function, which is a method that represents the combination of model parameter values that maximize the probability of drawing the sample obtained. In this model, age, weekly pocket money, mother's years of schooling, the variable "completed the questionnaire more days after last weekend" and family alcohol consumption continue to be statistically significant. There was a positive association between age, weekly pocket money, family alcohol consumption and the number of occasions of binge drinking and a negative association between the mother's years of schooling and the variable "completed the questionnaire more days after last weekend". On

the one hand, in relation to variables that have shown a positive association, this means that the average of BD occasions increases 0.265 times per additional year, 0.022 times for weekly pocket money euros and 0.502 times as frequency of BD increases in the family. On the other hand, with regards those variables showing a negative association, the average of BD occasions decreases 0.002 times for an additional schooling year of the adolescent´s mother and decreases 0.33 times for any additional day far from the last weekend the adolescent completing the questionnaire. Furthermore, in terms of how big are these associations, only age and family alcohol consumption showed a relatively high value, 0.14- and 0.26-times standard deviation for the control group at baseline period.

Discussion

This study analysed socioeconomic and family factors associated with binge drinking in adolescents between 15 and 19 years of age enrolled in public high schools. The related variables, according to the model that showed the highest performance level in terms of statistical measures, were age, pocket money, questionnaire completed more days after last weekend and family alcohol consumption. Several studies have explored the relationship between socioeconomic variables and drinking behaviour in adolescence through cross-sectional studies [42, 43], although the use of longitudinal studies on substance use is growing. These studies have the potential to contribute to prevention science on how best to reduce problem substance use. Importantly, our findings extend research in this field by analysing and quantifying an association between socioeconomic factors and behavioural patterns of binge drinking in adolescence.

Regarding age, our findings are consistent with those of other studies [33, 44-46] that show that alcohol use, as well as the use of other drugs, increases with age. Moreover, this study showed an association between availability of money and excessive alcohol use, finding that as weekly pocket money increases, so does the likelihood of consuming alcohol. Bosque-Prous et al. [47] reported similar findings, such as that high weekly student income was associated with a higher likelihood of alcohol consumption for different drinking measures (weekly binge drinking and weekly alcohol consumption). This finding is important for informing families that a greater availability of money could contribute to this risk behaviour.

In relation to completion of the questionnaire more days after the last weekend and its association with lower drinking, it could be assumed that memory could explain this finding

and as a consequence underestimate the reported data related to binge drinking frequency, due to this is an alcohol consumption pattern that usually occurs during weekends [46].

Family alcohol consumption, as mentioned above, was positively and significantly associated with the number of occasions of binge drinking in the last month. Along the same lines, Pedersen and von Soest [48] found that binge drinking among parents was predictive of binge drinking among their children, just as the frequency of alcohol use by parents is predictive of the frequency of alcohol use by their children. Others authors, such as Moore et al. [49], affirm that parents' behaviours are central influences on adolescent activities and, specifically, on alcohol use.

No consistent and significant findings were found in our study between perceived economic situation at home and binge drinking. However, Liu et al. [23] showed that girls from high perceived family wealth groups were more likely to be abstainers than girls from low perceived family wealth groups. Conversely, the Spanish Survey on Drug Use in Secondary Schools (ESTUDES) 2016-2017 [16] found an association between higher family socioeconomic level and higher alcohol use in adolescents. In addition, Moure-Rodríguez et al. [50] found that a high maternal education level, understanding this variable as a reflection of a high socioeconomic level, was a risk factor for risk consumption (drinking 5 alcoholic beverages or more for girls and 6 or more for boys) among Spanish youth. Notwithstanding, they did not found association between maternal education level and heavy episodic drinking (frequency of drinking 6 or more alcoholic beverages per occasion). On the one hand, this inconsistent association could be related with the positive perception (normalization) of alcohol consumption in Spanish culture, and the easy accessibility to this substance independently of the economic status. On the other hand, it is argued that, especially in Andalusia, Spain, there is a high tendency to street drinking among adolescents, where they can get alcoholic drinks on stores at a lower price than other regions.

Regarding gender, this study found that the number of occasions of binge drinking is higher in girls. There are various recent studies that reflect this trend towards equalizing consumption between women and men [33, 50]. Other studies have found different results using other variables. For example, Wilkinson et al. [51] measured the association between adherence to gender-typical behaviour and substance use from adolescence into young adulthood, and found that greater gender-adherence in females is associated with lower odds of high-frequency substance use. Equally, male adolescents who are more gender-adherent, compared with less adherent males, have a higher frequency of binge drinking. The data from

the Health Behaviour in School-aged Children survey (2013-2014) at the European level showed that alcohol use still tends to be more common among boys, but gender differences appear to be decreasing, particularly in relation to weekly drinking and drunkenness on more than one occasion. These differences could be related to population and date studied [44].

Spanish students reported higher alcohol consumption than non-Spanish students. This finding is similar to a study carried out in the United States [52], which showed that US-born adolescents reported higher use. It seems that living in one's birth country is related to alcohol use in the Spanish context. In their study, Díaz Geada et al. [33] found that being a non-immigrant increases the probability of buying alcohol among adolescents between 14 and 18 years of age. This fact could be associated to a higher socioeconomic level or greater availability of economic resources, as well as the ease of access or acquisition of alcoholic beverages for natives [33]. Moreover, it is known that for many years alcohol has been an integral part of the cultural and culinary heritage of western European countries, particularly those that border the Mediterranean Sea [53, 54].

One of the main limitations of our study might be missing data from the post-test, which was mainly related to the early completion of classes by vocational training students (whose classes ended before those of the other participants). In addition, the date for administering the post-intervention or follow-up questionnaire fell close to the final examination period in the schools involved, which made it difficult to ensure that the questionnaire was completed at school. The high dropout rate prevented us from using multiple imputation. High attrition rates, which are known to be common in eHealth interventions, may have affected the outcomes of the analysis [55, 56]. In this line, this attrition rate limited us to use only the variable "economic situation at home" as a mirror of family socioeconomic status, due to the loss of data in a question about the parents´ occupation. Another limitation is that the questionnaire was self-reported. This could have caused students to respond according to what they consider socially acceptable, although confidentiality was ensured during the completion of the questionnaire. The upside side of using data collected from self-reported measures is that if answers had been given by other people, such as parents, they might have been estimates that bore little resemblance to the reality, since parents' perceptions of their children's behaviour and substance use can be very different from those reported by the children themselves, as shown by Jander et al. [38]. The association between binge drinking and completing the questionnaire more days after the

last weekend could be another limitation, as the passage of more time could have resulted in recall bias as to the amount consumed, since adolescents drink more frequently on weekends. Another limitation could be the non-collection of information about the type of alcoholic beverage consumed, while other authors have found differences in terms of sex and family affluence, among other factors [57]. Finally, it is important to note the use of the definition of binge drinking and its equivalence in grams of alcohol per standard beverage unit as a limitation, given the difference between the grams of alcohol contained in a standard beverage in the USA and Spain.

Future research should include families of adolescents to explore other factors that might influence adolescent binge drinking, as well as other socioeconomic variables that might make it possible to measure the influence of socioeconomic status in the acquisition of this pattern of consumption.

Conclusions

In conclusion, the results of this study could complement prevention policies by emphasizing the importance of a reduction of weekly pocket money or of the economic availability to adolescents, as well as the importance of binge drinking by parents and siblings, and highlighting the need for the inclusion of families in interventions aimed at preventing alcohol use in adolescence. In this line, given that family members´ alcohol use predicts binge drinking in adolescents, future studies may need to consider interventions aimed at preventing alcohol use in family members too. In addition, given the findings relating to age, future research aimed at intervening in early adolescence to prevent binge drinking would be justified.

Abbreviations

BD: binge drinking; IG: intervention group; CG: control group; WHO: World Health Organization; DALYs: disability-adjusted life years; ESPAD: European School Survey Project on Alcohol and Drugs; ESTUDES: Spanish Survey on Drug Use in Secondary Schools; SD: Standard Deviation

Declarations

Ethics approval and consent to participate

The study received approval from the Bioethics Committee of Andalusia. Written informed consent was obtained from parents and students prior to participation in the study. The questionnaires were self-completed by the adolescents and confidentiality was ensured.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors´contributions

MLS, MTB and AMVM have made substantial contributions to the conceptualization and design of the study. TM and AMVM have contributed to formal analysis. AMVM has prepared the original draft of the work. MTB and MLS have supervised the work. All authors have read and approved the final version of the manuscript.

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Chapter 4

Paper 3. Measuring the Effects on Quality of Life and Alcohol Consumption of a Program to Reduce Binge Drinking in Spanish Adolescents

4.1. Main messages learned

This chapter includes the third paper of this thesis. This paper was written in response to the dearth of relevant data on the association between BD and HRQoL in adolescence. As mentioned in the introduction of this thesis, there is extensive knowledge about the acute consequences of BD and its long-term consequences in terms of morbidity. BD not only kills but also affects the HRQoL of individuals. It is therefore important to measure the association between BD and HRQoL. To do so, we decided to use QALYs as the health benefit measure, although it would also have been interesting to measure the association between DALYs and BD. In line with already published economic evaluations relating to alcohol use, this study measured the effectiveness of the intervention in terms of reducing the number of BD occasions and increasing QALYs.

While drafting this paper, I realized the importance of assessing interventions and programmes that are carried out over a long period, particularly in the field of public health, where the effects are expected to be found and maintained in the longer term. Lack of resources and difficulties in carrying out this evaluation prevented us from measuring the effects of the programme beyond four months, which meant that there were certain limitations regarding the extrapolation of the results found in this study. Additionally, since the effects of treatments, interventions, and programmes are not maintained to the same extent over time, costs also vary over time, which is something that must be considered in economic evaluation. It was at this time that I began to understand the concept of the discount rate and its importance.

Among the lessons learned from this paper, I would also highlight the depth of learning and understanding of the concepts of "utility" and "preference". I learned about the great work that takes place in the development of a set of values for measuring health states based on the preferences of different populations through the use of different methodologies, such

as discrete choice experiments (DCE) and time trade-off (TTO). This work was part of the analysis needed to conduct the final economic evaluation of the *Alerta Alcohol* programme.

This paper was submitted to and published in the journal *Drug and Alcohol Dependence*.[5] The review process for this paper helped me to hone skills related to the writing of scientific articles and the synthesis of research results.

In conclusion, this paper reflects my learning with regard to evaluating the effectiveness of public health interventions in terms of their health benefits and the management of tools used in health economics, such as the generic Euroqol Group questionnaire mentioned in Chapter 2.

This paper expands the scant scientific evidence available on the association between quality of life and BD and on the possible effects on QALYs of an intervention aimed at preventing BD in adolescence, which could help in future policy decision-making on the implementation of such interventions. In addition, the analyses carried out in this paper helped lay the groundwork for the paper described in Chapter 5.

[5] This journal is indexed in Journal Citation Report (JCR). It has an impact factor of 3.466 and is positioned within the "Substance Abuse" category in Q1 (5/35) of the Social Science Citation Index (SSCI) and Q1 (4/19) of the Science Citation index (SCI).

4.2. Abstract

Aim: To present a comparison between the effects on health due to a reduction in binge drinking (BD) and health-related quality of life (HRQoL), as a result of ALERTA ALCOHOL, an intervention aimed at reducing BD in Spanish adolescents.

Methods: A two-arm cluster randomized controlled trial was conducted with an intervention and a control group, randomized at the school level, following individuals over four months. The study population consisted of Andalusian adolescents aged 15 to 19 years who were enrolled in urban public high schools (n = 1247). Participants were assigned randomly to receive the intervention. The main outcome studied was the number of occasions of BD in the last 30 days, which was directly obtained from the answers given by the adolescents, and HRQoL measured with the EQ-5D-5L questionnaire. The model of estimation was the generalized estimating equations (GEE) approach.

Results: The program showed a BD reduction at the 4-month follow-up, although it was not shown to significantly increase the HRQoL in adolescents who reduced the number of occasions of BD and had received the intervention. However, it was shown that those who would predictably reduce the number of occasions of BD controlled by several sociodemographic variables perceived a higher HRQoL, as did those who had a greater adherence to the program.

Conclusions: Higher adherence to a web-based computer-tailored intervention to prevent BD in adolescents has a positive effect on decreasing the number of occasions of BD in adolescents as well as on increasing participants' HRQoL, although this second effect is very small, which could be due to the short follow-up time. This fact is quite important and should be assessed extensively to corroborate the results and to be translated into health policy.

Keywords: adolescents, health-related quality of life, EQ-5D-5L, binge drinking, alcohol, intervention, prevention

4.3. Unique selling points

- The *Alerta Alcohol* programme was effective in reducing the number of binge drinking (BD) occasions.
- Higher adherence to the programme increased health-related quality of life (HRQoL).
- Higher age, family alcohol consumption, and having a partner who belonged to the intervention group and reduced his/her BD occasions negatively affected HRQoL.
- Girls reported lower scores in "pain/discomfort" and "anxiety/depression" on the EQ-5D-5L instrument.

4.4. Main body of the paper

Based on:

Vargas-Martínez, A.M., Trapero-Bertran, M., Lima-Serrano, M., Annokye, N., Pokhrel, S., Mora, T. (2019). **Measuring the Effects on Quality of Life and Alcohol Consumption of a Program to Reduce Binge Drinking in Spanish Adolescents.** *Drug and Alcohol Dependence, 205,* 107597. Doi: 10.1016/j.drugalcdep.2019.107597

Chapter 5

Paper 4. Cost-effectiveness and cost-utility analysis of a web-based computer tailored for prevention of binge drinking in adolescents:

Alerta Alcohol

5.1. Main lessons learned

This chapter includes the fourth and final paper of this thesis. This research arose from the need to evaluate the efficiency of public health interventions to help decision-makers obtain the maximum health benefit with the resources available. The process of developing this paper involved my participation at the 6th EuHEA PhD Student-Supervisor and Early Career Researcher Conference (European Health Economics Association), held in Porto, Portugal, on 4–6 September 2019. At the conference, a senior health economist from University College London, Caroline Clarke, discussed a full preliminary version of this paper, highlighting several needed improvements that were later incorporated. This experience greatly enriched the paper and also gave me the opportunity to present part of my thesis work at an international congress where many international health economics experts meet and share knowledge in a positive and constructive atmosphere. The input from that conference could be considered the first external review of the paper prior to publication. I worked on all of Dr Clarke's comments, and we kept in contact after the conference.

In addition, a couple of months later, when I was attending a seminar entitled "Modelling in Economic Evaluation of Pharmaceuticals and Health Programmes (blended learning)", offered by the Barcelona School of Management at the Universitat Pompeu Fabra, I decided to review not only the model but also the calculations and settings of the model design of the economic evaluation that I built for the *Alerta Alcohol* programme. That process also helped me to revise the calculations and make improvements to the model setting for this and future economic evaluations. This intensive course was very useful to me, as it enabled me to continue learning about modelling approaches in economic evaluation, something I would like to continue working on after my thesis.

Regarding the lessons learned from the findings of this paper, I realized the importance of including the societal perspective in public health interventions in order to capture all of the costs and benefits generated by an intervention, which often lead to external effects. Another lesson learned relates to short-term assessments. Despite having obtained positive results in the cost-effectiveness analysis for a time horizon of four months, the intervention's effects in terms of both reducing the number of BD occasions and HRQoL were very small, indicating that longer periods of follow-up should probably be considered in the future.

Given the lack of literature on this topic and the fact that the Editorial Board of *BMC Public Health*, the journal that published paper 2, "Social, economic and family factors associated with binge drinking in Spanish adolescents", was interested in knowing more about the results of this economic evaluation, I submitted this paper to that journal.

In conclusion, this paper reflects my journey and learning experiences during the thesis process in relation to both methodological aspects and experience as a researcher in scientific dissemination at the international level.

5.2. Abstract

Background: Worldwide, binge drinking (BD) today follows being a public health concern among adolescents. This study sought to assess the cost-effectiveness and cost-utility of a web-based computer-tailored intervention to prevent BD in adolescence.

Methods: The sample was drawn from a study evaluating the *Alerta Alcohol* programme. The population consisted of adolescents aged 15-19. Decision tree analysis was used to estimate costs and health outcomes, as measured by number of BD occasions and quality-adjusted life years (QALYs). Incremental Cost-Effectiveness and Cost-Utility Ratios were also calculated from National Health Service (NHS) and societal perspective and for a time horizon of four months. Multivariate deterministic sensitivity analysis of best/worst scenarios by subgroups was used to account for uncertainty.

Results: The intervention was dominant from the societal perspective resulting in savings of €7,986.37 by one BD occasion averted per month. With regard to Incremental Cost-Utility Ratios, the intervention resulted in an incremental cost of €71.05 per QALY gained from NHS perspective and this was dominant, from societal perspective, resulting in savings of €34,126.64 per QALY gained in comparison with the control group. Subgroup analyses showed that the intervention resulted dominant for girls from both perspectives, and for those who were older (17 years or more) from NHS perspective.

Conclusion: Computer-tailored feedback is a cost-effective way to reduce BD and to increase QALYs among adolescents. However, long-term follow-up would probably be needed to capture major changes both in reduction of BD and in increasing of health-related quality of life.

Keywords: cost-effectiveness, cost-utility, binge drinking, alcohol, adolescents, Spain

Trial registration (ClinicalTrials.gov): NCT03288896. Registration date: September 20, 2017. "Retrospectively registered".

5.3. Unique selling points

- The *Alerta Alcohol* programme showed a statistically significant reduction in the number of BD occasions in the older adolescent group (≥17 years).
- Greater adherence to the intervention among females and those who had available pocket money of between €1 and €20 was associated with a reduction in the number of BD occasions.
- ICERs differed for the two perspectives studied (societal and National Health Service). The intervention was dominant from the societal perspective, resulting in monetary savings per BD occasion per month averted and per QALY gained.
- A possible cost-effectiveness in terms of BD occasions averted and QALYs gained from the NHS perspective was observed.

5.4. Main body of the paper

Based on:

Vargas-Martínez, A.M., Lima-Serrano, M., Trapero-Bertran, M. **Cost-effectiveness and cost-utility analysis of a web-based computer tailored for prevention of binge drinking in adolescents: *Alerta Alcohol.*** *BMC Public Health (submitted).*

Chapter 6

General discussion

6. General discussion

6.1. Introduction

In this chapter, the first section provides a summary of the results obtained in the study in relation to the research questions. This is followed by an in-depth discussion of the findings in relation to existing literature, following the order of the papers that make up this thesis. In the subsection entitled "General aspects of the thesis", the strengths and limitations of this work are discussed in terms of methodological quality, contribution to the existing literature in the field of study, and implementation of the evaluated intervention. Finally, the contributions and implications of this work are summarized, and ideas for future research in this area and the researcher's prospects are explored. The chapter ends with the conclusions of this thesis, summarizing the additional value and knowledge added by it.

6.2. Summary of findings

Prior to the actual economic evaluation of the Alerta Alcohol programme, a literature review was conducted to gain more insight into the current situation with regard to BD prevalence in adolescence at the international and national levels; the health, social, and economic repercussions of BD; existing interventions to prevent this harmful behaviour; and the effectiveness and efficiency of these interventions. Among the most important findings, it seems relevant to note the high prevalence of BD in this population, both globally and at the European and country (Spain) levels where the rates exceed 30%.

Exploring possible differences by gender, some studies have found variations in relation to risky alcohol consumption and, in particular, to the pattern of alcohol consumption under study, but the results have not been conclusive. This pattern of alcohol consumption has been found to have health and social repercussions, mainly related to acute events such as acute intoxication, accidental and intentional injuries, low school performance associated with brain alterations, and unprotected and unplanned sex. All this gives rise to economic consequences, such as the use of health, police, or justice resources, although data in the literature on these consequences is scarce, especially at the European and national level for BD in particular. The information found usually relates to costs attributable to alcohol in general. The preliminary literature review also revealed a lack of public health interventions to prevent BD among adolescents, globally and specifically in Spain, and a scarcity of evaluations of the effectiveness and efficiency of interventions (Chapter 2).

Following the implementation of the intervention, analyses were carried out to identify determinants of BD in adolescence in light of the disparities and inconclusive findings identified in the literature regarding the factors associated with this pattern of alcohol consumption. Prior to these analyses, a sample of Spanish adolescents were found to have a higher BD prevalence (around 36%) in comparison with European adolescents, according to data reported by ESTUDES 2016-2017 (OEDA, 2018). Among the social, economic, and family factors studied, a statistically significant association between BD frequency in family members (parents and siblings) and BD in adolescents was found, indicating that family drinking patterns are a risk factor for this behaviour. Similarly, BD frequency was found to increase as age and weekly pocket money increased (Chapter 3).

Subsequently, given the health outcome data collected to assess the cost-effectiveness of the Alerta Alcohol programme, the effects of a reduction in the number of BD occasions on HRQoL were analysed, together with the socioeconomic and family factors associated with HRQoL, and the effects on health of this intervention in terms of HRQoL and reduction of BD frequency. These analyses found a statistically significant association between a decrease in the number of BD occasions and HRQoL. This finding was related to higher adherence to the programme (i.e. completion of a higher number of intervention sessions). Unfortunately, after these preliminary analyses of the four-month follow-up assessment, the intervention was not shown to be significantly effective in increasing HRQoL among adolescents Additionally, a negative effect on HRQoL was found in relation to age, family alcohol consumption, and having a partner: lower HRQoL was found as age and family alcohol consumption increased and among adolescents who had a partner who belonged to the intervention group and reduced his/her number of BD occasions. Nevertheless, the Alerta Alcohol programme was shown to be effective in reducing the probability of BD (Chapter 4). In line with the foregoing findings, the intervention was shown to be more effective in specific subgroups of adolescents, namely girls, older adolescents (17 years of age or older), and those who had available weekly pocket money of between €1 and €20. These findings are derived from analyses carried out prior to the economic evaluation of the Alerta Alcohol programme (not yet published). The costs arising from BD and the intervention were also studied, and a large difference was found between costs in the intervention and control groups. Costs in the intervention group decreased, while costs in the control group increased. In relation to the cost-effectiveness and cost-utility analysis, the Alerta Alcohol programme showed dominance versus not doing anything from the societal perspective using both outcome measures: BD occasions averted per month and

QALYs gained. From the NHS perspective, the ICUR was €71.05 per QALY gained and the ICER was €16.63 per BD occasion averted. Sensitivity analyses showed differences in terms of efficiency by gender, age, and weekly pocket money subgroups. In summary, the intervention was found to be dominant for reducing the number of BD occasions per month for girls, for older adolescents (≥17 years), and for those who had no weekly pocket money. However, when the outcome measure used was QALYs gained, different results were obtained. Specifically, the intervention was dominant for both girls and boys from the societal perspective, with no differences by age group. From the NHS perspective, the Alerta Alcohol programme was cost-effective for both girls and boys (€2,710.92 per QALY gained) and for younger adolescents (<17 years) (€213.64 per QALY gained) (Chapter 5).

Notwithstanding these general findings, there are some important considerations that should be taken into account when interpreting the results of this study. Limitations, implications for future research, and practical applications are discussed in this chapter.

6.3. Specific discussion by findings

Binge drinking prevalence and determinants

The first paper in this thesis, which contextualized the current situation of BD prevalence among the young population, found no great differences between European and Spanish national data, with an approximate figure of around one in three adolescents (above 30%) who drinks a large amount of alcohol within a very short period of time (ESPAD Group, 2016; ESTUDES, 2018). However, when worldwide and European/Spanish data are compared, a slight difference is observed. Globally, more recent data reported by the World Health Organization (WHO) in relation to an alcohol use pattern similar to binge drinking, known as heavy episodic drinking (defined as 60 or more grams of pure alcohol on at least one occasion in the previous month), are slightly lower, with rates of 13.6% among adolescents aged 15 to 19 and 21.8% among young people aged 20 to 24 in 2016. Although a decrease in this unhealthy behaviour among adolescents aged 15 to 19 was observed during the period from 2010 to 2016 (from 17.1% to 13.6%), the prevalence remains high. According to the WHO report, at European level, 24.1% of adolescents aged 15 to 19 and 33.9% of young people aged 20 to 24 reported having engaged in heavy episodic drinking in 2016. Those figures represented a reduction of 11% for the first group and a reduction of 12.1% for the second group with respect to 2010, when the rates were 35.1% among adolescents aged 15 to 19 and 46.0% among young people aged 20 to 24 (WHO, 2018b). These differences between European and global data could be due to lower prevalence of

this unhealthy behaviour in regions such as the WHO Eastern Mediterranean Region, the WHO South-East Asia Region, and the WHO African Region (0.2%, 10.2%, and 12.7%, respectively). It is known that high-income countries tend to have higher levels of alcohol use than low- and middle-income countries. It is thought that this is due to a large number of abstainers in the latter countries (Cook, Bond & Greenfield, 2014; Rehm et al., 2009; Sornpaisarn, Shield & Rehm, 2012).

BD prevalence figures similar to the WHO data were found in other sources. For example, the latest European School Survey Project on Alcohol and Drugs reported a rate of 35% (ESPAD Group, 2016), while the latest survey on drug use in Spanish secondary education (ESTUDES, 2018) found a prevalence of 32.3% among Spanish young people aged 14 to 18. The prevalence of BD obtained in our study (among adolescents aged 15 to 19), through the responses of adolescents to the question: "In the last 30 days, how many times did you drink four or more glasses of alcohol (if you are a girl) or five or more glasses of alcohol (if you are a boy) on a single occasion?", was higher at around 37%. This difference might be related to differences in the definition of BD used in ESTUDES (at least five standard drinks in a two-hour period) and in our study (five standard drinks or more for boys and four standard drinks or more for girls on a single occasion). Nevertheless, given that the percentage of current smokers and the age range explored in our study were similar to those in European and in Spanish adolescents by the ESPAD Group (ESPAD Group, 2016), our sample could be considered representative of this population.

In relation to socioeconomic and family factors associated with BD in adolescents found in this study, the strong association between frequency of BD in family members (parents and siblings) and adolescent BD is remarkable. The data from the ESTUDES survey, which found an increase in the prevalence of alcohol consumption and BD as the frequency of parents' alcohol consumption increased (ESTUDES, 2018), also suggests this association. This finding represents a great challenge for healthcare providers in Spain, where alcohol consumption has been normalized as a social habit (March Cerdá et al., 2010).

The finding of a strong association between rising age of the adolescent and increased BD did not contribute anything new to what had already been found in the literature. But the positive association, which means that the frequency of BD increases with age, might indicate a need for further assessment of the effectiveness of interventions designed to prevent this risk to the health of the adolescent population.

Economic, health and social repercussions of binge drinking

Through the review carried out in the first paper that forms part of this thesis, economic repercussions (direct healthcare and social costs) arising from binge drinking were identified. Nevertheless, the scarcity of information about this at both the European and national levels is remarkable. In particular, it is noteworthy that the most up-to-date data about binge drinking costs come from United States (Sacks et al., 2015).

In relation to social and health repercussions of BD in young people, which translate into costs, more studies addressing this topic were found. Many of these repercussions are associated with the effects of BD on brain development and activity described by several authors (López-Caneda et al., 2013; Pulido et al., 2014; Squeglia et al., 2014; Stephens et al., 2008; Windle & Windle, 2017). The findings regarding the relationship between BD in adolescence and the development of an alcohol use disorder or dependence in adulthood (Caamaño-Isorna et al., 2017; Grant et al., 2001; Spoelder et al., 2015; Windle & Windle, 2017) are noteworthy and highlight the need to prevent this behaviour at an early age. Although this consequence could be classified as a medium-/long-term effect, the majority of the repercussions of BD in youth are acute. Some examples of these acute consequences at the social level would be violence, low school achievement, road traffic accidents, unprotected and unplanned sex, and use of other substances. All of them, in addition to direct health repercussions such as acute alcohol intoxication, result in health expenditures, for hospital stays, pharmaceuticals, and ambulance services, for example, as well as police and criminal justice expenditures (Pulido et al., 2014; Institute for Alcohol Studies, 2016). These findings should encourage reflection on the numerous risk behaviours that may be initiated in adolescence and the myriad consequences that they may produce both for the individual and the community.

Effects of Alerta Alcohol on Binge Drinking and Health-Related Quality of Life

Given the negative consequences of alcohol use and binge drinking, in particular, on adolescent health, it seemed important to analyse the relationship between this pattern of alcohol consumption and health-related quality of life (HRQoL). This association was studied in the third paper, in which reduction in the number of BD occasions was found to have an impact on HRQoL, although this finding was not related to having participated in the Alerta Alcohol programme. Nevertheless, this effect on HRQoL indicates that it is important to continue studying the prevention of this risk behaviour, given the importance of HRQoL for the population as a whole, as well as for decision-makers. This finding should

also prompt reflection on the multifactorial nature of HRQoL, especially in the healthy adolescent population, as well as future research on the effects of the Alerta Alcohol intervention in the long term. In addition, since the tool used to measure HRQoL, the EQ-5D-5L instrument, can be used to calculate quality-adjusted life years (QALYs), which is a generic measure of health improvement, it should be possible to make comparisons on the same scale of different types of health effects across different healthcare programmes (Bergmo, 2015).

In relation to the socioeconomic and family factors associated with adolescents' HRQoL, there is a clear need to continue studying the association between having a relationship with someone and HRQoL, given the lack of relevant studies and the negative effect of having a partner found in the study described in Chapter 4 of this thesis. In relation to age, the findings are similar to previous studies. The decrease in HRQoL as adolescents age increases could be the result of the physical and social transition experienced at this stage, in which young people begin to develop their own cultural values and norms and are continually being challenged with new developmental tasks, including the perceived and self-imposed pressure of being socially accepted (Bolton et al., 2014). This suggests a greater need for intervention at this stage of life filled with changes and potential risks for the adolescent.

The findings coming from this analysis suggest that, given the effectiveness of the Alerta Alcohol programme in specific subgroups of adolescents (girls, young people aged 17 years or older, and those who had available pocket money of between €1 and €20), it is necessary to study how and/or when to intervene in the rest of the adolescent population. In this connection, a recently developed eHealth app (Digital Alcohol Risk Alertness Notifying Network for Adolescents [D-ARIANNA]) predicts short-term BD episodes and classifies adolescents' risk levels (Crocamo, Bartoli, Montomoli & Carra, 2018). This tool could help to identify adolescents who present a higher risk of engaging in BD behaviour in order to adapt the Alerta Alcohol programme to these subgroups and consider its use in other subgroups of the adolescent population.

Limited interventions to prevent binge drinking

Another finding from this thesis is the scarcity of interventions to prevent BD in the young population, despite it being a major public health concern. This situation could be related to specific characteristics of public health programmes compared with healthcare technology-related interventions (Hill et al., 2017). The aim in public health is prevention of

future morbidity, which requires long-term assessment. Public health interventions are also broader in scope compared with healthcare technologies, which focus on specific individuals (Hill et al., 2017). In spite of these difficulties, a meta-analysis of computer-tailored interventions for health behaviour change was found, which demonstrates the potential of this type of intervention, although the analysis did not include any programmes aimed at preventing excessive alcohol use, due to the insufficient number of studies available for comparison (Krebs, Prochaska & Rossi, 2010).

Currently, at the national level in Spain, preventive interventions for risk reduction are part of one of the action areas under the National Addiction Strategy 2017–2024, "Towards a healthier and more informed society". The prevention of intensive alcohol consumption such as binge drinking is included in this area. The evaluation of the National Drug Strategy 2009–2016 (Delegación del Gobierno para el Plan Nacional sobre Drogas, 2017) concluded that the Strategy's people-centred orientation would need to be balanced with other strategies aimed at reducing risk factors and promoting protection in specific environments. Furthermore, although varied and structured prevention programmes exist, there is a clear need to increase the coverage of these programmes, ensuring universal coverage of those supported by evidence. It is also clear that, given the new challenges that prevention poses today owing to new forms of addiction and the perception of normality surrounding alcohol consumption among young people, these programmes must adapt to new contexts and forms of relationship in which consumption occurs, in particular by taking advantage of the opportunities that these new contexts offer for prevention (Delegación del Gobierno para el Plan Nacional sobre Drogas, 2018).

In addition to a national strategy, each autonomous region in Spain develops its own plans and programmes aimed at preventing substance use. Andalusia, the autonomous region from which the study sample was drawn, now has the Third Andalusian Plan on Drugs and Addictions 2016–2021 (Consejería de Igualdad y Políticas Sociales, 2016). This plan includes a battery of programmes for preventing drug use and addictions in schools (*DINO*, *Prevenir para Vivir*, *Y tú, ¿qué piensas?*, and *Forma Joven*), developed by health authorities in collaboration with the Department of Education. These programmes, which target a population between 10 and 18 years of age, have been integrated into the educational plan of each affiliated centre, where the interventions are carried out by the teaching staff, with training, materials, and support provided by technical personnel specializing in drug use and addiction. A common feature of these programmes is that they are aimed at preventing addictions in

general. They do not focus on alcohol consumption or specifically on binge drinking. Moreover, there have been few evaluations of their effectiveness, apart from an assessment of their implementation and of teacher and student satisfaction and an exploration of proposals for improvement of the *DINO* and *Prevenir para Vivir* programmes (Antolín Suárez et al., 2009) and an evaluation of the implementation features and effects of *Forma Joven* on attitudes and behaviours relating to nutrition, physical activity, sexuality, drugs, and road safety (Lima-Serrano, 2012). Regarding the *DINO* and *Prevenir es Vivir* evaluation, the teachers surveyed largely agreed on the need to improve the characteristics of the material of both programmes in terms of updating the format, including audiovisual and computer materials, and using more dynamic methodology. Other proposed improvements were related to the need for specialized external support and the involvement of parents in carrying out the programme. Students, like the teachers, highlighted the need to update the programme material (methodology and content), increase the length of the programme, increase the variability in the application schedule, increase the variability in the staff responsible for implementation (including both professionals from the centre and external staff), and promote the involvement of families (Antolín Suárez et al., 2009). In relation to the assessment of *Forma Joven*, low magnitude effects and counter-effects were found that were not conclusive. The weaknesses detected were related to organization, loyalty, professional training, and resources and to low response by the young people, which could have influenced the lack of effects of interest (Lima-Serrano, 2012).

The main reason for providing information about the programmes carried out in the Andalusian region is that the sample for the studies discussed in this thesis came from Andalusia. In addition, as García-Lorenzo and Trapero-Bertran (2020) report in a literature review on evaluations of the impact of structured programmes and specific actions for the prevention and treatment of alcohol consumption in Spain, there is an evaluation gap and a need to build a culture of evaluation. The current situation does not promote transparency regarding accountability to society for public health expenditures, nor does it facilitate decision-making regarding health policies in this field. Furthermore, these authors in their review report that the evaluation of the quality of these Spanish programmes is low, despite the investment made to reduce this public health problem. In this review it was found that most programmes (72%) include objectives related to other drugs in addition to alcohol and that results were evaluated for only a quarter of the programmes.

Efficiency of Public Health Interventions

Another issue examined in the literature review carried out for the first paper was assessment of the efficiency of interventions aimed at preventing BD in adolescence. Hoang et al. (2016) conducted a systematic review of modelling approaches in economic evaluations of health interventions for substance use problems, but no interventions aimed specifically at preventing binge drinking. This study found a need to enhance the quality of economic evaluations of this type of intervention.

In the review carried out for my paper, only one study was found which assessed the cost-effectiveness of a programme aimed at preventing this alcohol consumption pattern (Drost et al. 2016). Among the reasons why there is a scarcity of studies involving economic evaluation of interventions in the field of public health, one is the difficulty of attributing results in this type of study. The recommended clinical trials are much less frequent (and sometimes not feasible) in public health. Moreover, the results of public health interventions usually occur in the long term, whereas many clinical results are measured in the short term, which favours the allocation of resources to the healthcare system rather than to public health programmes (García-Altés et al., 2011).

A systematic review carried out after Hoang et al. (2016) by Bardach et al. (2019) sought to establish the burden of disease attributable to alcohol and identify the cost-effectiveness models that have been tested worldwide. Three evaluation models were identified: (a) state transition models, i.e. decision-analysis models such as cohort simulations of the Markov model and individual microsimulations; (b) multi-stage life table models; and (c) modelling studies for estimating population attributable and preventable fractions. Most of the studies used the latter model (46%), followed by the state transition and life table models.

Efficiency of Alerta Alcohol

In relation to costs and health effects in terms of reduction in the number of BD occasions and QALYs gained as a result of the *Alerta Alcohol* programme in comparison with no active intervention, it was observed that there was a small incremental effect in terms of reduction in the number of BD occasions in the intervention group and that the costs (without counting intervention costs) in this group decreased between the pre-intervention and post-intervention periods, whereas the costs in the control group increased in the post-intervention period, leading to large differences in the costs between the two groups in the post-intervention period. This difference derives from the high cost of the consequences related to alcohol consumption and specifically to BD behaviour (traffic accidents, hospital

stays, emergency medical transport, and others). Hence, it could be concluded that small effects in reducing the number of BD occasions produce great savings in relation to the efficiency of an intervention in young people (Foxcroft & Tsertsvadze, 2012).

Given that the findings regarding the efficiency of the *Alerta Alcohol* programme reflect the dominance of this intervention from the societal perspective, it seems important that policymakers should be made aware of the impact of perspective and should take it into account in their decisions about resource allocation. Jönsson (2009) provides ten arguments for taking a broad societal perspective in health technology assessment (HTA) studies, one of which is that, since regulatory decisions about market authorization of new medical technologies are based on an assessment of the benefits and risks from a societal perspective, HTA studies should take the same perspective. Another argument is that adopting a payer perspective instead of a societal perspective will create a bias against investments aimed at improving health through healthcare spending. This author also notes that, since it has been widely accepted that economic evaluations should include all potential health effects, then costs should also be taken into account from a societal perspective. Another argument is that specific payer perspectives should be assessed within the societal perspective, because it will thus be possible to identify the most relevant perspective, depending on the specific policy issue to be addressed. Jönsson (2009) also proposes that the use of a societal perspective supports an informed public discussion and democratic decisions, since it is the public that pays for and receives the benefits of new technologies or healthcare interventions.

Finally, with regard to the need for data on the effectiveness and costs of public health interventions, Puig-Junoy and Oliva Moreno (2020) recently concluded that there are many elements that must be taken into account when analysing the evolution of public health spending, such as improvement in the quality of life. They stress that, although some elements are not controllable or are difficult to control, others can be controlled, such as regulatory changes and generation and dissemination of information on the effectiveness and costs and prices of new health technologies.

Concerning subgroup differences in cost-effectiveness of the intervention, it is known that alcohol use patterns vary by gender. Although, adolescent males generally have higher rates of alcohol use, including binge drinking, this is not the case in all countries. For instance, in the US, girls aged 12 to 20 have slightly higher rates of alcohol use and BD than boys (Center for Behavioral Health Statistics and Quality, 2017). Similarly, ESTUDES (2019), the survey on drug and alcohol use among adolescents in secondary education in Spain, found

that the prevalence of BD is higher among girls than boys in the group aged 14 to 17 years, whereas at 18 years this prevalence is slightly higher among boys than girls. In addition, the metabolism of alcohol is different for males and females owing to differences in gastric tissue activity. This results in higher blood concentrations of ethanol in women than in men after drinking similar amounts of alcohol (Frezza et al., 1990; Lieber, 2000, NIAAA, 1999; NIAAA, 2003). As a result, women become intoxicated with lower amounts of alcohol than men (NIAAA, 1999). Therefore, it seems important to use strategies, interventions, and/or programmes to prevent this pattern of alcohol use specifically among girls.

With regard to age, differences were found in the cost-effectiveness of the intervention depending on the outcome measure used (BD occasion averted or QALY gained). The *Alerta Alcohol* programme was found to be dominant and cost-effective for older adolescents (≥17 years) from both the NHS and societal perspectives in relation to BD occasions averted. However, when the outcome measure was QALYs gained, the intervention was dominant and cost-effective for younger adolescents (<17 years) from the societal and NHS perspectives. These differences regarding the cost-effectiveness of the intervention by age group might be related to the fact that the aim of the intervention was to prevent BD, not to increase QALYs. In addition, this finding in relation to QALYs gained might be confusing, since the perception of HRQoL in adolescence is known to be associated with abilities to interact socially, and adolescents with high levels of alcohol consumption might therefore show low perceived impact on HRQoL (Luquiens et al., 2018). Therefore, it does not necessarily follow that the perception of HRQoL would improve among adolescents who reduce their number of BD occasions. However, the fact that the intervention proved more cost-effective, in terms of reducing the number of BD occasions, among the group aged between 17 and 19 years is positive, since as confirmed by ESTUDES (2019), both alcohol use and binge drinking increase with age, with BD prevalence of over 40% among those 17 years of age or older.

Regarding the cost-effectiveness of the intervention depending on the weekly pocket money available, it is worth highlighting the difference in results depending on whether the measure of health effect used was reduction in the number of BD occasions or increase in QALYs. As demonstrated in the study, the *Alerta Alcohol* programme was shown to be cost-effective for those who had no weekly pocket money from both the NHS and societal perspectives, with an incremental cost of €167.53 and €1,128.25 per QALY gained, respectively. The intervention could also be cost-effective in reducing the number of BD

occasions avoided, depending on the willingness to pay of society and the NHS (€72.42 and €10.75, respectively). For adolescents who had weekly pocket money of over €20, the intervention was effective in increasing QALYs, resulting in savings from both perspectives, but not in reducing the number of BD occasions. This finding may be attributable to the fact that greater availability of weekly pocket money has been found to be a risk factor for BD (Crocamo et al., 2018) and that better quality of life has also been associated with greater economic availability (Nur, Kıbık, Kılıç & Sümer, 2017).

Other studies have found negative effects of higher weekly pocket money not only in relation to alcohol consumption but also tobacco and cannabis use (Gaete & Araya, 2017; Ma et al., 2013). For example, Gaete and Araya (2017) found that those who had more pocket money had a higher risk of having smoked cigarettes and a higher risk of cannabis use during the 30 days preceding their study. In that study, a higher risk of alcohol use was also found among those who had more pocket money, similar to findings of our study. In a study carried out by Ma et al. (2013) among Chinese adolescents, the prevalence of current smokers increased as amounts of monthly pocket money rose.

6.4. General aspects of the thesis

Limitations

Dropout

One of the most important aspects to mention is the *high dropout rate* in the study. The main reasons for this high rate are related to intervention design, data collection, administration of questionnaires, and information bias. Adolescents, classes, and schools may drop out during the intervention (not completing all the sessions that the intervention includes) or in the follow-up assessment (Jander et al., 2015; Jander, 2016). When dropout occurs during an intervention, the participants do not receive the full content of the intervention, which can influence any intervention study (Jander et al., 2016). For an intervention to be effective, it must be used in the way it was designed; otherwise, the impact of the intervention on public health may be weakened (Eysenbach, 2005; Glasgow et al., 1999; Jander, 2016).

A high attrition rate is common in studies aimed at the adolescent population and, in particular, in studies that use web-based interventions or programmes, in which data for assessment are collected through self-reporting. The dropout rates in such studies reach around 50% (Wangberg, Bergmo & Johnsen, 2008; Kelders, Kok, Ossebaard & Van Gemert-

Pijnen, 2012), and many difficulties may be encountered in maintaining the number of subjects over the course of these studies (Etter, 2005, Farvolden, Denisoff, Selby, Bagby, & Rudy, 2005). Additionally, the use of web-based interventions and other technologies may make it easier for participants to be distracted, and it is easier for them to drop out of this type of study, for instance by simply closing the browser window (Birnbaum, 2004). This concept, called "attrition", is defined by Eysenbach (2005) as "the phenomenon of participants stopping usage and/or being lost to follow-up". Attrition is one of the fundamental methodological challenges in evaluating eHealth interventions. This author distinguishes between two processes when talking about attrition in longitudinal studies. On the one hand, attrition refers to the loss of participants to follow-up – that is, these subjects do not return to complete the follow-up and evaluation questionnaires, which the author calls "dropout attrition". On the other hand, attrition refers to the non-use of the programme, which is called "non-usage attrition" (Eysenbach, 2005).

One of the main consequences of the high dropout rates in computer-based prevention and intervention programmes could be the small effect sizes found. Based on the experience of our study and those found in the literature, it is necessary in this type of clinical trial to invest in human resources. In the review of the literature carried out by Schinke and Schwinn (2017), it was found that a quarter of recent studies that managed to reduce attrition rates through increased use of human capital showed significant differences in substance use among youth, with larger effect size. Nonetheless, the literature supports the increased use of new technologies, although improvements are required in order to maintain high standards of rigour in research (Schinke & Schwinn, 2017).

In relation to the problem of attrition, in addition to improving the monitoring and scope of the sample, it could be concluded that it is very important to closely supervise data collection in a research project. This thesis has been developed on the basis of the data collected in a clinical trial in which a single research technician was recruited, but it would have been preferable to hire a larger number of people to oversee data collection, since the technician could not be present in all schools at both the first and last sessions, which were aimed at the evaluation.

Regarding the *design of the intervention*, better use could have been made of electronic technologies to achieve greater acceptance and adherence, as well as to reduce loss to follow-up. The feedback to the adolescent in this programme is provided through text messages that come from an avatar that each adolescent chooses when registering on the programme's

website, and this avatar accompanies them during all sessions. A review of the literature on computer-based interventions and prevention programmes to reduce alcohol use among young people notes that few programmes exploit the potential of technologies using elements of gamification, smartphones apps, or social media to complement the design of interventions such as the *Alerta Alcohol* programme, which are based on a programme personalized for the youth's individual demographic characteristics, risk factors, and vulnerabilities (Schinke & Schwinn, 2017).

Gamification, in particular, has been found to be a useful tool for increasing participation and adherence in web-based programmes and interventions (Lumsden, Edwards, Lawrence, Coyle & Munafò, 2016; Lumsden, Skinner, Coyle, Lawrence & Munafo, 2017; Primack et al., 2012; Cugelman, 2013), although there is considerable controversy in the literature regarding the definition of gamification (Sardi, Idri & Fernández-Alemán, 2017; Deterding, Dixon & Khaled, 2011; Deterding, Dixon, Khaled & Nacke, 2011; Werbach, 2015). The most commonly accepted definition is that of Deterding, Dixon, and Khaled (2011), who define gamification as "the use of game design elements in non-game contexts". It follows that this technique could be used to modify the behaviour and motivation of users through experiences similar to games (Hamari & Koivisto, 2013). One of the main uses of gamification is the leveraging of social networks with the aim of increasing engagement and interaction between users (Palmer, Lunceford & Patton, 2012). Some examples of gamification techniques are narrative stories, avatar-based self-representation, and onboarding tutorials (Cugelman, 2013). According to Turan, Avinc, Kara, and Goktas (2016), the use of gamification improves interventions from two convergent perspectives: on the one hand, it makes the activities included in the intervention more enjoyable and, on the other hand, by making activities more enjoyable, it helps to ensure the long-term commitment of users to activities or tasks that they may perceive as demotivating or not interesting for them. These authors highlight emotional, cognitive, and social benefits of using gamification (Turan et al., 2016). Schinke & Schwinn (2017) point out the importance of involving parents, teachers, and other sources of guidance and social support in these programmes.

While the design of the intervention may have contributed to the high dropout rate and, thus, to a possible bias in the information, another possible reason for the high attrition rate may have been the seasonal period in which the intervention was assessed. The collection of baseline data, prior to the start of the intervention, took place in January and early February,

after the Christmas holidays. This is a period in Andalusia in which there are often many events involving family and friends, an environment in which alcohol consumption is more frequent. The data collection carried out four months later, in the months of May and June, coincided with several different situations. At this time, students are usually busy preparing for the final examinations of the academic year. In addition, part of the sample consisted of students enrolled in vocational training, who finished their course before the rest of the sample (in May), which meant that many of those participants could not be contacted during the follow-up period. Furthermore, teachers were engaged in a number of activities (meetings, evaluations, etc.) at the end of the school year and were therefore less willing to carry out the last session. Finally, in Andalusia, numerous local festive events (fairs, pilgrimages, street parties), at which alcohol consumption is more frequent, take place during this period.

We chose these dates to assess the alcohol intervention because the academic year begins in September and ends in June. Schools were contacted in September and either agreed to participate or not. A pilot test of the intervention was carried out during the first months of the academic year, but we had to wait until January to begin the intervention itself. We could not start in December, since it is the period in which students are assessed for the first quarter of the academic year. A four- month follow-up period was selected because that was the period selected in the Dutch study on which this intervention was based (Jander et al., 2014), since a six-month follow-up assessment, as indicated in the design of the original intervention, would have coincided with students' summer holidays. This period was also chosen to avoid greater attrition. If the follow-up assessment had been postponed to the following September, many adolescents might have changed schools or classes, which would have made it much more difficult to reach them.

The lack of close monitoring mentioned above, especially in the collection of data to be used in evaluating the effectiveness and cost-effectiveness of the intervention, resulted in some mistakes in the collection of data on certain variables, which could therefore not be used in the analyses. For instance, one of the specific objectives of this thesis initially was to analyse, through network methods, peer effects on binge drinking by adolescents and on the impact of and adherence to the intervention. This research objective was formulated in recognition of the role that peer relationships play in the healthy or unhealthy development of an adolescent (Brown, 2004; Rubin et al., 2011; Ali & Dwyer, 2010; Duncan et al., 2006). Ivaniushina, Titkova & Alexandrov (2019) identified three systematic reviews which analysed

the interrelationships between adolescents' health risk behaviour and peer relationships (Jeon & Goodson, 2015; Jacobs, Goodson, Barry & McLeroy, 2016; Leung, Toumbourou & Hemphill, 2014). To carry out these analyses, we needed to identify peer effects, specifying who were the friends of each adolescent within their class. Given the legal requirement for data protection, students were asked to identify their friends by their number in the class list. To do this, data were collected during the session, with the collaboration of teachers, who provided all students with a class list, either on paper or in an electronic document projected in class. These constraints made it difficult to collect the data, and it was therefore not possible to evaluate peer effects.

Another measure initially included in the design for data collection related to students' academic performance. Owing to the aforementioned problems, these data could not be collected or analysed, either. Such data could have been an indirect measure of the effectiveness of the intervention, as indicated by Weimer, Moberg, French, Tanner-Smith, and Finch (2019) in their study on the efficiency of a tertiary prevention measure such as "recovery high schools" that provide education and therapy for young people who have been treated for some substance use disorder. This study measured effectiveness in terms of the number of students graduating and found average net benefits ranging from $16.1 thousand and $51.9 thousand per participant and incremental benefit-cost ratios ranging from 3.0 to 7.2.

In addition to what has already been mentioned in relation to the possible reasons for high attrition, which affected the final sample size, it seems important to add that some variables were not included in the analyses because of lack of data on some variables included in the evaluation questionnaire and because of the need to avoid possible biases, given the answers in some items. An example is the variables related to the frequency of other substance use.

Given that the questionnaire was *self-reported*, one of the reasons for the lack of response might be the length of the questionnaire, which might have led to respondent fatigue. The original questionnaire from the clinical trial was expanded to enable us to study additional socioeconomic variables and variables related to healthcare and non-healthcare costs in order to carry out an economic evaluation of the *Alerta Alcohol* programme. We might have been able to shorten the questionnaire by collecting some of these data from the NHS databases. Moreover, data from the NHS databases would have been more detailed than those collected from the adolescents. As with all data sources, however, there are limits to both use of and

access to NHS data, making it difficult to collect. Furthermore, some limitations have been noted in data collected from the NHS, such as the quality of data related to the accuracy of some diagnoses and procedures encoded with the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), including erroneous coding, omission of comorbidities, and missing data. Another problem might be related to the expected source of payment, since some adolescents may have received care in a public healthcare service and others in a private healthcare service, which could further complicate data collection (Andrews, 2015).

Another limitation might be related to the social desirability effect, which may lead to bias in responding based on what is considered "socially acceptable" and therefore to underestimation of alcohol use and binge drinking prevalence (Koning, Harakeh, Engels & Vollebergh, 2010; Petróczi & Nepusz, 2011). Another possible reason for the lack of answers on these items could be proximity bias, or the tendency to give responses that are similar to previous responses, since all these items had the same categories of answers and the questions were presented in tables that differed only in terms of the substance concerned (hallucinogens, amphetamines or speed, cannabis, cocaine, ecstasy or MDMA, heroine, etc.).

After this in-depth analysis of the dropout rate and missing data and the possible underestimation of substance use in this study, it seems appropriate to discuss one of the possible solutions to these problems: the use of multiple imputation. Although this is one of the methods of choice for handling missing data (Blankers, Koeter & Schippers, 2010), given the high number of missing values in our database, its use could have led to unreliable estimates, as reported in the literature (White, Royston & Wood, 2011). There seems to be no clear consensus as to the percentage of missing data and the number of imputed data sets needed to carry out multiple imputation (Bodner, 2008; Blankers et al., 2010; White et al., 2011; Allison, 2012; Graham, Olchowski & Gilreath, 2007).

Particular characteristics of public health interventions

In addition to the aspects related to attrition in this study, it seems appropriate to address the difficulty of conducting an economic evaluation of a prevention programme, as opposed to a health technology such as a medication or screening test. Public health has unique characteristics which make it difficult to assess interventions carried out in this field. In general, the scope of the consequences and/or effects of public health interventions is much broader than that of health technology interventions, in which the result is focused on

an individual's health. In addition, the time horizon between the intervention and the effect that it produces is usually considerably longer in public health, as the aim is to achieve a long-term goal of morbidity prevention. This makes economic evaluation difficult, since a discount has to be applied to future costs and benefits, thus modelling the effects in the longer term, since generally the present value of costs and benefits generated by an intervention is higher than the future value. The application of this discount rate is necessary to inform decision-making in the present and it must therefore be chosen carefully (Weatherly et al., 2009). The effects of public health interventions, and specifically behaviour change interventions, are known to be observed over the long term. (Alayli-Goebbels et al., 2014; Pokhrel et al., 2017). Since the future situation is subject to much more uncertainty than the present, measuring the effect of a behavioural intervention in the future is always difficult and surrounded by uncertainty.

Nevertheless, the difficulty in carrying out both economic and effectiveness evaluations of public health interventions aimed at prevention does not obviate the need for evidence-based public health. Decision-makers have to make decisions based on the evidence currently available on public health interventions, as they do with health technologies (Wang et al., 2006). However, the evidence in this area of action is scarce, in part because public health interventions depend on the context in which they are implemented, "context" being understood to mean the social and cultural environment and the particular political and organizational system of a society (Wang et al., 2006). This means that an intervention that has proven effective in one context may be ineffective in another, even assuming it can be implemented there. For this type of intervention, there is therefore a need to assess applicability and transferability (Rychetnik & Frommer, 2002; Rychetnik et al., 2002), an area of interest for the Cochrane Health Promotion and Public Health Field (Frommer et al., 2003). The term "acceptability" was defined in the work carried out by Wang et al. (2006) as the extent to which an intervention could be implemented in another context, and the term "transferability" was defined as the degree to which the measured effectiveness of an applicable intervention could be achieved in another setting.

Longitudinal assessment

In addition to the applicability and transferability of public health programmes and interventions, it seems important to discuss the *long-term assessment* of behaviour change interventions, since the intervention carried out in this study was aimed not only at prevention but also at inducing a change in behaviour, in line with the Integrated Change or

I-Change Model (De Vries, Dijkstra & Kuhlman, 1988; De Vries & Mudde, 1998), which integrates several theories (Ajzen's Theory of Planned Behaviour, Bandura's Social Cognitive Theory, Prochaska's Transtheoretical Model, the Health Belief Model, and goal-setting theories) (Ajzen, 1987; Prochaska & Velicer, 1997; Janz & Becker, 1984; Gollwitzer, 1999). Owing to the difficulties described above and lack of resources for research, it was not possible to successfully carry out a long-term assessment, which, as discussed in the papers that make up this thesis, was a limitation of the study.

It is known that people who initiate a change in health behaviour often relapse when the intervention is withdrawn (Hendershot, Witkiewitz, George & Marlatt, 2011; Jeffery et al., 2000; Marcus et al., 2000). According to Jander et al. (2016), it is advisable to carry out longer-term evaluations to assess effects after 12 or 24 months or an even longer period of time.

Strengths

Despite all the limitations mentioned above, tools aimed at changing behaviour through multimedia and mobile technologies have been shown to strengthen health promotion and disease prevention (Lau et al., 2012; Gonzales, Ang, Murphy, Glik & Anglin, 2014; Whittaker et al, 2012). One of the main advantages of the use of such technologies could be their wide reach and their normally low cost. One of main strengths of the design of the *Alerta Alcohol* programme may have been the use of text messages sent through a website, given that several studies have shown that text and video messages sent by mobile phones elicit a higher response rate than messages sent by email (Geckle, 2016).

In relation to adolescent self-reporting and the option of using NHS databases to complete the information needed to assess the efficiency of the programme, I would point out that the design of the evaluation questionnaire prior to the intervention has the advantage of ensuring homogeneity with regard to the units of measure for the variables incorporated. Additionally, the uncertainty analysis carried out through a deterministic sensitivity analysis attempted to address the problem of high dropout and the consequent lack of results certainty.

As mentioned earlier, a deterministic sensitivity analysis of best and worst scenarios was carried out instead of a probabilistic analysis. This type of analysis consists of modifying the values of several parameters, choosing values that combine the values of the parameters that

produce the best and the worst cost-effectiveness ratios and the most optimistic and pessimistic scenarios, and then checking to see if the intervention is cost-effective even in such extreme scenarios. One of the disadvantages of this type of sensitivity analysis is the difficulty of presenting and interpreting results. If the intervention evaluated is preferable in the general case or base case, as well as in the best and worst scenarios, we can be very confident in the evaluation results. Probabilistic sensitivity analysis is advisable when it is possible that the cost-effectiveness ratios will show significant changes or there is a possibility that the parameters are interdependent (Pinto Prades & Sánchez Martínez, 2003). Probabilistic sensitivity analysis is specifically used in economic evaluations based on models and not to analyse results but to predict them (Fox-Rushby & Cairns, 2005). This type of sensitivity analysis was not used in our study because the use of a decision tree for the economic evaluation of *Alerta Alcohol*, which only shows the progress of an adolescent through the model in one direction, meant that subjects were not able to move back and forth between states, and events occurred only once. One of the main reasons for this choice was the decision to have a single follow-up measure at four months, without being able to use modelling approaches, given the absence of evaluation in other follow-up periods that would have made it possible to determine the length of cycles and calculate the probabilities of a change of state (Fox-Rushby & Cairns, 2005).

6.5. Contributions of the thesis

What does this thesis change?

Given the results of this thesis, this work represents a modest advance in the study of the determinants of binge drinking in adolescence and provides a basis to continue working on measures to prevent this pattern of behaviour and to develop interventions that may be more effective in reducing alcohol consumption. This study provides evidence on a possible approach for preventing and treating this public health problem, which affects many adolescents. The evidence includes data that reflect a possible cost-effectiveness, which is so important for decision-makers in the political sphere who make decisions concerning the allocation of resources.

Regarding the progress made in identifying the factors associated with binge drinking, we can conclude that this problem is not only the responsibility of governments, but also of families and others in the environment surrounding the adolescent. For instance, despite the laws restricting the purchase and consumption of alcoholic beverages by young people under the age of 18 in Spain, alcoholic beverages can be obtained through family and friends, whose

consumption patterns have been shown to influence teenagers' alcohol consumption. Given the findings in relation to the influence of families in adolescents' BD behaviour, it seems important to involve them, although this would not necessarily be easy, as noted by Jander et al. (2015), who encountered difficulties both in recruitment and in avoiding dropout in their study. Jander et al. (2015) concluded that more research is needed on the best method for including families, taking into account specific research needs, such as, for example, the need for coincident data (family-student dyad) and anonymity. Among the strategies identified in the third round of the study for reducing dropout of parents were: email reminders, SMS reminders (text messages), use of highly relevant material; interesting topics; use of language that does not sound pompous or that may be interpreted as condescending; making clear that it is understood that parents are the best experts when it comes to their children, and that parents want what's best for their children, and that being a parent can be extremely difficult; and making the need for the intervention salient to parents.

Regarding the cost-effectiveness of this intervention, caution must be exercised in interpreting the results, given the high attrition rate. Nevertheless, this intervention could be considered cost-effective using the number of BD occasions averted as a result outcome measure (irrespective of the perspective applied – NHS or societal). However, it is difficult to make recommendations, since cost-effectiveness depends on the willingness to pay by society and the NHS and since there is no reference cost-effectiveness threshold for reducing binge drinking. In relation to the cost-effectiveness of the intervention as measured by QALYs gained, the *Alerta Alcohol* programme could be considered cost-effective based on the cost-utility threshold for Spain (Vallejo-Torres et al., 2016), although the interpretation of data in relation to QALYs gained should also be approached with caution, given the small incremental effect found between the control group and the intervention group and the non-association between the impact of the intervention, as measured by the reduction in BD occasions and belonging to the intervention group, and HRQoL found in the analyses undertaken prior to the economic evaluation. Despite this, the ICERs and ICURs obtained point to a probability of cost-effectiveness for a wide range of population scenarios and subgroups.

Given that the results of this work can only be interpreted cautiously due to the high dropout rate, further studies of adherence to these types of interventions in the population studied would be needed in order to promote their implementation in practice and confirm their effectiveness, cost-effectiveness, and impact on public health.

Contribution of this thesis to my knowledge

In thinking about the knowledge that I acquired while developing this thesis, I would begin by highlighting the importance of studying and carefully designing the field work and the importance of high adherence to public health interventions. In this way, the results obtained in future investigations would have greater external validity. One of the aspects that I would try to improve is the motivation for behaviour change in adolescents through the various elements discussed below. Another is the use of elements such as gamification, smartphone apps, and social media, which, as previously reported, improve adherence to this type of intervention.

Although during the intervention, the sessions focused on factors associated with the motivational phase of behaviour change, such as attitudes, social influences, self-efficacy, and action plans (de Vries, Kremers, Smeets, Brug & Eijmael, 2008; de Vries et al., 2003), it seems that focusing first on pre-motivational factors, such as knowledge, action signals recognition, and risk perception (de Vries et al., 2008; de Vries et al., 2003), could be beneficial for the motivation of study participants (Jander, 2016). Bartholomew, Parcel, Kok, Gottlieb & Fernandez (2011) suggest that some methods for influencing these pre-motivational factors might be awareness, scenario-based risk information, fear arousal, and signal delivery.

In a study carried out by Kells, Burke, Parker, Jonestrask & Shrier (2019) aimed at engaging young people in order to reduce frequent marijuana use, the authors concluded that motivational interviews (MI)/motivational enhancement therapy (MET) can provide appropriate goals and encourage healthy values and ambivalence about cannabis use that can be used later to facilitate movement through the stages of behaviour change towards reduced use. MI has been defined by Miller and Rollnick (2013) as: "…a collaborative, goal-oriented style of communication with particular attention to the language of change. It is designed to strengthen the personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion." This approach has been shown to work well with adolescents and young adults (Naar-King & Suárez, 2011). MET combined with MI along with structured personalized feedback has been shown to be a promising intervention for adolescents with problematic substance use (Blevins, Walker, Stephens, Banes & Roffman, 2018; Cornelius et al., 2011; Dennis et al., 2004; Jensen et al., 2011).

Gaume, Bertholet, Faouzi, Gmel & Daeppen (2013) explored and tested the different categorizations and measures of Change Talk (CT) as predictors of change in alcohol consumption at six-month follow-up among 20-year-old men who received a single brief motivational interview (BMI) session in an army recruitment centre. CT is defined as the process of obtaining and shaping the client's language in favour of change during sessions in an MI (Miller & Rollnick, 2002). In their study, Miller and Rollnick (2002) concluded that CT, or some of its dimensions (ability, desire, and need for language), predicts a real subsequent change. Perhaps the inclusion of a pre-intervention session focused on these pre-motivational factors and discussed through the use of some of these techniques could have improved the motivation for adolescent behaviour change, thus improving the effect of the *Alerta Alcohol* programme on the binge drinking behaviour of adolescents.

In addition to the aforementioned interventions aimed at improving motivation to change among adolescents, a change in the design of the intervention through the use of games, following the same strategy of computer-tailoring-based interventions, might improve such motivation. However, the intervention evaluated in this thesis was based on a Dutch programme (Jander et al., 2016) that used a game, and although it proved effective for adolescents aged 15 and 16 years, it did not yield the expected results, due largely to the high dropout rate. The study by Jander et al. (2016) proposed improving the game, rather than rejecting its use in eHealth interventions, given the effectiveness reported in other studies (Connolly, Boyle, MacArthur, Hainey & Boyle, 2012; DeSmet et al., 2014; Papastergiou, 2009; Tüzün, Yılmaz-Soylu, Karakus, I˙nal & Kızılkaya, 2009). One of the suggestions for improvement was to make the entire intervention a game, without asking explicit questions about attitude and modelling. Jander (2016) proposed an example based on the popular game SimCity, in which the player takes the role of mayor and takes control of the economic development of a city so that all his/her decisions affect the wealth of the city. In the case of an intervention aimed at preventing alcohol consumption, the adolescent could play the role of a health worker trying to deal with the consequences of alcohol consumption among young people.

Policy implications of the findings from the thesis

The findings of this thesis suggest that, although there is no cost-effectiveness threshold for the reduction of binge drinking, the inclusion of the societal perspective, and not only the NHS perspective, in economic evaluations of interventions focused on preventing and/or treating a health-related problem can change policy decisions regarding the allocation

of resources. In addition, it is worth recalling that the evaluation of the efficiency of the intervention analysed in this thesis was conducted from two perspectives: cost-effectiveness in terms of costs for reducing the number of BD occasions and costs for gaining QALYs. Using subject survival and HRQoL – and therefore QALYs – as measures of the impact of the intervention allows comparisons to be made in different areas of health care and between different interventions or programmes (Whitehead & Ali, 2010). This measure has been developed to inform decision-making on health resources (Whitehead & Ali, 2010). Hence, the economic evaluation carried out as part of this thesis makes a contribution that, to our knowledge, had not previously been made to the existing literature, adding evidence on interventions aimed at preventing and reducing this public health problem in Spain.

These findings should be of interest to political and legal decision-makers, since they could be used as a preliminary step for the development and implementation of new policies on alcohol consumption and the adoption of preventive programmes to reduce alcohol consumption, in particular binge drinking, which is a current public health concern.

Additionally, considering the effect size of the intervention evaluated in this thesis, it seems that all the efforts being made in different areas (education, health, government) are not sufficient, as indicated in the previous section. Greater effort is needed in this area at the policy level. In 2018, the Spanish Society of Epidemiology produced a report putting forward 11 measures that were considered priorities for inclusion in the Spanish law on alcohol and minors. These measures included: prohibiting alcohol advertisements on street furniture or in shop windows visible from the outside; reducing the affordability (through increased rates and minimum prices) and availability of alcohol and prohibiting advertising, promotion, and sponsorship of alcoholic beverages at any sports, cultural, or leisure activity at which minors might be present; and prohibiting sales of alcohol at reduced prices (happy hours), which promotes binge drinking (Sociedad Española de Epidemiología, 2018).

This thesis has also helped to highlight the fact that this pattern of alcohol consumption is more prevalent in certain population subgroups, such as adolescents, which results in numerous health, social, and economic repercussions. This finding may help decision-makers to design public health policies for this population subgroup.

Dissemination and communication

Four scientific articles were produced as part of this thesis, in addition to a number of presentations made at national and international conferences in the fields of health economics, prevention research, and child and adolescent psychology. These presentations are listed below:

- "Gaps in the literature about the socioeconomic determinants of alcohol consumption in adolescents". EUSPR (European Society For Prevention Research), Eighth Conference and Members' Meeting. Vienna, Austria, 20-22 September 2017.

  EUSPR promotes the development of prevention science, and its application to practice so as to promote human health and well-being through high-quality research, evidence-based interventions, policies, and practices.
- "Sociodemographic variables associated with binge drinking in adolescence: *Alerta Alcohol*". XXXVIII Jornadas de Economía de la Salud, Asociación de Economía de la Salud (AES), "Compartiendo decisiones: ¿Qué cambios se requieren?". Las Palmas de Gran Canaria, Spain, 20-22 June 2018.

  AES seeks to promote and disseminate health economics studies by facilitating training for experts, exchanges between professionals, and the comparison of studies and research.
- "Effectiveness of binge drinking reduction of *Alerta Alcohol* programme in quality of life of adolescents in Spain", EuHEA (European Health Economics Association. Twelfth European Conference on Health Economics. Maastricht, Netherlands, 11-14 July 2018.

  The purpose of EuHEA is to promote cooperation among national health economics associations and groups in Europe, as well as to foster the study of health economics at European universities.
- "Binge drinking and health-related quality of life in adolescence: Alerta Alcohol". Fourth International Congress of Clinical and Health Psychology on Children and Adolescents. Palma de Mallorca, Spain, 15-17 November 2018.

  These congresses are organized by the AITANA Research Group, which is part of the Miguel Hernández University in Elche, Spain. The AITANA Group promotes the dissemination of the latest advances in the field of child and adolescent psychology. The International Congress of Clinical and Health Psychology on Children and Adolescents brings together researchers, professionals, and students interested in the fields of clinical psychology and health in childhood and adolescence.
- "Cost-effectiveness and cost-utility analysis of a web-based computer-tailored programme for prevention of binge drinking among Spanish adolescents". Sixth EuHEA

PhD Student-Supervisor and Early Career Researcher Conference, European Health Economics Association (EuHEA). Porto, Portugal, 4-6 September 2019.

- "Coste-efectividad y coste-utilidad de una intervención a medida basada en la web diseñada para prevenir el consumo episódico excesivo de alcohol en adolescentes españoles" (Cost-effectiveness and cost-utility of a computer-tailored web-based intervention designed to prevent heavy episodic drinking among Spanish adolescents), Fifth International Congress of Clinical and Health Psychology on Children and Adolescents. Oviedo, Spain, 14-16 November 2019.

In addition, this thesis is part of the output from (a) the research project "Alerta Alcohol: design, validation and evaluation of the programme of selective prevention of alcohol abuse in adolescents: web-based computer-tailored intervention" (PI-0031-2014), financed by the Andalusian Public Foundation "Progress and Health" for the financing of research and innovation in the biomedical field and the health sciences in Andalusia for the year 2014 (Health Counselling); (b) the research project "Activos para la salud positiva en la adolescencia: intervención familiar basada en nuevas tecnologías- web para la prevención del consumo episódico excesivo de alcohol" (PI-0012-2017 CP-1), financed by the Andalusian Public Foundation "Progress and Health" for the financing of research and innovation in the biomedical field and the health sciences in Andalusia for the year 2017 (Health Counselling); and (c) the project: "Estilos de vida no saludables: herramientas para el análisis de políticas de salud" (Unhealthy lifestyles: tools for health policy analysis), Grant ECO2017–83771-C3–3-R, funded by the Spanish Ministry of Economy and Competitiveness (MINECO).

6.6. Research agenda

Future research could now be taken forward by (a) incorporating economic evaluation in public health programmes, and (b) improving the research agenda for the prevention of the alcohol use pattern known as binge drinking among adolescents. This research agenda could include studies aimed at improving the design of programmes through the inclusion of other resources based on technologies such as gamification, social media, and smartphone applications, whose effectiveness has been evaluated and demonstrated in the literature.

With regard to social media as part of the daily social life of young people, Hendriks, Van den Putte, Gebhardt & Moreno (2018) studied the importance of the social aspects of alcohol consumption and social networks through an analysis of the social content of alcohol-related social media posts and the social processes related to such posts on social

network sites. The authors found an association between the social elements in the posts and the reactions of young people, noting that a greater number of social elements in the post led to more (positive) responses such as "likes" and comments. These authors suggest that future research should be aimed at reducing alcohol-related posts through interventions focused on the individual in a social networking context. One proposal would be to increase people's awareness of the unintended negative consequences of posts about social gatherings where alcohol is visible and to motivate them not to allow tags in such posts and to encourage others not to post alcohol-related content (Hendriks et al., 2018).

Champion et al. (2019) did not identify any interventions based on mobile technology (mHealth), a finding that the authors attribute to the fact that school policies prohibit the use of mobile phones in the classroom, among other causes. Nevertheless, the use of mobile technology-based interventions is mentioned in the literature as a particularly appropriate way to address the limitations of traditional interventions (Fowler, Holt & Joshi, 2016). Other authors have pointed out the benefits of using this technology in interventions aimed at changing alcohol consumption behaviour. Recently, for example, Hides et al. (2018) assessed the efficacy of an app called Ray's Night Out and found that it showed an increase in alcohol-related knowledge, which is very important given the positive correlation of such knowledge with drinking behaviour in adolescents (Thadani, Huchting & LaBrie, 2009). According to Anderson and Jiang (2018), 95% of US adolescents own a smartphone, and 85% of the population worldwide owns one (Pew Research Center, 2012). In Spain, according to the National Institute of Statistics (INE), almost 70% of young people aged 10 to 15 years have a mobile phone, and the percentage rises as age increases, reaching 94.8% among 15-year-olds. The INE report, published in 2019, notes that smartphones are the main means of connecting to the Internet (INE, 2019). All of this suggests that the potential of mHealth apps is not being sufficiently harnessed to complement web-based programmes for adolescents.

Among the advantages of mHealth are the ability to deliver messages with high fidelity, in a precise and consistent manner, through automated systems that also allow the adaptation of messages based on the needs and individual responses of adolescents (Suffoletto, Callaway, Kristan, Kraemer & Clark, 2012; Weitzel, Bernhardt, Usdan, Mays & Glanz, 2007); the anonymity that these interventions provide, given the stigma surrounding addictions (Savic, Best, Rodda & Lubman, 2013; Heron & Smyth, 2010); and the ability to send messages to large numbers of people at low cost (Arbanowski et al., 2004; Gibbons, 2007;

SAMHSA, 2015). Furthermore, downloading mobile applications is considered an easy task (Free et al., 2013), and a decrease in the cost of mobile phones has been observed in recent years (Ben-Zeev et al., 2014). In addition, it should be noted that mobile technology is widely accessible, both for individuals seeking treatment and for those who do not (Fowler et al., 2016). Finally, a major public health agency, the US Centers for Disease Control and Prevention (CDC), has endorsed the use of mobile-based interventions to prevent substance use through evidence-based approaches (Mason, Ola, Zaharakis & Zhang, 2014). Therefore, this type of intervention should be designed and evaluated.

Another matter to address in the research agenda would be the inclusion of family members and teachers in the implementation of interventions to prevent BD among adolescents. Gilligan et al. (2019), in a recent systematic review carried out on the effectiveness of family-based programmes to prevent alcohol consumption or drinking problems in school-age children (up to 18 years of age), suggest that these programmes alone are not effective in reducing alcohol consumption among adolescents. These authors emphasize that the frequency and volume of alcohol consumption should be considered in prevention programmes, taking into account the characteristics of the target group in order to ensure that the intensity of the programme is appropriate to the group's age and level of risk. This review identified a small number of studies on the different types of family-based interventions (universal, selective, and indicated) and concluded that there is a need to measure the impact of the intensity and context of the programme as well as its differential effects on the key outcome.

After the proposed improvements to reduce the dropout rate and increase adherence to the intervention have been introduced, a long-term assessment of this intervention should be conducted to determine to what extent its effects were maintained, and then the intervention should be re-evaluated. The importance of long-term assessment of web-based prevention interventions aimed at behaviour change has been recognized by several authors (Kohl, Crutzen & de Vries, 2013). According to Glasgow, Vogt, and Boles (1999), the factors that contribute to the public health impact of an intervention are reach, effectiveness, adoption, implementation, and maintenance. Other studies found in the literature indicate that effect size decreases with over the course of the intervention and after the intervention ends and that the changes in behaviour are not maintained over time because the initial effect sizes were quite small (Maon, Edirippulige, Ware & Batch, 2012; Vandelanotte, Spathonis, Eakin & Owen, 2007; Tait & Christensen, 2010).

This research agenda should also include studies to evaluate the cost-effectiveness of interventions to reduce the alcohol consumption among adolescents incorporated in the NHS Public Health Strategy. The interest in such studies is evidenced by the progress observed in the last decade regarding the incorporation of health economics in the evaluation of public health interventions. This is also reflected in guidelines developed by NICE in the United Kingdom, "Methods for the Development of NICE Public Health Guidance" (NICE, 2012) and those prepared by the Centers for Disease Control and Prevention (CDC) in the United States (Messonnier, 2006; Honeycutt et al., 2006).

As described in Chapter 1 of this thesis, public health interventions have particular characteristics, and as Forster and Pertile (2013) point out, it would be interesting to evaluate, given the long-term results of this type of intervention, whether in some situations it would be advisable to stop an evaluation before the predetermined time in the research project because the evidence that has been gathered up to that point is considered conclusive. This would reduce costs in the research process. At the same time, it would be interesting to investigate how to reduce uncertainty regarding the estimation of the efficiency of an intervention in reducing the probability of making the wrong decision.

Personally, in my agenda as an early career researcher, I would like to see these types of interventions incorporated into the public health system. I would also like to continue conducting research, through economic evaluations, on the efficiency of public health interventions related to alcohol and other issues. As a nurse practitioner working in the area of family and community nursing, I have personally seen the need for these types of evaluations so that research in this area can be translated into health practice and policy.

Chapter 7

Conclusions

7. Concluding remarks

This thesis contributes to the existing knowledge in a variety of ways. Before mentioning these contributions, it is important to remark that this thesis has described promising indications of the effectiveness and efficiency of the *Alerta Alcohol* programme for the reduction of binge drinking in adolescence. However, given the high dropout rate, the results should be interpreted with caution. It would be advisable to apply the proposed improvements outlined in this thesis and re-evaluate the intervention after the changes have been incorporated, considering the importance of evaluating its long-term effects.

Firstly, recalling the objectives proposed in this thesis, it can be concluded that there are significant gaps in the information about social and health-related harms associated with binge drinking among adolescents in Spain, especially in regard to estimation of the mortality and morbidity burden, the prevalence of alcohol use disorders, the social costs of consumption, and the efficiency of preventive interventions or programmes. Therefore, it seems important to assess the economic burden of BD and carry out economic evaluations of interventions aimed at preventing BD.

Secondly, the findings of this study in relation to social, family, and economic factors associated with BD in adolescence could complement existing prevention policies by emphasizing the importance of reducing weekly pocket money, or economic availability of alcohol to adolescents, and including families in the implementation of interventions aimed at preventing this pattern of consumption.

Thirdly, the analyses carried out took into account adherence as measured by partial or full attendance at the six sessions of the intervention. Higher adherence to this type of web-based computer-tailored (WBCT) intervention to prevent BD among adolescents, meaning that the adolescents attend more sessions, could have a positive effect in terms of both decreasing the number of BD occasions among adolescents and increasing participants' HRQoL, although this second effect was found to be very small in our study, due to the short follow-up period. This finding suggests improvements that need to be considered in order to capture greater changes both in reduction of the number of BD occasions and in enhanced HRQoL and greater savings in healthcare costs due to a behavioural change intervention, in particular through long-term follow-up of the intervention participants. Currently, long-term assessments of this type of intervention are scarce, but such

assessments are needed to inform policymakers and guide the allocation of healthcare resources.

Fourthly, this type of intervention based on computer-tailored feedback is recommendable and should be considered for use in other countries to inform the design of public health policies targeting alcohol use among adolescents. This study provides the first economic evaluation in Spain to analyse the cost-effectiveness and cost-utility of a web-based computer-tailored programme aimed at preventing and reducing binge drinking among the adolescent population, and the findings could help to inform decision-making processes from both the national health system and societal perspectives. The analysis shows that the *Alerta Alcohol* programme could be a cost-effective tool for preventing binge drinking in terms of reducing the number of BD occasions and increasing QALYs among adolescents and, especially, among specific subgroups within this population.

Finally, this work has helped to lay the groundwork for a future research agenda aimed at improving the efficiency of public health interventions through economic evaluations of alcohol prevention interventions.

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APPENDICES

Appendix 1. Health-related Quality of Life instruments in children and adolescents.

In this appendix, other tools used to assess HRQL in children and adolescents are described other than EQ-5D, HUI and SF-6D which were described and detailed in the introduction of this thesis.

The Quality of Well-Being Scale (QWB) was developed as a measure of HRQoL in general population. It is a preference-based measure that combines functioning and symptoms to calculate a well-being index ranging from 0 (death) to 1 (full, symptom-free functioning). This tool can used to calculate QALYs, and although initially, was created to be administered for an interviewer, a self-reported version was developed (QWB-SA). This scale is comprised of 74 items: 58 symptoms including 19 chronic symptoms, 25 cute physical symptoms, and 14 mental health symptoms; 2 items to evaluate self-care; 3 items for mobility and 3 items for usual activity; and, finally, 8 items to evaluate physical activity. The use of this measurement tool has been low due to its length (Busija et al., 2011).

The sixteen-dimensional measure of HRQoL (16D) and the seventeen-dimensional measure of HRQoL (17D) are generic self-assessment measure of HRQoL which have demonstrated its use with children aged 12-15 and 8-11, respectively (Apajasalo et al., 1996a, Apajasalo et al., 1996b).

The AQoL-6D Adolescent (15-17 years old) is an adaptation of the existing AQoL-6D instrument, which is a measure of HRQoL designed initially for adults. This utility measure is composed of 6 dimensions ((independent living, mental health, coping, relationships, pain, and senses) and 20 items with four to six response levels, each representing increasing levels of severity. The AQoL utility score ranges from -0.04 (health state worse than death) to 0.00 (death) and 1.00 (full health) No Spanish version has been described in the literature (Hawthorne, Richardson and Osborne, 1999; Richardson, Peacock and Iezzi; 2004, Moodie, et al., 2010).

The original CHU9D is an English measure and is valid for children and adolescents aged 7-17 years old. Although it was originally designed for English speaking countries, it is already being extended to other countries (Chen and Ratcliffe, 2015; Ratcliffe et al., 2012;

Stevens & Ratcliffe, 2012). The CHU9D consisted of nine dimensions, including worried, sad, pain, tired, annoyed, schoolwork, sleep, daily routine and ability to join in activities. Within each dimension, there are five different levels indicating increasing levels of severity (Yang et al., 2018). This measure has been validated for use in older adolescent populations aged 11-17 years (Ratcliffe et al., 2011, Ratcliffe, Stevens, Flynn, Brazier & Sawyer, 2012, Stevens & Ratcliffe, 2012, Stevens, 2012).

The Adolescent Health Utility Measure (AHUM) describes key impacts of having a chronic condition from the perspective of children or adolescents. AHUM is comprised of six dimensions: self-care, pain, limitations in walking around (mobility), perception of ability to do strenuous activities, self-image and, perceptions about current health in relation to the past (Beusterien et al., 2012).

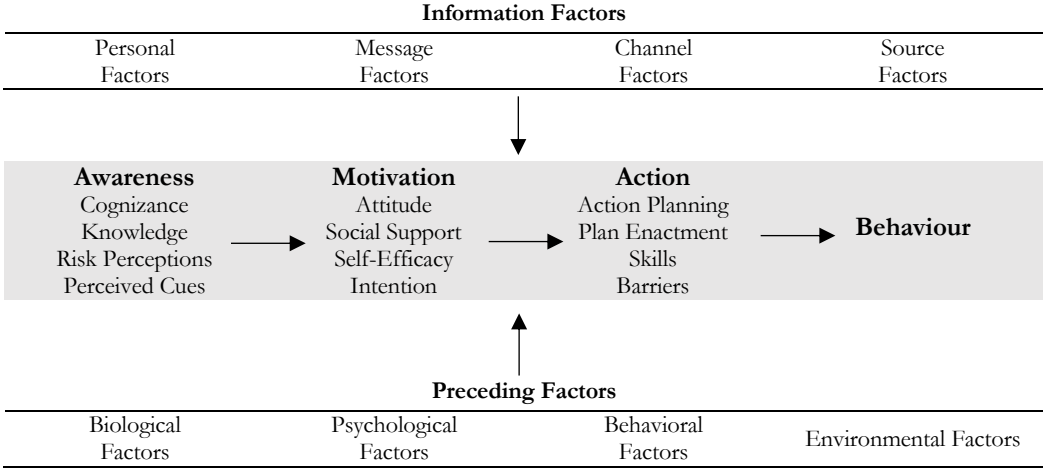
Appendix 2. *Alerta Alcohol* programme.

The *Alerta Alcohol* programme is based on *Alcohol Alert*, a Dutch web-based computer tailored intervention developed by Jander, Crutzen, Mercken, Candel & de Vries (2016). The description in detail of this programme carried out in this study is based on study protocol (Lima-Serrano et al., 2018).

This program consists of preventive and informative messages about the benefits of not consuming alcohol, reducing positive attitudes and encouraging negative attitudes towards alcohol consumption and binge drinking, as well as social influences and self-efficacy, with personalized feedback based on of the answers given to questions included in a questionnaire completed at the beginning of the intervention and during the sessions that make up this program. In addition, these messages are customized with the name and gender of the adolescent, since the latter chooses between different avatars that are offered when the adolescent registers on the programme´s website and creates an account to get access to the intervention. This avatar accompanies the student throughout the intervention in the different sessions. The intervention encourages skills and action plans aimed at rejecting binge drinking to help teens deal with this unhealthy behavior.

These questions and feedback are related to alcohol consumption and binge drinking and are based on the *I Change Model* and its relevant concepts (attitude, social influences, self-efficacy, and action planning) (Figure A1), an integrated model based on theories such as the Attitude-Social Influence-Self-efficacy Model (De Vries & Mudde, 1998), the Theory of Reasoned Action (Fishbein, 1980), the Theory of Planned Behavior (Ajzen, 1991), the Cognitive Social Theory (Bandura, 1986), the Health Believe Model (Janz & Becker, 1984), the precautionary adoption model (Weinstein, 1988) and the transtheoretical model (Prochaska, DiClemente, & Norcross, 1992). This model, which tries to explain the motivational and behavioral change of a person in the face of unhealthy behavior, has been used successfully in the design and evaluation of previous health interventions (Elfeddali, Bolman, Candel, Wiers & de Vries, 2012; Schulz et al., 2014; Stanczyk et al., 2014).

Figure A1. The I-Change Model



Source: taken from "An Integrated Approach for Understanding Health Behavior; The I-Change Model as an Example", by Hein d V., 2017, *Psychology and Behavioral Science International Journal*, 2(2),555-585. Doi: 10.19080/PBSIJ.2017.02.555585.

The Alerta Alcohol programme consists of short stories in which the main character wakes up after a night of heavy drinking and can't remember what happened. Then a friend calls him/her to tell him/her what happened. These stories take place in different settings: at home, at celebrations or parties, and in public places. After presenting the story, questions and messages are offered, using reinforcement strategies for certain positive behaviors and motivational feedback.

The intervention consists of six sessions in total, which could be summarized in (table A1): a baseline or pre-intervention questionnaire (session 1) followed by three scenarios (sessions 2 and 3), the challenge of not binge drinking and its assessment (sessions 4 and 5), and the follow-up or post-intervention questionnaire to evaluate the intervention. All participants must be able to access to a computer in their school's computer room.

In detail, session 1 is based on a baseline questionnaire including sociodemographic variables, alcohol use behaviours, other substances use, mediator variables such as motivational determinants (attitude, social influences, self-efficacy), and economic measures (health services use, non-health services use,…). This session is performed at schools in the presence of a member of the research team. In sessions 2 and 3, adolescents face different scenarios (at home, at celebrations, and in public places). In theses sessions, the knowledge and risk of alcohol consumption and binge drinking, as well as the degree of danger of binge drinking are addressed. In addition, social influences (friends, peers, relatives) are also treated

in these sessions, helping the adolescent to choose the social models considered most appropriate. The feedback focuses on increasing awareness of the negative aspects of binge drinking and reinforcing negative beliefs about it, thus working on the attitudes towards this behavior. Likewise, this feedback is based on the training of skills and action plans to manage self-efficacy and face social pressure. These sessions take place at schools. Session 4 takes place a week after the last scenario, and it is held at the adolescent's home. A challenge is proposed consisting of not consuming alcohol in excess in an upcoming event. Prior to the challenge proposal, participants receive an email inviting them to answer a question about their alcohol consumption during the previous week and subsequently receive comments on their behavior compared to what was answered in the basic questionnaire about their own alcohol consumption. Next, they are asked if they have an event in the next 30 days in which they could binge drink, and if yes, they are given the option to accept the challenge specifying the following: "I challenge you NOT to drink alcohol in this event, or at least, don't have four or more glasses if you're a girl or five glasses or more if you're a boy. " If they accept it, they must record the date of the event as well as where it takes place (at home, celebration, public place) and you are invited to develop your own action plan. If they are not willing to develop their own action plan, they are provided with a list of plans that were suggested in the previous sessions. Two days before the event date, they are reminded by email of the acceptance of the challenge. Session 5 consists of evaluating the challenge, taking place on different dates depending on the date of the event recorded by the adolescent in the previous session. In this session, a brief questionnaire about the achievement of the stated objective is provided to fill in two days after the event. If the adolescent manages to overcome the challenge, they are congratulated by positively reinforcing their behavior. If, on the other hand, they did not meet the challenge, the reasons are explored and the adolescents are given information on what to do about it and you are encouraged for a new challenge. However, all adolescents are asked to repeat the challenge if they so choose. This session is completed at adolescent´s home such as session 4. Finally, session 6 consist of an assessment questionnaire, which takes place 4 months after the first session at schools, including the same measurement variables that baseline questionnaire.

Table A1. Structure and functioning of *Alerta Alcohol* programme.

- 6 sessions in total, of which 4 sessions were carried out in the high schools (the 4th y 5th sessions were carried out from the adolescent´s home). (January/February-May/June). The time interval between the first and last session is 4 months.
- Each session had a duration of 45 minutes y were performed in hours of tutoring, in computer rooms to be able to access the Internet.
- Session 1: the participants completed a baseline questionnaire on the *Alerta Alcohol* website. (January/February)
- Session: 2 and 3: the participants entered a story in which an adolescent played a character that wakes up after a night of binge drinking. Participants received in-story questions concerning alcohol-related sociocognitive factors, including attitude, social influences, self-efficacy expectations, and action plans toward alcohol drinking. Based on their answers, they received computer-tailored feedback on these determinants. The story takes three scenarios within two sessions. (March)
- Session 4: A week after the third scenario, the participants were asked if they had an event (e.g., party, wedding) in the upcoming 30 days then they were challenged to drink less than usual and asked for the maximum amount they wanted to drink. An email, with a reminder of accepting the challenge, was sent to them two days before the event.
- Session 5: Two days after the event, they were asked to visit the intervention website and fill in their alcohol use. If the participant failed the challenge, they received computer-tailored feedback with tailored advice and had the opportunity to take on a new challenge. If the participant met the challenge, he or she received congratulations and the intervention was over. (March/April)
- Session 6: the participants completed a follow-up questionnaire for evaluating the effectiveness of the intervention.
- Members of research team attended the first session of all the high schools and if was necessary also attended the rest of the sessions. In the session 1 they were given detailed information both spoken and written to guide them about the procedure to follow in the following sessions.
- Detailed information on the *Alerta Alcohol* intervention can be found on the website **http://institucionales.us.es/alertalcohol/**

Appendix 3. First page of published papers

letter to the editor adicciones vol. 30, nº 2 · 2018

Impact of Binge Drinking (BD) in Adolescence. Are we doing it right?

Impacto del consumo episódico excesivo de alcohol en la adolescencia. ¿Lo estamos haciendo bien?

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Dear Editor,

Excessive alcohol use and alcohol use disorders are major causes of death and disability worldwide (WHO, 2014). According to the World Health Organization, 10% of adolescent deaths (those aged 15 to 19 years) in the European Region were attributable to alcohol (Drost et al. 2016).

Nowadays, one of the most prevalent patterns of alcohol consumption is called binge drinking (BD). In 2015 it was estimated that about 35% of European adolescents of 15–16 years old have had at least one BD occasion in the past 30 days (The ESPAD Group, 2016). Moreover, in Spain, the series of surveys on the use of drugs in adolescents of secondary education, ESTUDES 2014-2015, stated that 32.2% have performed at least one BD occasion in the last month (National Plan on Drugs, 2016) whereas a recent study by Golpe, Gómez, Braña, Varela & Rial (2017) concluded that 33.1% of Spanish adolescents were doing intensive consumption last year and 20% last month (3 or more alcoholic drinks per sitting and drunkenness). Moreover, 19.8% of adolescents were doing a risk alcohol consumption without significant differences by gender. Romo-Avilés, Marcos-Marcos, Tarragona-Camacho, Gil-García & Marquina-Márquez (2016) found small differences between the amount of alcohol consumed or in "botellón" participation between boys and girls. This suggests that intensive alcohol consumption and BD have increased in girls.

In the European Union, alcohol-attributable costs were estimated at €125 billion in 2003. In Spain, the total social costs of alcohol consumption can be around 1% of gross domestic product (more than 10.000 million euros) (Pulido, Indave-Ruiz, Ruiz-García, Bartroli & Barrio, 2014).

We did not find any study regarding costs associated with BD and underage drinking in Europe but previous works have shown youthful drinkers are at greater risk of: being victimized and perpetrating youth violence; low educational attainment; and low college expectations, putting a financial burden on the criminal justice system and educational sector. (WHO, 2014).

Based on the evidence, BD is mainly related to acute effects in young people, such as acute intoxication, accidental and intentional injuries, road crashes, scholar problems due to lower cognitive performance and brain alterations as well as school absenteeism caused by the symptoms caused by the hangover after acute alcohol intoxication, unprotected and unplanned sex, consumption of other drugs, legal problems due to the reduction of cognitive and verbal ability to resolve conflicts and developing an alcohol use disorder in adulthood (Pulido et al., 2014, Windle & Windle, 2017). In a research carried out by Windle & Windle in 2017 found that diagnostic accuracy of adolescent alcohol problems in predicting alcohol dependence 7 years later was 74%. In Spain, the annual prevalence self-informed about acute alcohol intoxication was higher than 30% in population between 15 and 34 years

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RESEARCH ARTICLE Open Access

Social, economic and family factors associated with binge drinking in Spanish adolescents

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Abstract

Background: The main aim of this study was to determine the socioeconomic and family factors associated with binge drinking (BD) in Spanish adolescents who participated in a web-based computer intervention for the prevention of binge drinking known as *Alerta Alcohol*.

Methods: Longitudinal analyses were carried out in a sample of Andalusian adolescents aged 15 to 19 enrolled in public schools, which was part of a two-arm cluster randomized controlled trial with an intervention group (IG) who received the *Alerta Alcohol* programme and a control group (CG) who did not receive any active intervention. Panel count data and the following econometric procedures were used: negative binomial, a two-part model and a finite mixture model. The endogenous variable in all models was the number of BD occasions in the last 30 days. A total of 1247 subjects in the pre-intervention period, with an average age of 16.8 years, plus 612 adolescents in the follow-up period (4 months later), were included in the analysis.

Results: In relation to findings, being older (≥ 17 years old), having more pocket money and higher family alcohol consumption were associated with greater BD. By contrast, subjects who completed the questionnaire on Wednesday, Thursday or Friday, further from the previous weekend, indicated a lower number of BD occasions.

Conclusions: Our results suggest the need to include families, especially parents and siblings, in interventions aimed at preventing alcohol use among adolescents, given the association shown between BD and both family alcohol consumption and weekly pocket money or availability of money to adolescents. Given the findings with regard to age, future research aimed at intervening in early adolescence to prevent BD would be justified.

Trial registration: (ClinicalTrials.gov): NCT03288896. Registration date: September 20, 2017. "Retrospectively registered".

Keywords: Binge drinking, Adolescence, Socioeconomic factors, Intervention

Background

According the World Health Organization (WHO), alcohol was the seventh cause of disease and premature death among the world's population in 2016. Also, alcohol is the cause of more than 200 health conditions, in addition to diseases with a high mortality burden such as liver cirrhosis, cancer and cardiovascular diseases [1, 2]. In Europe, alcohol accounts for 10.1% of all deaths and 10.8% of all disability-adjusted life years (DALYs) [1, 2].

With regard to alcohol use in different life stages, it is known that alcohol abuse is a public health concern across all age groups. Nevertheless, it is important to highlight that alcohol is the most widely used substance

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Full length article

Measuring the effects on quality of life and alcohol consumption of a program to reduce binge drinking in Spanish adolescents

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ABSTRACT

Aim: To present a comparison between the effects on health due to a reduction in binge drinking (BD) and health-related quality of life (HRQoL), as a result of ALERTA ALCOHOL, an intervention aimed at reducing BD in Spanish adolescents.
Methods: A two-arm cluster randomized controlled trial was conducted with an intervention and a control group, randomized at the school level, following individuals over four months. The study population consisted of Andalusian adolescents aged 15 to 19 years who were enrolled in urban public high schools (n = 1247). Participants were assigned randomly to receive the intervention. The main outcomes studied were the number of occasions of BD in the last 30 days, which was directly obtained from the answers given by the adolescents, and HRQoL measured with the EQ-5D-5L questionnaire. The model of estimation was the generalized estimating equations (GEE) approach.
Results: The program showed a BD reduction at the 4-month follow-up, although it was not shown to significantly increase the HRQoL in adolescents who reduced the number of occasions of BD and had received the intervention. However, it was shown that those who would predictably reduce the number of occasions of BD controlled by several sociodemographic variables perceived a higher HRQoL, as did those who had a greater adherence to the program.
Conclusions: Higher adherence to a web-based computer-tailored intervention to prevent BD in adolescents has a positive effect on decreasing the number of occasions of BD in adolescents as well as on increasing participants' HRQoL, although this second effect is very small, which could be due to the short follow-up time. This fact is quite important and should be assessed extensively to corroborate the results and translate into health policy.

1. Introduction

According to the World Health Organization, in 2012, approximately 3.3 million deaths globally, 139 million DALYs (disability-adjusted life years), and 5% of the global burden of disease and injury were attributable to alcohol consumption (World Health Organization (WHO), 2014). Moreover, it is known that children, adolescents and elderly people are typically more vulnerable to the negative effects of excessive alcohol consumption than other age groups (Hilton, 1987; Mäkelä and Mustonen, 2000; Midanik and Clark, 1995). Among young people, this vulnerability is related to binge drinking (BD), when a great amount of alcohol is consumed during short periods of time, mainly on weekends (Anderson, 2014; Calafat Far, 2007; Cortés et al., 2007; US Surgeon General, 2007).

BD has become a concern for health policy makers. At the international level, in 2015, the European School Survey Project on Alcohol and Other Drugs (ESPAD) study investigated the drinking habits of 96,046 adolescents born in 1999 and found that every third student (35%) reported heavy episodic drinking in the past month. The term "heavy episodic drinking" is defined as drinking a minimum of five alcoholic beverages on one occasion at least once in the last 30 days and is therefore similar to BD. This study found high rates of alcohol use, particularly heavy alcohol use, although temporal trends over the past twenty years (between 1995 and 2015) indicated a positive

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Cost-Effectiveness and Cost-Utility Analysis of a Web-Based Computer-Tailored Programme For Prevention of Binge Drinking in Adolescents: ALERTA ALCOHOL Project

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