UNIVERSITÀ DEGLI STUDI DI PAVIA
CORSO DI DOTTORATO IN

PSICOLOGIA E SCIENZE STATISTICHE E SANITARIE
Psychology, Health and Statistical Sciences
Direttore: Chiar.mo Prof. Gabriella Bottini

The Digital–Alcohol Risk Alertness Notifying Network for Adolescents and Young Adults Project (D-ARIANNA):

Risk estimation model and impact of a mobile eHealth Intervention on Binge Drinking in Young People

Tutor: Professor Cristina Montomoli

PhD Candidate
Cristina Crocamo
Mat. Nr. 424325

A.A. 2015-2016 – XXIX ciclo

INDEX

ABSTRACT

Background. The Digital–Alcohol Risk Alertness Notifying Network for Adolescents and Young Adults Project (D-ARIANNA) addresses a topic of growing interest in the field of substance abuse among adolescents and young adults, i.e., risk estimation models for binge drinking (BD) using eHealth apps. According to relevant research, this study novelty value may bring an important contribution to the substance abuse community. BD is common among young people, but often risk is not recognized. eHealth apps, attractive for young people, may be useful to enhance awareness of this problem. We aimed to develop a risk estimation model for BD, incorporated into an eHealth app, D-ARIANNA, for young people.

Methods. A longitudinal approach with phase 1 (risk estimation), phase 2 (design), phase 3 (feasibility study) was followed. Ten risk and two protective factors identified from the literature were used to develop a current risk estimation model for BD. Relevant odds ratios were pooled through meta-analytic techniques, deriving weighted estimates to be introduced in a final model. The model, nested in an eHealth app interview, provided in percent an overall risk score, accompanied by appropriate images and a summary message with factors that mostly contributed. The D-ARIANNA questionnaire, matching identified risk factors, was assessed for wording, content and acceptability. Feasibility study was a quasi-experimental, pre-/post-test study. Subjects were recruited in pubs, discos, or live music events in Milan urban locations. They were requested to self-administer D-ARIANNA and were re-evaluated after 2 further weeks.

Feasibility Study Results. Young (18–24 years) people (N = 590) reported reduced two-week BD (18% vs. 37% at baseline). Most of subjects considered D-ARIANNA helpful. To exclude systematic errors involving those lost at follow-up (14%), the diminution in BD was also evaluated through an appropriate generalized estimating equation model.

Conclusions. D-ARIANNA is the first evidence-based eHealth app for BD in young people, cited in the European Monitoring Centre for Drugs and Drug Addiction (http://www.emcdda.europa.eu/html.cfm/index98829EN.html) and the NHS health apps libraries (http://apps.nhs.uk/apps/alcohol/). Although a more advanced study is pending by through of an adequately powered trial, the promising results point to the potential of a smartphone tool for preventing relapse in BD and its application in real word practice, thus enabling further studies. D-ARIANNA, focused on personal communication and BD risk awareness, influences responsible drinking, and could be tested in an environmental-based community intervention.

INTRODUCTION

Binge drinking: definition and prevalence

Binge drinking (BD) can be described as heavy alcohol use over a short period of time, and it is typically defined by a consumption of four or five drinks in a row among women and men, respectively (*Wechsler et al., 1995*). BD is problematic and dangerous, resulting not only in acute impairment, but also over half of the annual 80,000 deaths caused by excessive alcohol consumption are attributable to BD (*WHO, 2011*). In the U.S. this dangerous pattern of alcohol consumption is considered a public health concern (*Naimi et al., 2003*), as more than 15% of young people aged between 18 and 24 years are engaged in BD, with a male/female ratio of 3:1 (*CDC, 2011*), and in the high risk group with hazardous alcohol use young adults age range contributes for 40% (*SAMHSA, 2012*). In addition, data from the 2001 National Household Survey on Drug Abuse on 19-21 years U.S. adults, highlighted a weekly BD prevalence of 12% and 27% among females and males, respectively (*Slutske, 2005*).

At the same time, relevant research showed an increase of BD among young people also across Europe (*Plant et al., 2009*; *Kuntsche et al., 2007*; *Farke and Anderson, 2007*). For instance, the European School Survey Project on Alcohol and Other Drugs (ESPAD), gathering information on substance abuse among students in 35 European countries, showed that in France, UK, Finland, Denmark, and Belgium, 45% of males and 36% of females aged between 15 and 16 years consumed five or more drinks on a single occasion during the last 30 days (*Hibell et al., 2009*). In addition, a six European countries (Germany, Iceland, Italy, Netherlands, Poland, and Scotland) cross-sectional survey on 16,551 students from 114 public schools showed that 27% of the sample had consumed >5 drinks in a row on at least one occasion in their life (*Hanewinkel et al., 2012*). Also in culturally distinct Southern Europe countries like Spain, with possibly healthier drinking cultures, more than 15% of young adults experienced BD at least once in the past month (*Soler-Vila et al., 2013*).

Binge drinking and young people

High persisting rates of frequent, intense alcohol use or BD might lead to alcohol dependence in young adults (*Bonomo et al., 2004*). Furthermore, adolescents and young adults who engage in BD are more likely to report other health risk behaviours, such as

riding with a driver who had been drinking, smoking cigarettes, being a victim of violence, attempting suicide or using illicit drugs (*Miller et al., 2007*; *Jones et al., 2001*; *Siliquini et al., 2012*; *Martinotti et al., 2011*; *Haberstick et al., 2014*). The impact of BD among young people has been also associated with an increased risk of social and clinical consequences in the adulthood, such as psychiatric morbidity, homelessness, convictions, lack of qualifications, and accidents (*Martinotti et al., 2009*; *Viner and Taylor, 2007*).

Common reasons for alcohol drinking during adolescence and early adulthood are related to expected benefits with anticipated consequences perceived as personally desirable, and include pleasure, habit, social/recreational increasing confidence, anxiety or stress, coping with negative affect reasons and social pressures (*Patrick et al.,2011*; *Newbury-Birch et al., 2000*). Also, comorbid mental disorders might play a role in alcohol misusing risk (*Carrà et al., 2012*).

Decision making

On the other hand, BD is associated with long-term changes in cognitive processes, which may explain the loss of control over excessive alcohol consumption. These modifications include increased subjective craving for alcohol, positive and arousing outcome expectancies and implicit associations for alcohol use, increased action tendencies to approach alcohol, impulsive decision-making, and impaired inhibitory control over drives and behaviour (*Field et al., 2008*). In particular, expected benefits have a key role for decision-making impaired mechanisms, involving individuals' tendencies to prefer an immediate to a delayed reward, even when this is associated with significant negative consequences (*Goudriaan et al, 2007*).

Impaired decision-making is actually a common issue for substance users, who show little regard for consequences, and often deny or are unaware that they have a problem (*Bechara, 2003*). This seems even more true for college students who binge drink, though they are more likely to report adverse consequences of drinking (e.g., missing classes, spending less time studying, experiencing unplanned and/or unsafe sex, becoming injured, and getting into legal trouble) (*Figlock, 2010*). Since compromised decision-making mechanisms make people unable to consider the negative consequences of their misuse and to learn from previous mistakes, its role in substance use has been acknowledged (*Bechara, 2003*). In particular, recent studies showed that BD among college students is predictive of disadvantageous decision-making, though

this should be nearly or fully developed in young people (*Goudriaan et al., 2007*). Indeed, young people's knowledge and awareness of BD consequences are often low (*De Visser and Birch, 2012*), and perception in terms of risky behaviour is scant (*SAMHSA, 2013*). In addition, even if they might be able to anticipate BD consequences, they often don't care or consider consequences not relevant to themselves (*Goudriaan et al., 2007*).

Moreover, young people behaviour is connected to peers and friendships actions. A relevant research on college friendships (*Borsari and Carey, 2006*) provides evidence for quality of peer relationships influence on alcohol use in young people. In particular, stability, intimacy and support appear to be key components of this connection. Young people behaviours are strictly related to a combination of these three components, involving young people number of social interactions, long-term, rather than quickly, friendships, feeling interpersonally close with friends and decreasing loneliness, and the extent to which the individual is accepted, including self-confidence and sociability (*Borsari and Carey, 2006*).

Strategies dealing with decision-making in young people

In order to find common strategies to approach young people and their decision-making, new eHealth platforms have recently designed and implemented, based on social media and multimedia networks (*Norman and Yip, 2012*). eHealth tools, engaging young people across diverse contexts, appear able to support behavioural changes.

Indeed, eHealth technology encompasses a wide range of delivery formats (e.g., computer-based, smartphones, tablets), types of intervention (e.g., brief interventions, behavioural therapy, treatment adherence tools), and have been used across various substances of abuse (e.g., opioid, cocaine, alcohol, cannabis, etc.) (*Kiluk and Carroll, 2013*), for an array of populations (adults, adolescents and young adults, criminal justice populations, postpartum women), and in a number of different settings (addiction specialty treatment programs, schools, emergency rooms, criminal justice settings) (*Marsch et al., 2014*). Nowadays 90% of individuals worldwide have access to mobile phone services, including vulnerable populations, such as people with substance use disorders (*McClure et al., 2013*). Accessibility and availability across settings, enhanced patient-clinician communication, conveyance of information in an engaging manner, individualization and tailoring of intervention, all are eHealth advantages appropriate

for people with addiction problems (*Olmstead et al., 2010*). As nearly 90% of individuals with a drug or alcohol problem does not access treatment (*SAMHSA, 2012*), technology-based interventions may allow improved perceived privacy and anonymity, coping with stigmatization or embarrassment about drug use, and increasing the number of people receiving treatment for illicit recreational drug use (*Wood et al., 2014*). In particular, relevant trials have been conducted for mobile phone text message interventions with participants receiving feedbacks tailored to their individual responses (*Suffoletto et al., 2013*). As a whole, eHealth tools for prevention programs have shown encouraging results as regards identification of BD, alcohol use reduction and behavioural support among young people (*Fraeyman et al., 2012*; *Kypri et al., 2009a*).

On the other hand, traditional preventive interventions on BD have shown poor effectiveness among young people (*Ferri et al., 2013*), and possibly, impaired decision-making in young people who binge drink makes this attempt even more difficult. eHealth tools might instead address these difficulties, taking advantage of young people propensity to, and expertise with, electronic devices. However, studies on BD characteristics and correlates conducted in Southern Europe are sparse (*Digrande et al., 2000; D'Alessio et al., 2006; Laghi et al., 2012; Soler-Vila et al., 2013*), though relatively healthier drinking culture might moderate magnitude and consequences of excessive alcohol intake among young people (*Mäkelä et al., 2006*). Furthermore, there is a lack of research exploring prevalence and correlates of BD in natural settings, whereas most of studies were specifically conducted among high school (*Miller et al., 2007; Laghi et al., 2012*) or college/university students (*Wechsler et al., 1995; Digrande et al., 2000; D'Alessio et al., 2006*).

AIMS

The primary aim of this study was to develop an evidence-based current risk estimation model for binge drinking, to be incorporated into an eHealth app for adolescents and young adults. This innovative approach could be useful in designing prevention strategies for BD in young people and includes on phase 1 risk estimation, phase 2 design, and phase 3 feasibility of the D-ARIANNA study.

Secondly, we explored BD correlates in a representative sample of not abstemious young adults recruited in areas of the Milan nightlife scene, evaluating the impact of D-ARIANNA eHealth app.

MATERIALS AND METHODS

Evidence-based risk estimation model

Scientific literature search

Search Strategy

First, we aimed at exploring scientific literature in order to investigate studies on BD among young people. Thus, we conducted a systematic review of the scientific literature in order to identify risk and protective factors of BD and their relative effect, enabling the implementation of the risk prediction model. We used PubMed electronic database for search purposes in order to identify relevant studies published up to May 2013. No time limits, neither language restrictions, were applied. Search phrases combined index and free-text search terms, i.e., "Binge Drinking" and "Risk Factors". We also used Medline's Medical Subject Headings terms (MeSH) to avoid too general and broad concepts. Results were filtered to include only articles on adolescents (13-18 years) and young adults (18-24 years). Furthermore, we hand-searched reference lists of relevant systematic or narrative reviews on BD among young adults or adolescents.

Eligibility

We included any observational study based on a cross-sectional, case-control or prospective design with the following characteristics: (1) estimates of BD proportion; (2) analysis of variables potentially associated with BD; (3) samples of young adults or adolescents. If we found the same data published in multiple works, we retained only the study with more complete information to avoid duplicate results. We included only studies published on peer reviewed journals and dissertations, excluding conference abstracts.

Data collection process

We made a preliminary screening based on titles and abstracts. Papers were then retrieved in full text to test the final eligibility according to inclusion criteria. According to standard procedures, the eligibility assessment was performed by two researchers independently. Discordance on the inclusion or the exclusion of articles was analysed, and disagreements resolved by consensus.

We built a data extraction template, including for all the eligible studies key items based on year of publication, country, recruited population, sample size, methods to assess risk factors and BD, and main results.

Identifying risk factors for binge drinking and deriving estimates

Review of the scientific literature addressed the identification of BD risk and protective factors, enabling the implementation of the risk prediction model. Furthermore, as National young binge drinkers may have different drinking cultures, as compared with their U.S. and Northern Europe peers, we also explored correlates of BD from the National Institute of Statistics databases.

We aimed at identifying several factors associated with BD, with a coverage on socio-demographic, clinical, individual, and lifestyle characteristics, as well as substance-related behaviours. Since different results for the same risk/protective factor might be retrieved from several published studies, evidence regarding identified risk factors, in terms of strength of association, was collapsed into single estimates for each risk/protective factor. Relevant odds ratios were pooled through meta-analytic techniques with a random-effects model, deriving for each risk/protective factor weighted estimates to be introduced in a final model. Moreover, where raw data were available, binge drinkers were considered as cases, and subjects who were not engaged in BD as controls. Data on potential risk factors for BD were collected for both cases and controls. We considered for meta-analyses only risk/protective factors for BD with data available at least from two different studies. Only clinically relevant factors with sufficient evidence for the association with the outcome BD were included in the final model.

Risk estimation model for binge drinking

The equation model and the risk score

Risk estimation models have been used to investigate an outcome of interest determined by multiple interacting risk/protective factors, balancing their relative contributions, to enhance individual's decision-making abilities (*D'Agostino et al., 2001*). Since several variables may influence BD risk, there is the need to develop a model which can take into account multiple components, cumulative and, sometimes, synergistic effects,

providing a more tailored approach with a set of identified factors. Similarly to other biomedical fields (e.g., cardiovascular diseases), factors related with an increased risk of developing an unhealthy behaviour such as BD can be modelled. Although the use of only factors that are potentially modifiable might appear reasonable, including in a model all those that improve risk estimation could encourage individuals at high risk to change remaining risk factors. Furthermore, factors included in estimation models need to be weighted, according to their prevalence in relevant populations, to obtain risk-estimation functions. In the cardiovascular field, for example, the most common approach is based on proportional hazards model, either Cox (semiparametric) or Weibull (parametric), accounting for variable follow-up times and losses to follow-up (*Cooney et al., 2010*). However, logistic regression is also used for risk estimation functions, translating coefficients into more intuitive clinical interpretations.

Estimation models have been shown to effectively reduce risk factors levels for cardiovascular diseases (e.g., *Cooney et al., 2010*), and logistic regressions have been used in models dealing also with different outcomes, e.g., breast cancer (*Ayer et al., 2010*), postoperative complications (*Toner et al., 1996*), and stroke (*Aviv et al., 2009*). Model performance is assessed in terms of several domains: discrimination (maximum achievable sensitivity and specificity); calibration (measuring how closely predicted outcomes agree with actual ones in an external dataset); ability to detect implicit interactions among different risk factors; generation of confidence intervals, and ease of clinical interpretation (*Cooney et al., 2010*). In sum, logistic regression may represent a powerful statistical method of modelling a binary outcome through the combination of predictor variables. In the regression model each regression coefficient provides a description of the size of the contribution of the corresponding predictor variable to the outcome. Therefore, combining relevant predictor variables leads to a regression equation and allows calculating the expected probability that outcome is "presence of condition of interest" for a given combination of predictors, through a composite function that reflects the relationship between the predictor variables and presence of condition of interest. Thus, a logistic regression estimation model, comprehensively including relevant associated risk and protective factors, and nested in an appropriately drafted questionnaire, is adequate to predict BD risk. Developed regression equation can then be translated into a predicted probability value for a given combination of predictors (scenario). Each scenario shows therefore a percentage for current risk estimate (overall risk score).

The following formulas in Equations (1) and (2) were used for the predictive model in order to build a risk score for binge drinking current risk.

$$\log odds = \beta_0 + \beta_1 x_1 + ... + \beta_n x_n \tag{1}$$

$$risk\ score = \frac{1}{1+e^{-\log odds}} * 100 \tag{2}$$

Model Design

Results on identified risk/protective factors

The vast majority of samples of included studies, ranging from 76 to 44,610 individuals, were made of school, college and university students from Anglo-Saxon countries. We identified different risk/protective factors of BD that might be included in a risk estimation model. These factors were grouped according to the following categories.

a) *Socio-demographic characteristics*. Standard socio-demographic information regarding age, gender, country of birth, educational and employment status, living condition, was included along with school proficiency (*Miller et al., 2007*) and more behaviour-specific correlates, such as relationships (*Jasinski and Ford, 2007; Borsari and Carey, 2006*), and young people financial availability (*Bellis et al., 2007*).

b) *Clinical and individual characteristics.* As there is a strong association between substance-related behaviours and mental disorders (*Carrà and Johnson, 2009; Carrà et al., 2006; Carrà et al., 2014*), particularly between BD and depression (*Paljärvi et al., 2009*), we took into account presence of depressive and anxiety symptoms. Furthermore, impulsivity, as measured by the Substance Use Risk Profile scale (SURPs) (*Woicik et al., 2009*), was also found likely associated with the risk of BD among young adults, being related to alcohol abuse and physiological dependence symptoms (*Balodis et al. 2009; Townshend et al., 2014*).

c) *Lifestyle characteristics*. Previous studies found that several lifestyle habits could influence BD behaviour. First, the interest for joining events and attending recreational settings where it may be easier engaging in BD, such as night parties or discos might influence young people alcohol consumption (*Gallimberti et al., 2011; Wechsler et al., 1995*). Second, participation to sport activities involving violent social identity and antisocial norms might affect alcohol use (*Sønderlund et al., 2014).* The same link could be found for videogame use (*Sanchez et al., 2011*). In addition, an association was found also between risky behaviour and young people religious participation and volunteering activities (*Weitzman and Chen, 2005*). Religion might directly reduce risky behaviours through moral guidance and strong social networks that reinforce social norms (*Mellor and Freeborn, 2011; Gruber, 2005*).

d) *Substance and alcohol-related behaviours*. Other substance-related behaviours, such as smoking nicotine cigarettes and/or cannabis, were found potentially associated with BD (*Siliquini et al., 2012; Reed et al. 2007*). This aspect included also electronic cigarettes (e-cigarettes) growing phenomenon (*Sutfin et al., 2013; Choi et al., 2014*). Moreover, role of decision-making mechanisms for alcohol consumption is emphasised when choices in real life situations and environments condition young people alcohol expectancies and drinking behaviours. This leads to the definition of alcohol environments, such as live music events, alcohol outlets where young people meet up, but also influence of peers and family drinking habits. Thus, since young people daily life is highly linked to peers and friendships (*Borsari and Carey, 2006*), we considered as important factors from previous evidence peers' alcohol consumption and positive alcohol expectancies, as estimated by the Alcohol Expectancies Questionnaire (AEQ-AB) seven-item Likert scale exploring related domains (global positive changes, changes in social behaviour, improved cognitive and motor abilities, sexual enhancement, cognitive and motor impairment, increased arousal, and relaxation and tension reduction) (*Weitzman et al., 2003; Townshend et al., 2014; Stein et al., 2007*).

Final model

We selected factors based on several features, i.e., the strength of association with BD, consistency among the definitions of the independent variable provided by different studies, and sensitive nature of the topic. Modifiable nature of risk factors was also

considered. Unfortunately, several different risk factors, originally identified from the literature review, were not included. Indeed, we deliberately excluded from the model those that could look inappropriate in terms of sensitiveness, specifically according to the local cultural background and therefore with potentially biased answers and missing values, i.e., sexual orientation (*Jasinski and Ford, 2007*), history of sexual abuse (*Mouilso et al., 2012*), flat-share (*Kypri et al., 2009b*), single-parent family (*Fisher et al., 2007*), having a religion (*Sanchez et al., 2011*). Factors with paucity of data, including videogames, financial availability in terms of pocket money, ethnicity, and drunk-driving (*Sanchez et al., 2011; Bellis et al., 2007; Elton-Marshall et al., 2011; Tin et al., 2008*), were also excluded, as well as those without specific measures appropriate to be nested in an easy-to-use eHealth app (i.e., alcohol expectancies, anxiety and depression) (*Eaton et al., 2004; Oei and Morawska, 2004; Mitchell and Coyne, 2007*), though comorbid mental disorders might play an important role (*Carrà and Johnson, 2009; Carrà et al., 2012; Bartoli et al., 2014; Carrà et al., 2014*). Other factors were omitted for other different reasons, such as equivocal findings, i.e., socio-economic status (*Sanchez et al., 2011*), wide range of legal drinking ages in different countries, i.e., ease of alcohol availability (*Weitzman and Chen, 2005*), heterogeneity of risk factor definitions, i.e., playing sports and media influence (*Tao et al., 2007; Hanewinkel et al., 2012*), overlapping/correlation, e.g., impulsivity and engage in physical fighting (*Swahn et al., 2004*). Therefore, given appropriateness of retrieved data and quality of evidence, ten risk (five modifiable), and two protective factors showed relevant associations with BD in young people and were included into the model. Thus, we developed a risk estimation logistic regression model using the following factors, ranked in order of estimates magnitude: past 30 days cannabis use, interest for clubs and parties, smoking cigarettes, gender, past two weeks excessive alcohol consumption, drinking onset at age 17 or younger, peers influence, parental alcohol misuse, age, impulsivity as measured by SURPSs (*Woicik et al., 2009*). In addition, two protective factors were identified and included in the model, i.e., volunteering, and school proficiency (*Miller et al., 2007*). Main factors and relevant studies are shown in Table 1.

Regression equation needed then to be translated back into a predicted probability value for a given combination of predictors. Thus, each possible combination of predictors has an expected probability calculated from regression equation.

Table 1. Factors contributing to risk estimation model. Characteristics of included studies.

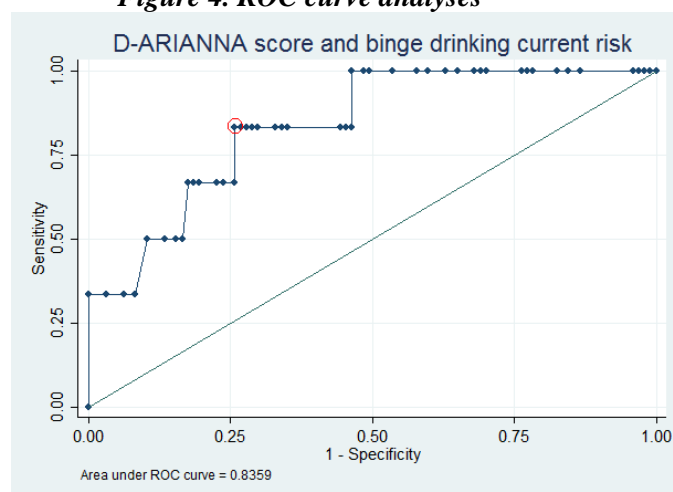| Risk/Protective Factor	Source*	Country	Setting	Size	Odds ratio (95% CI)
Cannabis use (Yes vs. No) **(past 30 days)**	McGee et al, 2010	New Zealand	university students	1356	10.34 [6.39-16.73]
	Digrande et al, 2000	Italy	university students	1911	9.55 [6.99-13.06]
	Wechsler et al, 1995	USA	college students	17592	7.13 [6.36-7.99]
	Vickers et al, 2004	USA	university students	412	11.05 [5.10-23.96]
Interest for discos and parties (Yes vs. No)	Gallimberti et al, 2011	Italy	high school students	802	5.04 [2.03-12.52]
	Sanchez et al, 2011	Brazil	high school students	2582	5.26 [4.40-6.29]
	Wechsler et al, 1995	USA	college students	17592	5.38 [5.00-5.80]
Smoking cigarettes (Yes vs. No)	Wechsler al., 1997b	USA	college students	17592	4.69 [4.37-5.00]
	Griffiths et al, 2006	China	university freshmen students	2630	4.20 [2.50-7.20]
	Schorling et al, 1994	USA	college students	3374	4.11 [3.28-5.15]
	Harrison et al, 2008	USA	young adults	5838	2.57 [2.12-3.12]
	Wickholm et al, 2003	Sweden	high school students	6287	5.90 [5.00-6.90]
	Jonas et al, 2000	UK	young adults	14762	3.54 [3.16-3.97]
Gender (Male vs. Female)	ISTAT National Institute of Statistics, 2012	Italy	adolescents and young adults	8325	2.88 [2.44-3.42]
Binge (Yes vs. No) **(past two weeks)**	Wechsler et al, 1997a	USA	college students	17592	2.84 [2.6-3.1]
	Beets et al, 2009	USA	college freshmen	827	1.23 [1.15-1.32]
Drinking onset at age 17 or younger (Yes vs. No)	Cranford et al, 2006	USA	college students	4580	2.74 [2.34-3.20]
	Digrande et al, 2000	Italy	university students	1911	7.62 [5.66-10.26]
	Youth Risk Behavior Surveillance System 2011	USA	young adults	14751	2.03 [1.65-2.49]
	Youth Risk Behavior Surveillance System 2003	USA	young adults	10387	2.32 [1.89-2.85]
	Maggs et al, 2011	USA	college freshmen	200	2.35 [1.48-3.72]
Parental alcohol misuse (Yes vs. No)	Sanchez et al, 2011	Brazil	high school students	2582	1.94 [1.55-2.43]
	Wechsler et al, 1995	USA	college students	17592	2.15 [1.97-2.34]

Table 1 *Continued*

Risk/Protective Factor	Source*	Country	Setting	Size	Odds ratio (95% CI)
Age (ref. younger age)	ISTAT, National Institute of Statistics, 2012	Italy	adolescents and young adults	8325	1.91 [1.78-2.06]
Peers influence (Yes vs. No)	Hanewinkel and Sargent, 2009	Germany	secondary school students	2708	1.53 [1.25-1.88]
	Eaton et al, 2004	USA	high school students	2004	1.31 [1.08-1.61]
	Harakeh et al, 2012	The Netherlands	secondary school students	1742	1.40 [1.02-1.92]
	Gallimberti et al, 2011	Italy	secondary school students	845	1.25 [1.10-1.43]
	Kim et al, 2009	China	1st and 2nd year university students	3041	4.10 [2.30-7.60]
Impulsivity[§]	Castellanos-Ryan et al, 2011	UK	secondary school students	76	1.27 [1.02-1.58]
	Friedel, 2011 dissertation	The Netherlands	adolescents	210	1.33 [1.15-1.54]
Volunteering (Yes vs. No)	Weitzman and Chen, 2005	USA	college students	27687	0.69 [0.65-0.73]
	Weitzman and Kawachi, 2000	USA	college students	17592	0.77 [0.71-0.83]
School proficiency (good vs. low performance)	Miller et al, 2007	USA	high school students	14114	0.44 [0.39-0.51]
	Engs et al, 1997	USA	college and university students	11621	0.46 [0.34-0.63]
	Hanewinkel et al, 2012	Italy	secondary and high school students	2668	0.39 [0.31-0.49]
	Donath et al, 2012	Germany	high school students	44610	0.84 [0.82-0.87]
	Wechsler et al, 1995	USA	college students	17592	0.64 [0.60-0.68]
	Porter and Pryor, 2007	USA	college and university students	41599	0.75 [0.72-0.78]
	Rasic et al, 2011	Canada	high school students	1615	0.48 [0.38-0.61]

*Full references of studies used to develop risk estimation model are listed in Appendix 2 (eReferences). [§]Assessed by SURPS (Substance Use Risk Profile Scale).

However, developed model was refined according to a pilot sample (N=110), involving subjects assessed at baseline and follow-up, using the preliminary version of D-ARIANNA model (evidence-based overall score). However, previously estimated parameters used for risk assessment purposes were likely to be overestimated due to high heterogeneity across studies. Thus, we refined the modelled effects according to

more realistic site-specific source characteristics. In addition, as the modelling provided 9,216 scenarios based on possible combinations, distribution data were split into five equal groups, thus calculating four quintiles (*Altman and Bland, 1994*). Relevant cut-off points, rounded to the nearest integers, were 43, 62, 82, and 93. However, for ease of interpretation these were amalgamated, deriving a simple percentage scoring system. Based on the coefficients of the model, we identified low (0-43%), moderate and moderate-high (43.1-62% and 62.1-82%), and high (82.1-100%) risk levels. Though most of risk factors can be generalizable across different populations, accounting for variability due to local drinking cultures, prevalence data for age groups and gender of young binge drinkers were collected from the National Institute of Statistics databases. Thereby, the model can be easily adapted if analogous national data can be retrieved.

Model performance was assessed through ROC curve analysis (Figure 4). This analysis revealed a probability that randomly selected member of high binge drinking risk score would have a larger classifier value than a randomly selected member of low risk group of 0.84 (0.69-0.98) with a cut-off value of 73% for D-ARIANNA overall score (sensitivity 83% and specificity 75%). According to selected cut-off, young people were to get a positive or negative test (overall score showing a high risk of BD) if they have BD condition (BD episode in the past two weeks), compared with a person without that condition with positive likelihood (LR+) ratio of 3.23 and a negative likelihood ratio (LR-) of 0.22, respectively. The tool appeared reaching a good threshold of accuracy even though showing only a small increase in the likelihood of BD. However, because of paucity of appropriate data in scientific literature (see Final Model paragraph), the model took into account only a restricted set of factors influencing BD current risk, not accounting for a considerable portion of variability and interactions.

Figure 4. ROC curve analyses

Implementing the model based on risk/protective factors in an interview

Questionnaire drafting

In order to carry out the interview, an unambiguous but not alarming questionnaire was needed catching youth attention. Young people may have specific insights in terms of appearance, and peculiar key questions/impediments/facilitators need to be considered. Thus, we designed a specific questionnaire investigating domains derived from identified risk/protective factors in an engaging manner (see Appendix 1). We took into account features that could affect response, in particular order and wording of the questions based on theoretical concepts applied to research in health (*Bowling, 2002*). We utilized closed questions in order to develop easily suitable response codes, providing comprehensive and unambiguous categories and, if necessary, an "other" category if we felt that there might be some unexpected answers. We built short queries, banning negatives since these are confusing and ambiguous. Wording was based on familiar statements and phrases that young people can understand. Hence, we avoided, when not strictly necessary, an excessively formal lexicon preferring a smooth and easy-to-understand language. Furthermore, also duration of questionnaire administration was taken into account, developing a ten minutes interview. We placed first simple and basic questions in order to retain rapport and goodwill, and those that seemed most sensitive at a later stage. For questions on impulsivity, as required by Substance Use Risk Profile Scale (SURPs), we used a Likert scale, a quick and popular method that contains a series of "opinion" statements about an issue (five in the case of SURPs), and that may be developed specifically for young people.

Along with questions investigating risk/factors status, the interview included also questions on excluded factors for descriptive purposes. For instance, we investigated financial availability in the weekend (pocket money) and use of violent videogames. Furthermore, we included some screening question about presence of depressive symptoms with a yes/no single item: "*Have you felt depressed or sad much of the time in the past year?"* and for anxiety symptoms in the same manner, asking: "*Have you felt anxious much of the time in the past year?"*. Even though not entirely reliable and not adequate to be nested in an easy-to-use eHealth app, single-item questions have been used for depressive disorders screening in both general and clinical populations (*Mitchell and Coyne, 2007; Carrà et al., 2011*), as well as for anxiety detection (*Teunissen et al., 2007*). We also explored if the subject had high alcohol expectancies

for social facilitation (*Townshend et al., 2014*) through the Alcohol Expectancies Questionnaire for Adolescents, Brief (AEQ-AB) (*Stein et al., 2007*). The AEQ-AB is a-seven item Likert scale exploring alcohol expectancies on global positive changes, changes in social behaviour, improved cognitive and motor abilities, sexual enhancement, cognitive and motor impairment, increased arousal, and relaxation and tension reduction (*Stein et al., 2007*).

Acceptability of the questionnaire

A pilot study was conducted involving high school students (N=110), aimed at verifying users' comprehensibility of the questionnaire, removing expressions or contents that could be experienced as offensive or provocative, and gathering feedback and suggestions about the graphics and usability of the eHealth app. We evaluated acceptability and wording of D-ARIANNA app, providing each enrolled with a form, immediately after interview completion. Ninety-eight percent of subjects considered D-ARIANNA an easy–to-use app and about 94% of subjects would recommend it to a friend. Nevertheless, 18% felt that some questions in the app sounded provocative either covered sensitive topics (i.e., parental alcohol misuse, school proficiency, past two weeks binge, past 30 days cannabis use, and drinking onset at age of 17 or younger). In addition, 13% of subjects suggested minor wording changes in questions on impulsivity, peers influence, smoking cigarettes, interest for clubs and parties.

Incorporating the model in an eHealth app

Finally, the questionnaire and the connected risk estimation model for BD were embedded in an eHealth app (D-ARIANNA-Digital - Alcohol RIsk Alertness Notifying Network for Adolescents and young adults), estimating user's percentage risk for BD. The statistical model was translated into an algorithm specifically designed for smartphones (i.e., iPhone and Android), with errors fixing in a process called debugging. Thus, the algorithm was verified in a version for personal computer and then it was integrated with a user graphical interface enabling use and appealing of eHealth app (e.g., questions placement, colours and fonts, specific graphic according to type of device, intuitive use of the app…). Thus, the eHealth app D-ARIANNA provides the described classification of different risk levels (from low to high), with user-friendly screens and simplified graphical interfaces. Moreover, a closing summary message shows risk factors that mostly contribute to the overall score. Examples of D-

ARIANNA screens are shown in Figure 1. Most information was recorded locally, with a support back-end area on a server. Each user identification was anonymized through an identification number. In addition, disclaimers for privacy regulations accompanied the implemented algorithm. The developed application was freely delivered in the market (Apple Store and Android Market) for the final release of the eHealth app.

Figure 1. Examples of eHealth app D-ARIANNA screens

Feasibility Study

Sample and study design

The study aimed to involve young people aged between 16 and 24 years, representative of youth general population susceptible to excessive alcohol consumption. Although studies of use of alcohol-related treatment have typically covered a very wide age range

-rather than focusing specifically on young adults- (*Grant, 1996; Hasin et al. 1995; Weisner and Matzger, 2002; Wu et al., 1999*), a prior study reported that only 6% of college students with alcohol dependence had received alcohol treatment services since starting college (*Knight et al., 2002*). The most common reasons for not using services were "not ready to stop using alcohol and/or drugs" (47%), "having no health care coverage and unable to afford the cost" (19%), "concerned that getting services might cause neighbours and community to have a negative opinion" (18%), and "not knowing where to go to get treatment" (15%). Thus, young people have a high prevalence of alcohol use disorders, but they are very unlikely to receive treatment or early intervention services or to perceive a need for such services. Underutilization of alcohol-related services among young adults deserves greater research attention (*Wu et al., 2007*). As a result, young people do not seek treatment for alcohol-related outcomes, just because they think they could handle the episodes themselves, or more likely, they did not consider excessive alcohol use serious or did not recognize it as a health problem. Indeed, young people's perception in terms of risky behaviour is scant (*SAMHSA, 2013*).

Because of the chosen setting (*Campostrini et al., 2006*), we consequently opted for a quasi-experimental, pre-post test design without a control group (*Harris et al., 2006*). As a result, we set this proof-of concept study (PoC), verifying that the D-ARIANNA tool has the potential for real-world application, for a first approach to young people with excessive alcohol use.

Setting and procedures

Recruitment took place in urban locations of Milan, for example live music events. Young people with the following characteristics were consecutively recruited: (1) aged between 16 and 24 years; (2) having exceeded with alcohol at least once in the last 6 months (screening question). We included only individuals able to sign the informed consent and excluded people who self-reported consumption of alcohol or drugs at the moment of the interview. Thus, those who joined the study received an information sheet and signed a written consent. In order to ease the sampling and to minimize embarrassment, the recruitment was conducted by peers, similar to the target population, introducing the tool and asking the screening question. Thus, the interviewers were students, peers aged between 18 and 24 years, selected from different Schools of Milano Bicocca University, and receiving 10 hrs training for the research

project about data collection procedures, including checking eligibility, providing information on the research project, obtaining consent, distributing and assisting with questionnaires. Questionnaires were administered through a smartphone application (D-ARIANNA eHealth app). Subjects who accepted to participate to the study received a €10.00 mobile phone recharge.

On the other hand, participants' drinking behaviour was evaluated after two further weeks using a single-item test asking '*How many times in the past two weeks have you had X or more drinks in a day*?' where X is 5 for men and 4 for women (*Wechsler et al., 1994*). This single-item test was considered as reference for assessment of participants' BD condition. A response of ≥ 1 was considered positive.

The study was approved by the Ethics Committee of University of Milano Bicocca (The D-ARIANNA study, approval: 0009873/13).

Outcome definition

We chose a short-term primary outcome, consistent with the expected impact of a one-shot self-administered eHealth app. We thus focused on detecting differences between the BD rates in the 2 weeks before and after the eHealth app self-administration.

The D-ARIANNA eHealth app

Through the interview, embedded in the D-ARIANNA (Digital - Alcohol Risk Alertness Notifying Network for Adolescents and young adults) eHealth app, users' answers about BD risk and protective factors populate an algorithm, providing an evidence-based current risk estimate for BD in young people (*Carrà et al., 2015*). Thus, the eHealth app identifies low (0-43%), moderate and moderate-high (43.1-62% and 62.1-82%), and high (82.1-100%) risk levels for the single subject, with user-friendly screens and simplified graphical interfaces.

As a whole, D-ARIANNA eHealth app uses a personalized risk communication to informed decision-making by individuals taking test, based on the nature of the population involved (*Edwards et al., 2013*). Information on risk factors that contribute most to the overall score are shown in a closing summary message, though this version of the app only predicts behaviour and it does not offer information on why to change behaviour. The feasibility study was aimed to explore the impact of D-ARIANNA on BD relapse outcome.

D-ARIANNA eHealth app is freely available from the main app-stores Google Play™ (https://play.google.com/store/apps/details?id=com.saysoon.d_arianna.en), and iTunes®

(https://itunes.apple.com/us/app/d-arianna-eng/id875252915?l=it&ls=1&mt=8). It was also included in the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (http://www.emcdda.europa.eu/html.cfm/index98829EN.html) and the NHS health apps libraries (http://apps.nhs.uk/apps/alcohol/).

Statistical analysis

For power calculation, we used information from the Italian Institute of Statistics databases, assuming that in the relevant age range the proportion of subjects who had recently binged on alcohol were 15% (*ISTAT, 2012*). Given a 5% level of significance, 90% power, and attrition of 20%, 589 participants would be needed to detect a 5% difference in BD prevalence rates at follow-up.

Mean (SD) and percentages were used for descriptive statistics, provided also by follow-up status. The normality of continuous data was checked with Shapiro-Wilk's test. Student's t-test was performed under the assumption of normally distributed continuous data, otherwise non-parametric Wilcoxon-Mann-Whitney test was used. Chi-square and Fisher's exact tests were applied for categorical variables. Where appropriate Bonferroni multiple testing correction was used. Association with BD was shown as odds ratio (OR) with related 95% confidence intervals (CI) and relevant p-value.

In order to investigate the longitudinal course over the study period of 2 weeks we performed Generalized Estimating Equation (GEE) analyses. Indeed, GEE regression model takes into account the correlation of repeated within-person measures (*Zeger et al., 1998*). Specifically, we used a logistic GEE model for the binary outcome binge drinking in the past 2 weeks. However, risk and protective factors identified in the risk estimation model were also entered with a stepwise procedure in the GEE model, in order to take into account their effect on the outcome. Furthermore, we needed to exclude systematic errors involving those lost at follow up, verifying whether unobserved outcome data were missing: i) completely at random (MCAR, i.e., the probability of non-response depends neither on covariates nor on outcome); ii) simply at random (MAR, i.e., non-response is dependent on observed covariates and outcome values); or iii) not at random (MNAR, i.e., non-response depends on the value of the missing outcome itself, even when observed data are taken into account).

We therefore followed a structured approach (*He, 2010; Bell and Fairclough, 2014*). We first assumed that missing data did not influence our outcome, implementing an

unweighted GEE model under the MCAR assumption. Nevertheless missing outcome data might depend on observed covariates (the MAR condition). We consequently performed sensitivity analyses, via t-tests and cross tabulations, comparing those who dropped out versus those who did not, and implemented a weighted GEE model that accounted for data from those who dropped out. In addition, we used a multiple imputation (MI) procedure, based on replacing missing data by drawing from a distribution of likely values. If we detected differences from any of these estimations, there would be a reasonable chance of systematic error, and missing outcome data would hence be dependent on observed values. However, people who are binge drinkers might be reluctant to disclose their condition and to provide follow-up information about adverse drinking outcomes. This would imply that the probability of nonresponse depends on missing values, suggesting a MNAR condition. However, MAR and MNAR can never be proved or falsified (*He, 2010*). We therefore analysed our data further by systematically varying our assumptions about missing outcomes. We tested two extreme models, i.e., a) all drop-outs would be bingers; b) all drop-outs would be abstinent, and a more conservative one, i.e., c) using last observation carried forward (LOCF) data for binging in the past 2 weeks. We evaluated how the estimates would change under each of these assumptions. Large deviations in regression parameters would indicate possible departures from MCAR (*Chen and Little, 1999; Hogan et al., 2004*), implying the inadequacy of utilizing only complete data, while small deviations would justify a per-protocol analysis. We used Stata statistical software package (version 13.1; StataCorp, College Station, Texas).

Analysis of D-ARIANNA tool model performance

Furthermore, we provided an evaluation of D-ARIANNA tool for binge drinking current risk performance using thresholds from ROC curves and summary measures, including sensitivity (the ability to correctly identify those people who actually have the condition) and specificity (the ability to identify people in a group who do not have the condition under investigation), along with positive ($\frac{Sensitivity}{100-Specificity}$) and negative ($\frac{100-Sensitivity}{Specificity}$) likelihood ratios (LRs).

RESULTS – FEASIBILITY STUDY

Study Participants, Screening and Follow-up Assessment

The sample comprised 286 males (48%) and 304 females (52%). The mean age was 20.65 (SD=1.90) years, with no significant gender differences. The majority of young people were students (88%), lived with parents (76%), get on well with them (90%) and had no immigration background (87%). They had on average good academic performance and played sports (64% of the whole sample). Many of them started drinking at age 17 or younger (75%), smoked cigarettes (48%) or have used cannabis in the past 30 days (34%). In addition, almost all participants were in contact with BD peers (90%). Participant flow, follow-up rates, and the numbers analysed are presented in Figure 2 according to inclusion criteria described in Setting and Procedures paragraph. From potentially eligible consecutive subjects (N=654) we selected those who reported excessive alcohol consumption at least once in the previous six months (N=590, 90%). Of the 590 involved young people, 224 (38%) had reported - at baseline recruitment – BD at least once in the past two weeks.

Figure 2. Study Participant Flow and Follow-up Rates

Data on bingeing after D-ARIANNA self-administration were unavailable for 38 (17%) of the 224 subjects who reported bingeing in the past two weeks, and for 45 (12%) of the 366 who did not. Thus, we obtained follow-up data from 507 (86%) participants who had self-administered the D-ARIANNA e-Health app.

Table 2. Baseline characteristics of participants lost to follow-up relative to those followed-up

Variable [¥]	Total N=590	Follow-up N=507 (85.9)	Drop-out N=83 (14.1)	P
Female Gender	304 (51.5)	264 (52.1)	40 (48.2)	0.512[a]
Age (yrs), *mean (SD)*	20.7 (1.9)	20.6 (1.9)	20.9 (1.9)	0.137[b]
Living with parents	446 (75.6)	392 (77.3)	54 (65.1)	0.023[a]
Get on well with parents[1]				0.876[a]
Not at all	10 (1.7)	9 (1.8)	1 (1.2)	
Only a little	48 (8.1)	41 (8.1)	7 (8.4)	
Some	286 (48.5)	249 (49.1)	37 (44.6)	
A lot	244 (41.4)	207 (40.8)	37 (44.6)	
Immigration background				0.010[a]
No immigration background	515 (87.3)	451 (88.9)	64 (77.1)	
One parent born outside Italy	34 (5.8)	26 (5.1)	8 (9.6)	
Both parents born outside Italy	41 (6.9)	30 (5.9)	11 (13.2)	
In a relationship	237 (40.2)	205 (40.4)	32 (38.6)	0.893[a]
Educational attainment				0.122[a]
Not attending any course	71 (12.0)	57 (11.2)	14 (16.9)	
High school	168 (28.5)	151 (29.8)	17 (20.5)	
University	351 (59.5)	299 (59.0)	52 (62.6)	
School proficiency, *mean (SD)*				
High school (maximum 10)	7.0 (0.8)	7.1 (0.8)	6.9 (0.9)	0.377[b]
University (maximum 30)	25.5 (2.5)	25.5 (2.5)	25.5 (2.4)	0.886[b]
Employed or in occasional jobs	178 (30.2)	152 (30.0)	26 (31.3)	0.829[a]
Interest for discos and parties	214 (36.3)	181 (35.7)	33 (39.8)	0.476[a]
Self-assessed religiosity[1]	224 (38.0)	195 (38.5)	29 (34.9)	0.583[a]
Volunteering	166 (28.1)	147 (29.0)	19 (22.9)	0.252[a]
Playing sports	380 (64.4)	329 (65.3)	51 (62.2)	0.588[a]
Weekly pocket money				0.408[a]
0-20 Euros	202 (34.2)	177 (34.9)	25 (30.1)	
21-50 Euros	249 (42.2)	217 (42.8)	32 (38.6)	
51-100 Euros	102 (17.3)	84 (16.6)	18 (21.7)	
>100 Euros	35 (5.9)	28 (5.5)	7 (8.4)	
Self-assessed Depression#[1]	129 (21.9)	115 (22.7)	14 (16.9)	0.251[a]
Self-assessed Anxiety#[1]	289 (49.0)	254 (50.1)	35 (42.2)	0.207[a]
Impulsivity[§] *mean (SD)*	5.1 (2.1)	5.1 (2.1)	5.3 (2.1)	0.381[b]
Violent Video Game Use[1]	63 (10.7)	59 (11.6)	4 (4.8)	0.081[c]
SUBSTANCE-RELATED FACTORS				
Smoking cigarettes	284 (48.1)	238 (46.9)	46 (55.4)	0.152[a]
E-cigarettes	24 (4.1)	17 (3.4)	7 (8.4)	0.063[c]
Cannabis use	198 (33.6)	159 (31.4)	39 (38.5)	0.194[a]
Early onset of drinking	445 (75.4)	383 (75.5)	62 (74.7)	0.869[a]
Previous binge drinking	224 (38.0)	186 (36.7)	38 (45.8)	0.113[a]
Peers binge drinking				0.347[a]
Only a few	61 (10.3)	50 (9.9)	11 (13.2)	
Most of them	529 (89.7)	457 (90.1)	72 (86.8)	
Parental alcohol misuse	71 (12.0)	61 (12.0)	10 (12.1)	0.997[a]
Positive alcohol expectancies[†] *mean(SD)*	21.4 (3.8)	21.5 (3.6)	21.0 (4.7)	0.884

Values are numbers (%), unless stated. [¥]There are missing values for some variables: the greatest number of missing values is for relationship status, where there are 490 ratings for follow-up participants and 78 for drop-outs; and for current employment, 498 and 82 ratings respectively.

[1]Missing values for both follow-up participants and drop-outs=1

*drinking onset at age 17 or younger. †Assessed by AEQ-AB (Alcohol Expectancy Questionnaire-Adolescent, Brief).

#Assessed by K-10 relevant items. §Assessed by Substance Use Risk Profile Scale, see *Carrà et al., 2015* for details

[a]Pearson's Chi-square test; [b]Student's t test; [c]Fisher's exact test, [d]Mann-Whitney U test.
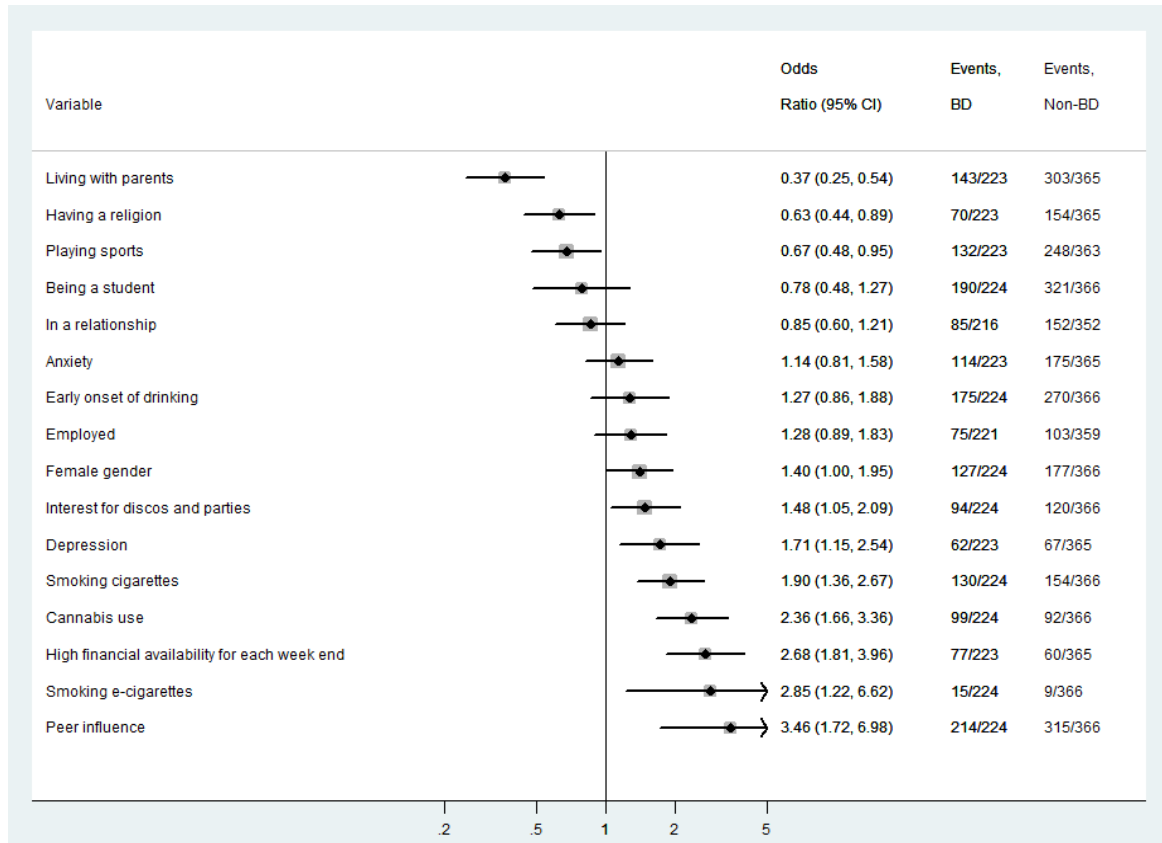
Table 2 presents baseline sociodemographic and clinical characteristics comparing those observed with those not observed at follow-up, together with several risk and protective factors. Although not included in the risk estimation model, other relevant variables were included for descriptive purposes in order to provide preliminary results. For most of the variables, we had no missing data, although for possibly sensitive items of questionnaire, response rates ranged from 96% (*being in a relationship*) to 99% (*religiosity*; *living alone or with parents*; *anxiety*; *depression*; *financial availability for each week-end*). Even if we should interpret this result with caution, young people dropping out were significantly more likely to have background of immigration (p=0.010) and less likely to live with parents (p=0.023). However, the two groups did not statistically differ on any of the remaining attributes, including previous BD, even though proportion was relatively higher in people who drop-out (37% vs 46%).

Correlates of binge drinking (BD)

Rates of an excessive alcohol consumption at baseline, before D-ARIANNA self-administration, were significantly higher among females than males (42% vs. 34%; p=0.049). However, at follow-up no statistically significant differences between gender groups were found. In addition, people who recently engaged in BD before D-ARIANNA showed higher scores of both impulsivity and alcohol expectancies (p<0.001) according to SURPs and AEQ-AB scales, respectively. This was confirmed at follow-up. Regarding investigation of clinical issues, depressive symptoms were at baseline more frequent among binge drinkers than in non-binge drinking individuals (28% vs. 18%), and, though not statistically significant (p=0.069), also at follow-up (23% vs. 16%). No statistical differences were found for what concerns anxiety, both at baseline (51.1% vs. 47.9%, p=0.455) and follow-up (50.7% vs. 47.8%, p=0.613). All smoking habits appeared significantly related to a recent BD episode both at baseline and follow-up. Cigarettes, cannabis, and e-cigarettes were regularly used by 58.0%, 44.2%, and 6.7% of binge drinkers, and by 42.1%, 25.1%, and 2.5% of non-binge drinkers at baseline, and by 62.2%, 50.0%, and 8.9% of binge drinkers, and by 43.6%, 27.3%, and 2.2% of non-binge drinkers at follow-up, respectively. Moreover, univariate analyses showed that, having more than €50 available *per* week-end (p<0.001), having most of friends drinking alcohol (p<0.001), all were associated with a recent BD episode both at baseline and follow-up. Having a high interest for parties and discos was associated with BD only at baseline (p=0.024). On the other hand, young people living

with parents, or who claimed to be religious, were less likely of having been recently engaged in BD also at follow-up. Categorical correlates of baseline previous two weeks BD are illustrated in *Figure 3*.

Figure 3. Correlates of previous binge drinking: univariate analysis

Variable	Odds Ratio (95% CI)	Events, BD	Events, Non-BD
Living with parents	0.37 (0.25, 0.54)	143/223	303/365
Having a religion	0.63 (0.44, 0.89)	70/223	154/365
Playing sports	0.67 (0.48, 0.95)	132/223	248/363
Being a student	0.78 (0.48, 1.27)	190/224	321/366
In a relationship	0.85 (0.60, 1.21)	85/216	152/352
Anxiety	1.14 (0.81, 1.58)	114/223	175/365
Early onset of drinking	1.27 (0.86, 1.88)	175/224	270/366
Employed	1.28 (0.89, 1.83)	75/221	103/359
Female gender	1.40 (1.00, 1.95)	127/224	177/366
Interest for discos and parties	1.48 (1.05, 2.09)	94/224	120/366
Depression	1.71 (1.15, 2.54)	62/223	67/365
Smoking cigarettes	1.90 (1.36, 2.67)	130/224	154/366
Cannabis use	2.36 (1.66, 3.36)	99/224	92/366
High financial availability for each week end	2.68 (1.81, 3.96)	77/223	60/365
Smoking e-cigarettes	2.85 (1.22, 6.62)	15/224	9/366
Peer influence	3.46 (1.72, 6.98)	214/224	315/366

BD = binge drinkers; Non-BD = non-binge drinkers

D-ARIANNA e-Health app impact

Of subjects with complete follow-up data (N=507), 186 participants (37%) had at least one BD occasion in the two weeks before baseline, and 90 (18%) in the two weeks before follow-up assessment. However, we needed to exclude systematic errors affecting those lost at follow up. Thus, we considered GEE and MI methods under the different assumptions about missing outcome data previously described. Each GEE-model compared follow-up drinking data with baseline assessments. In addition, we took into account the effect of risk and protective covariates for BD at multivariable level as reported in Table 3 that displays univariate and multivariable models under the different assumptions considered. Under the Missing Completely At Random assumption, analysis restricted to participants with complete data showed that the use of the eHealth app was associated with a statistically significant reduction in the

proportion who had binged in the two weeks before assessment (OR 0.36, 95% CI 0.29-0.45, P<0.001). We then applied the MAR assumption. Weighted GEE analysis and a multiple imputation with 100 iterations both showed statistically significant estimates similar to those from the MCAR model, with ORs (95%CI) of 0.38 (0.29-0.51) and 0.40 (0.31-0.50), respectively. Next, we investigated three distinct scenarios. First, we evaluated two extreme conditions: 1) that *all* the participants lost to follow-up had binged (the worst case scenario, OR=0.68, 95%CI: 0.55-0.83); and 2) that *none* of those lost to follow-up had done so (the best case scenario, OR=0.30, 95%CI: 0.23-0.37).

It can be seen that the worst case scenario provides a rather different estimate from the unweighted model. While this supports the need to dealing with missing outcome data, it is based on a rather unrealistic condition. The last observation carried forward (LOCF) method provides a less extreme assumption, which we think is more plausible, namely that the response remains constant at the last observed value (which is the baseline assessment). The relevant unweighted model gave an OR (95%CI) of 0.45 (0.37-0.55). Of all the models, this method provides the most appropriate and statistically meaningful estimate of the impact of the eHealth app, as it takes (reasonable) account of missing data. However, it allowed for the possibility that people who binge drink are more likely to drop out in order to avoid disclosing this condition: those lost to follow-up showed higher baseline rates, albeit not statistically significantly (see *Table 2*). Finally, multivariable models implemented under the different assumptions did not show clinically meaningful differences from their univariate counterparts, thus encouraging confidence in the estimates provided (*Table 3*).

Table 3. Binge drinking at two weeks follow-up

Assumption	GEE Method	OR (95% CI)	Robust SE	P
MCAR (Complete data)	Unweighted	0.36 (0.29- 0.45) 0.30 (0.23-0.40)*	0.04 0.04	<0.001
MAR	Weighted	0.38 (0.29-0.51) 0.31 (0.22-0.44)*	0.05 0.05	<0.001
	MI (N=100)	0.40 (0.31-0.50) 0.33 (0.25-0.44)*	0.05 0.05	<0.001
MNAR				
Missing as bingers	Unweighted	0.68 (0.55-0.83) 0.64 (0.51-0.82)*	0.07 0.08	<0.001
Missing as abstinent	Unweighted	0.30 (0.23-0.37) 0.24 (0.18-0.32)*	0.03 0.03	<0.001
LOCF (Last observation carried forward)	Unweighted	0.45 (0.37-0.55) 0.39 (0.31-0.49)*	0.04 0.04	<0.001

***Adjusted for:** Age, gender, cannabis use, peers binge drinking, parental alcohol misuse, alcohol expectancies, self-assessed religiosity, volunteering, weekly pocket money, impulsivity, interest for discos and parties, smoking cigarettes

In sum, at follow-up participants were significantly less likely to relapse than they were before D-ARIANNA self-administration, and missing data do not seem influencing these findings. *Table 4* shows the full model, including a significant interaction between gender and impulsivity score.

Table 4. Influence of risk factors on past two weeks binge drinking: GEE regression model

Variables	OR (95% CI)	Robust SE	P
Time effect	0.39 (0.31-0.49)	0.04	<0.001
Age	1.11 (1.01-1.23)	0.06	0.035
Female gender	3.38 (1.38-8.30)	1.55	0.008
Smoking cigarettes	1.18 (0.81-1.71)	0.22	0.395
Cannabis use	1.56 (1.07-2.29)	0.30	0.021
Peers binge drinking	2.29 (1.23-4.30)	0.73	0.009
Parental alcohol misuse	1.65 (1.03-2.65)	0.40	0.039
Positive alcohol expectancies	1.12 (1.07-1.18)	0.03	<0.001
Impulsivity (SURPs scale)	1.19 (1.06-1.33)	0.07	0.004
Female gender x Impulsivity	0.83 (0.71-0.97)	0.06	0.019
Interest for discos and parties	1.29 (0.92-1.81)	0.22	0.142
Weekly pocket money (ref. ≤20)			
21-50 euros	1.59 (1.01-2.51)	0.37	0.045
51-100 euros	2.43 (1.41-4.19)	0.67	0.001
>100 euros	2.63 (1.24-5.59)	1.01	0.012
Self-assessed religiosity	0.69 (0.48-0.99)	0.13	0.045
Volunteering	1.81 (1.26-2.61)	0.34	0.001

Last observation carried forward method was used

D-ARIANNA tool Model performance results

Five hundred and seven subjects were assessed at baseline and follow-up. Among those subjects who completed follow-up assessment, 126 reported a high (25%), 72 (14%) a moderate-high, 71 (14%) a moderate and 238 (47%) a low risk of BD. In addition, 90 (18%) subjects experienced at least one BD episode in the two weeks before follow-up assessment, of whom a considerable number of subjects (40%) did multiple times. The majority of subjects with at least a BD episode during the follow-up period had previously (baseline assessment) been considered at high (41%) or moderate-high risk (24%). The distribution in percentages of study participants' risk levels by the occurrence of binge drinking is shown in Figure 4. Furthermore, analysis of ROC curves (Figure 5) revealed a probability that randomly selected member of high BD risk score would have a larger classifier value than a randomly selected member of low risk group of 0.69 (0.63-0.75) with a cut-off value of 51% for D-ARIANNA overall score (sensitivity 76% and specificity 59%). According to selected cut-off, young people were

to get a positive or negative test (overall score showing a moderate/high risk of BD) if they have BD condition (BD episode in the past two weeks), compared with a person without that condition with positive likelihood (LR+) ratio of 1.84 and a negative likelihood ratio (LR-) of 0.41, respectively. Even though the tool appeared not reaching a good threshold of accuracy showing a minimal increase in the likelihood of BD, a more discriminatory ability was found regarding reported moderate-high and high risk level for BD (overall score cut-off = 62%) with LR+ 1.96 and LR- 0.51. However, because of paucity of appropriate data in scientific literature (see Final Model paragraph) the model took into account only a restricted set of factors influencing BD current risk, not accounting for a considerable portion of variability and interactions, thus considering the need of further research on excluded factors.

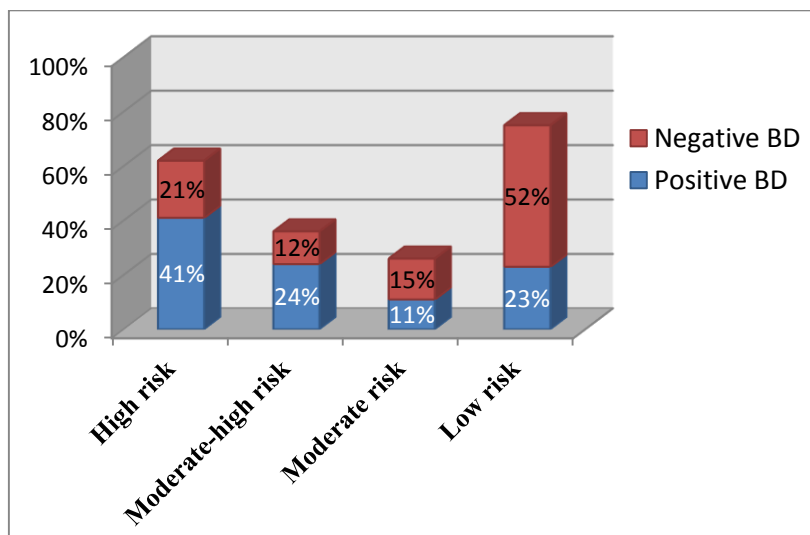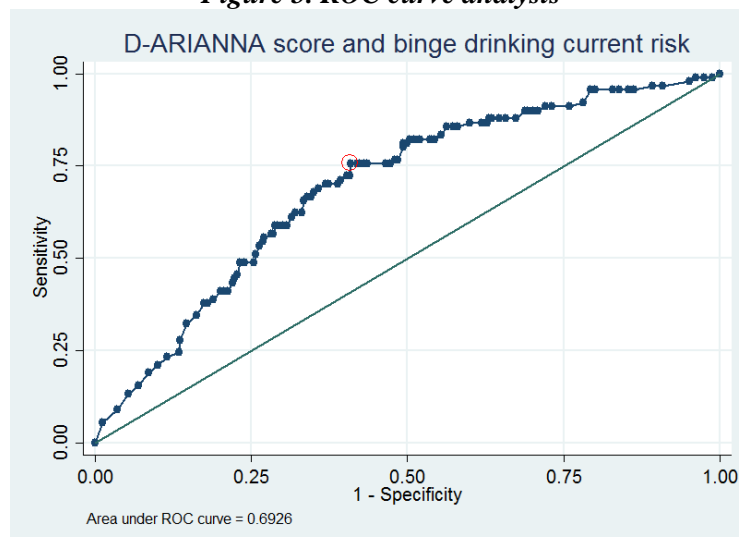*Figure 4. Distribution of participants' risk levels by the occurrence of binge drinking (BD)*

Figure 5. ROC curve analysis

DISCUSSION

Main findings

We could collect data from a large sample of subjects aged between 18 and 24 years with gender balance, including high school and university students but also young people not attending any course. Socio-demographic features of participants of our study characterized a sample of young people with apparently not problematic backgrounds, and a high community culture, despite of sampling strategy taking into account different deprivation-level areas of urban locations. Indeed, young people in our sample were more likely to live with parents, to get on well with them, with on average also a good academic performance and involvement in sports at different levels. Interestingly, despite the average positive background, the majority of them started drinking at age 17 or younger, and many of them smoked regularly cigarettes or have used cannabis in the past 30 days. As a result, an association between substance use and recent BD was found.

Findings from our proof-of concept study suggested a short-term beneficial impact of an eHealth tool for excessive alcohol consumption in young people, although needing a confirmatory trial (*Thorpe et al., 2009*). In this study, we showed that at follow-up, after D-ARIANNA self-administration, young people reported a reduction in BD in the preceding 2-week period (37% at baseline vs. 18% at follow-up). In addition, an appropriate model in handling of missing data, confirmed a significant diminution in rates over time. This preliminary evidence for a positive impact of the eHealth app was corroborated by the role of risk and protective factors in multivariable analyses, though we could not include in the risk estimation model some relevant domains, due to insufficient data or too sensitive topics. Moreover, levels of acceptance of the app and participation were very satisfactory with an increased knowledge and awareness in term of perception of risky behaviour after D-ARIANNA administration (*Carrà et al., 2015*). Our findings advocate the novelty value of an eHealth tool in dealing with alcohol consumption among young people. Actually, young people were approached in a natural setting, where real life situations and environments deeply condition their decision-making mechanisms and expectancies. Real life scenarios take account of the definition of alcohol environments, often crowded and with loud music, where young people meet up with each other, such as pubs, on-premises alcohol outlets and live

music events, where they can find a permissive environment and cheap alcohol availability. Alcohol use is considered a help to transform boring periods into enjoyable occasions (*Warwick et al., 2009*). Reported high scores of both alcohol expectancies and impulsivity of study participants who recently engaged in BD as compared with non-binge drinkers fall within these considerations, due to the representation of domains such as social confidence, tension reduction, little awareness of negative consequences, and thoughtless involvement in situations. Furthermore, according to previous evidence, it was unusual for young people not to consume alcohol at all, rarely reporting any difficulties in accessing alcoholic drinks (*Atkinson et al., 2011*). It is perhaps useful to note that several young people show a degree of creativity with regard to finding sufficient money to pay for alcohol and, if under age, finding ways to purchase it. Indeed, young people indicate that a life without alcohol would be undesirable, and they often talk about the considerable amounts of alcohol they drink as "amazing", rather than view the actual amount consumed as problematic (Warwick et al., 2009). In the Warwick et al. (2009) study, some participants suggested that if there were no alcohol around, this might result in other potentially risky practices related to other recreational drugs or to sexual activity. In addition, although violent or unwanted sexual incidents were considered somehow seriously, several alcohol negative consequences (e.g., encounters with the police, losing one's way home, vomiting in inappropriate places, hangovers and not remembering much about an evening in which alcohol was consumed) were often considered humorously (*Warwick et al., 2009*).

On the other hand, young people often consider challenging environments according to relationships they can establish (e.g., having friends nearby) (*Warwick et al., 2009*). Our study results confirmed the strong relationship between alcohol environment nature and perceived peers influence, along with family drinking habits. Peer influence was found as one of the most common factors that mostly contribute to the overall risk score, consistently with previous evidence. In previous research, peer influence has emerged as one of the most powerful predictors of the early initiation and maintenance of drinking in the transition from high school to college (*Reifman and Watson, 2003; Wood et al., 2001; Baer et al., 1995*). In addition, quality of peers' relationships enhances the influence of social reinforcement, modifying cognitive processes on personal alcohol use via three pathways: the lack or breakdown of quality peer relationships, alcohol use being an integral part of peer interactions, and if peers disapprove of alcohol use or do not drink (*Borsari and Carey, 2006*).

Strengths and Limitations

D-ARIANNA is, to the best of our knowledge, the first evidence-based eHealth app for young people, specifically evaluating risk for BD, relying exclusively on personalized risk communication for informed decision-making rather than on common technological means such as GPS to identify high-risk locations (*Gustafson et al., 2014*). Smartphone- and computer-based applications are available for alcohol use disorders, and effectiveness in the continuing care of patients has been reported (*Gustafson et al., 2014; Klein et al., 2012*). Previous studies relied on Web-based, feedback by e-mail and text-messaging approaches (Haug et al., 2013; Kypri et al, 2014; McCambridge et al., 2013) and they depicted behavioural (*Tanner-Smith and Lipsey, 2015*) and universal school-based prevention programs (*Foxcroft and Tsertsvadze, 2011*) with limited evidence in reducing BD, though their impact remains a cause for concern.

The involvement of a non-clinical population in real life settings, catching non-seeking treatment young people, and gathering relevant information from them represented an important challenge in the conception of this study. Appealing approaches were needed. Thus, eHealth seemed the most appropriate way in order to convey of information in an engaging manner, improving perceived privacy and anonymity, copying with stigmatization and embarrassment issues. Recent research in the UK (*Cox et al., 2006*), described young people rarely engaged in open communication with parents and health professionals about alcohol, though open communication, together with negotiation among family members allows alcohol use in a safe and supervised way. Finally, eHealth approach used for D-ARIANNA project took advantage of young people propensity to, and expertise with, electronic devices (i.e., smartphones applications).

However, this proof-of-concept study has several limitations mainly due to the lack of a control group and to the extremely short duration of the follow-up, both making difficult to establish whether the use of this eHealth app can change the attitude to BD in the target population. The difficulty of implementing a controlled study in the chosen natural setting led us to opt for a quasi-experimental, pre-/post-test design. This limitation is not unusual in e-Health interventions (*Harris et al., 2006*). Indeed, we used a convenience sample, though identifying every subject belonging to the target population would help randomize recruiting. Potential alternatives would include the

creation of another cohort where researchers simply assess BD before and after without an eHealth app or comparing outcome from young people using the e-Health app to a drinking diary completed by participants. However, assessment of alcohol and substance use through an interview not embedded in an eHealth app might not be adequately appealing for the target population, thus resulting in high risk of selection bias. Furthermore, our study was open to the methodological weaknesses of eHealth research, detecting subtle effects on behaviour with problematic attrition of participants not engaged in clinical settings (*Cunningham and Kypri, 2011*). Furthermore, limitations of this study are also related to considered self-report measure for BD and occurrence of recall bias when asking young people number of previous two-week BD episodes.

Although we are aware that the lack of a control group is a serious limitation, which cannot be overcome in any way, we chose a more pragmatic evaluation that at least minimizes interference by research artefacts stemming from intervention study participation. We maximized the external validity of the findings by using a large sample, more epidemiologically representative than special groups from specific settings such as school and college students. Our follow-up participation rates were good, and we addressed the potential for selection biases through our exhaustive methods of analysing the impact of missing outcome data.

However, it remains difficult to confirm an association between the change in outcome behaviour and the intervention in this study, not to mention that recruiting at pubs and clubs perhaps implied a peak point of BD, making possible a regression to the mean phenomenon. We cannot even exclude that participants engaged in a particularly heavy drinking session on the day of recruitment might have been especially likely to not drink over the next 2 weeks because of BD consequences.

In addition, we cannot rule out a Hawthorne observer effect, considering that participants knew their behaviour was being tracked. We attempted to reduce this effect, involving peer facilitators instead of standard researchers and health professionals.

Furthermore, we evaluated the persistence of BD using a 2-week follow-up, certainly a short-term outcome, not to consider that, although using the same exact wording previously used, baseline and follow-up questions were asked in different settings using different modes. Although consistent, in terms of dose–response relationship, with the impact of a one-shot eHealth app, this effect may decline over time, indicating a probable need for regular boosting.

Despite performed complex statistical analyses, these cannot overcome main limitations described and the proof-of-concept nature of our study. There is thus a requirement for an adequately powered randomized clinical trial, preferably based not on self-report, but on urine testing, to confirm our results and to ascertain whether the use of this app is of any benefit in the prevention of BD. Such a trial will establish the efficacy of the app using regular feedback and repeated administrations, possibly with motivational components such as *gamification* (*McCallum, 2012*). Those factors and processes could be enhanced in order to operate at the individual and community levels.

Implications

We could produce an evidence-based eHealth app for young people (D-ARIANNA), evaluating current risk for BD. The D-ARIANNA model includes several risk factors for BD and recognized protective factors. All are to some degree, modifiable, manageable conditions. It could be argued that provided information can improve decision-making mechanisms in young people who binge drink, supporting behavioural changes, thus improving relevant prevention strategies (*Goudriaan et al., 2007*). Attractive for young people, D-ARIANNA may be useful to enhance awareness of this risky behaviour. Working with difficult to engage young people experiencing alcohol-related harm may be less difficult using eHealth tools that fit their lifestyles. Also substance use professionals and families could use this novel instrument as a first approach for adolescents and young adults about their alcohol-related behaviours, even before they get involved in dangerous use. Our eHealth app shares the characteristics of usability, utility, and appeal typical of such applications (*Liu et al., 2011*), and it should in principle be capable of wide dissemination, reaching large numbers of young people. Of course, we need to consider the use of this eHealth app also in terms of ecologic validity. This would imply different approaches according to chosen dissemination strategies. Clinicians could actually prescribe this app to high-risk youth, taking advantage of risk levels categorization (low, moderate, moderate-high, and high risk), although the integration of this component in standard treatment programs needs to be considered. Alternatively, viral advertising also using existing social networking services could motivate youth, self-selecting to use this eHealth app. This could benefit from gamification to make the eHealth app more fun and motivational. In addition, existing features such as Breathalyzer can be incorporated in the eHealth app making this more appealing for young people rather than a simple screening approach.

CONCLUSIONS AND FUTURE RESEARCH

In sum, we observed that after D-ARIANNA use young people self-awareness increased and perception of risk for BD behaviour was grasped. The development of an eHealth tool, such as D-ARIANNA, focused on personal communication and BD risk awareness, also influences responsible drinking, and could be tested in an environmental-based community intervention (*Holder et al, 2000; Treno et al, 2007; Hingson et al, 2005*).

The novelty of the risk estimation design in the D-ARIANNA project was greater than the feasibility component. Indeed, it appears a more advanced study is pending, which could provide more power for definitive outcome results (e.g., adequately powered randomized clinical trial with gamified version of D-ARIANNA). Thus, our preliminary findings enable further studies on BD among young people and its correlates, promoting the translation of research results into effective prevention strategies.

REFERENCES

- Altman DG, Bland JM. Statistics Notes: Quartiles, quintiles, centiles, and other quantiles. BMJ 1994; 309: 996

- Atkinson A, Elliott G, Bellis M, Sumnall H. Young people, alcohol and the media. Liverpool John Moores University 2011. ISBN: 978-1-85935-853-5 (ebook) http://www.ias.org.uk/uploads/pdf/Underage%20drinking%20docs/young-people-alcohol-mediaEBOOK.pdf

- Aviv RI, d'Esterre CD, Murphy BD, et al. Hemorrhagic transformation of ischemic stroke: prediction with CT perfusion. Radiology. 2009; 250: 867–77.

- Ayer T, Chhatwal J, Alagoz O, Kahn CE Jr, Woods RW, Burnside ES. Comparison of Logistic Regression and Artificial Neural Network Models in Breast Cancer Risk Estimation. Radiographics. 2010; 30: 13–22.

- Baer JS, Kivlahan DR, Marlatt GA. High-risk drinking across the transition from high school to college. Alcohol Clin Exp Res 1995; 19: 54–61.

- Balodis IM, Potenza MN, Olmstead MC. Binge drinking in undergraduates: relationships with sex, drinking behaviors, impulsivity, and the perceived effects of alcohol. Behav Pharmacol. 2009; 20(5-6): 518-26.

- Bartoli F, Carrà G, Brambilla G, Carretta D, Crocamo C, Neufeind J, Baldacchino A, Humphris G, Clerici M. Association between depression and non-fatal overdoses among drug users: a systematic review and meta-analysis. Drug Alcohol Depend. 2014; 134: 12-21.

- Bechara A. Risky business: emotion, decision-making and addiction. J Gambl Stud. 2003; 19: 23–51.

- Bell ML, Fairclough DL. Practical and statistical issues in missing data for longitudinal patient reported outcomes. Stat Methods Med Res 2014; 23: 440-59.

- Bellis MA, Hughes K, Morleo M, et al. Predictors of risky alcohol consumption in schoolchildren and their implications for preventing alcohol-related harm. Subst Abuse Treat Prev Policy. 2007; 2: 15.

- Bonomo YA, Bowes G, Coffey C, Carlin JB, Patton GC. Teenage drinking and the onset of alcohol dependence: A cohort study over seven years. Addiction 2004;99(12): 1520–8.

- Borsari B, Carey KB. How the quality of peer relationships influences college alcohol use. *Drug and alcohol review*. 2006; 25(4): 361-70.

- Bowling A. The tools of quantitative research. In: Bowling A, ed. *Research methods in health*. 2nd ed. Philadelphia, PA: Open University Press, McGraw-Hill Education, 2002, 273-309.

- Campostrini S, Holtzman D, McQueen D, Boaretto E. Evaluating the effectiveness of health promotion policy: changes in the law on drinking and driving in California. Health Promotion International 2006; 21: 130-5.

- Carrà G and Johnson S. Variations in rates of comorbid substance use in psychosis between mental health settings and geographical areas in the UK. A systematic review. Soc Psychiatry Psychiatr Epidemiol. 2009; 44: 429-47.

- Carrà G, Bartoli F, Crocamo C, Brady KT, Clerici M. Attempted suicide in people with co-occurring bipolar and substance use disorders: Systematic review and meta-analysis. J Affect Disord. 2014; 167: 125-35.

- Carrà G, Crocamo C, Schivalocchi A, Bartoli F, Carretta D, Brambilla G, Clerici M. Risk Estimation Modeling and Feasibility Testing for a Mobile eHealth Intervention for Binge Drinking among Young People: The D-ARIANNA (Digital - Alcohol RIsk Alertness Notifying Network for Adolescents and young adults) Project. Subst Abus 2015; 36: 445-52.

- Carrà G, Johnson S, Bebbington P Angermeyer MC, Heider D, Brugha T, Azorin JM, Toumi M. The lifetime and past- ` year prevalence of dual diagnosis in people with schizophrenia across Europe: Findings from the European Schizophrenia Cohort (EuroSC). Eur Arch Psychiatry Clin Neurosci 2012; 262(7): 607–16.

- Carrà G, Johnson S. Variations in rates of comorbid substance use in psychosis between mental health settings and geographical areas in the UK. A systematic review. Soc Psychiatry Psychiatr Epidemiol. 2009; 44(6): 429-47.

- Carrà G, Sciarini P, Segagni-Lusignani G, Clerici M, Montomoli C, Kessler RC. Do they actually work across borders? Evaluation of two measures of psychological distress as screening instruments in a non Anglo-Saxon country. Eur Psychiatry. 2011; 26(2): 122-7.

- Carrà G, Scioli R, Monti MC, Marinoni A. Severity profiles of substance-abusing patients in Italian community addiction facilities: influence of psychiatric concurrent disorders. Eur Addict Res. 2006; 12(2): 96-101.

- CDC - Center for Disease Control and Prevention. CDC Health disparities and inequalities report—United States, 2011. MMWR Morb Mort Wkly Rep. 2011; 60(Suppl): 101–4.

- Chen HY, Little R. A test of missing completely at random for generalised estimating equations with missing data. Biometrika 1999; 86: 1–13.

- Choi K, Forster JL. Beliefs and experimentation with electronic cigarettes: a prospective analysis among young adults. Am J Prev Med. 2014; 46(2): 175-8.

- Cooney MT, Dudina A, D'Agostino R, Graham IM. Cardiovascular Risk-Estimation Systems in Primary Prevention: Do They Differ? Do They Make a Difference? Can We See the Future? Circulation. 2010; 122: 300-10.

- Cox L, Sherriff N, Coleman L, Roker D. Parent-young people communication about alcohol, Brighton: Trust for the Study of Adolescence 2006. Available from http://alcoholresearchuk.org/downloads/finalReports/AERC_FinalReport_0035.pdf

- Cunningham JA, Kypri K, McCambridge J. The use of emerging technologies in alcohol treatment. Alcohol Res Health 2011; 33(4): 320–6.

- D'Agostino RB, Grundy S, Sullivan LM, Wilson P, for the CHD Risk Prediction Group. Validation of the Framingham Coronary Heart Disease Prediction Scores Results of a Multiple Ethnic Groups Investigation. JAMA. 2001; 286: 180-7.

- D'Alessio M, Baiocco R, Laghi F. The problem of binge drinking among Italian university students: a preliminary investigation. Addict Behav. 2006; 31(12): 2328-33.

- De Visser RO, Birch JD. My cup runneth over: young people's lack of knowledge of low-risk drinking guidelines. Drug Alcohol Rev. 2012; 31: 206–212.

- Digrande L, Perrier MP, Lauro MG, Contu P. Alcohol use and correlates of binge drinking among university students on the Island of Sardinia, Italy. Subst Use Misuse. 2000; 35(10): 1471-83.

- Eaton DK, Forthofer MS, Zapata LB, et al. Factors related to alcohol use among 6th through 10th graders: the Sarasota County Demonstration Project. J Sch Health. 2004; 74: 95-104.

- Edwards AGK, Naik G, Ahmed H, Elwyn GJ, Pickles T, Hood K, Playle R. Personalised risk communication for informed decision making about taking screening tests. Cochrane Database Syst Rev 2013; (2):CD001865.

- Elton-Marshall T, Leatherdale ST, Burkhalter R. Tobacco, alcohol and illicit drug use among Aboriginal youth living off-reserve: results from the Youth Smoking Survey. CMAJ. 2011; 183: E480-6.

- Farke W, Anderson P. Binge drinking in Europe. Adicciones 2007; 19(4): 333–9.

- Ferri M, Allara E, Bo A, Gasparrini A, Faggiano F. Media Campaigns for the prevention of illicit drug use in young people. Cochrane Database Syst Rev. 2013; (6):CD009287. doi: 10.1002/14651858.CD009287.pub2.

- Field M, Schoenmakers T, Wiers RW. Cognitive Processes in Alcohol Binges: A Review and Research Agenda Current Drug Abuse Reviews 2008; 1(3): 263-79.

- Figlock D. Impaired Decision Making as a Risk Factor for College Student Drinking [PhD dissertation]. Ames, IA: University of Iowa; 2010. Available from: http://ir.uiowa.edu/etd/801.

- Fisher LB, Miles IW, Austin SB, Camargo CA Jr, Colditz GA. Predictors of Initiation of Alcohol Use Among US Adolescents Findings From a Prospective Cohort Study. Arch Pediatr Adolesc Med. 2007; 161: 959-66.

- Foxcroft DR, Tsertsvadze A. Universal school-based prevention programs for alcohol misuse in young people. Cochrane Database Syst Rev 2011; Art. No.: CD009113.

- Fraeyman J, Van Royen P, Vriesacker B, De Mey L, Van Hal G. How is an electronic screening and brief intervention tool on alcohol use received in a student population? A qualitative and quantitative evaluation. J Med Internet Res. 2012; 14:e56. doi: 10.2196/jmir.1869.

- Gallimberti L, Chindamo S, Buja A, Forza G, Tognazzo F, Galasso L, Vinelli A, Baldo V. Underage drinking on saturday nights, sociodemographic and environmental risk factors: a cross-sectional study. Subst Abuse Treat Prev Policy. 2011; 6:15.

- Goudriaan AE, Grekin ER, Sher KJ. Decision making and binge drinking: a longitudinal study. Alcohol Clin Exp Res. 2007; 31: 928–38.

- Grant BF. Toward an alcohol treatment model: a comparison of treated and untreated respondents with DSM-IV alcohol use disorders in the general population. Alcoholism, Clinical and Experimental Research 1996; 20: 372–378.

- Gruber JH. Religious market structure, religious participation, and outcomes: is religion good for you? *Advances in Economic Analysis and Policy* 2005; 5(1): 1–30. http://www.bepress.com/bejeap/advances/vol5/iss1/art5.

- Gustafson DH, McTavish FM, Chih MY, Atwood AK, Johnson RA, Boyle MG, Levy MS, Driscoll H, Chisholm SM, Dillenburg L, Isham A, Shah D. A smartphone application to support recovery from alcoholism: A randomized clinical trial. JAMA Psychiatry 2014; 71: 566–72.

- Haberstick BC, Young SE, Zeiger JS, Lessem JM, Hewitt JK, Hopfer CJ. Prevalence and correlates of alcohol and cannabis use disorders in the United States: results from the national longitudinal study of adolescent health. Drug and Alcohol Dependence 2014; 136: 158–61.

- Hanewinkel R, Sargent JD, Poelen EA, Scholte R, Florek E, Sweeting H, … Morgenstern M.. Alcohol Consumption in Movies and Adolescent Binge Drinking in 6 European Countries. Pediatrics. 2012; 129(4): 709-20.

- Harris AD, McGregor JC, Perencevich EN, Furuno JP, Zhu J, Peterson DE, Finkelstein J. The Use and Interpretation of Quasi-Experimental Studies in Medical Informatics. J Am Med Inform Assoc 2006; 13(1): 16–23.

- Hasin DS, Grant BF. AA and other helpseeking for alcohol problems: former drinkers in the U.S. general population. Journal of Substance Abuse 1995; 7: 281–92.

- Haug S, M.P. Schaub, V. Venzin, Meyer C, John U, Gmel G. A pre-post study on the appropriateness and effectiveness of a Web- and text messaging-based intervention to reduce problem drinking in emerging adults. J Med Internet Res 2013; 15: e196.

- He Y. Missing Data Analysis Using Multiple Imputation. Getting to the Heart of the Matter. Circ Cardiovasc Qual Outcomes 2010; 3: 98-105.

- Hibell B, Guttormsson U, Ahlstrom S, et al. The 2007 ESPAD report. Substance use among students in 35 European countries. Stockholm: CAN; 2009.

- Hingson RW, Zakocs RC, Heeren T, et al. Effects on alcohol related fatal crashes of a community based initiative to increase substance abuse treatment and reduce alcohol availability. Inj Prev. 2005; 11: 84–90.

- Hogan JW, Roy J, Korkontzelou C. Handling drop-out in longitudinal studies. Stat Med 2004; 23: 1455–97.

- Holder HD, Gruenewald PJ, Ponicki WR, et al. Effect of community-based interventions on high-risk drinking and alcohol-related injuries. JAMA 2000; 284: 2341–7.

- ISTAT - Italian Institute of Statistics databases. L'USO E L'ABUSO DI ALCOL IN ITALIA - REPORT 2011. ISTAT, 2012.
  http://www.istat.it/it/files/2012/04/alcol11aprileDEF.pdf Accessed July 15, 2015.

- Jasinski JL, Ford JA. Sexual orientation and alcohol use among college students: The influence of drinking motives and social norms. J Alcohol Drug Educ. 2007; 51: 63-82.

- Jones SE, Oeltmann J, Wilson TW, Brener ND, Hill CV. Binge drinking among undergraduate college students in the United States: implications for other substance use. The Journal of American College Health 2001; 50(1): 33–8.

- Kiluk BD, Carroll KM. New developments in behavioral treatments for substance use disorders. Curr Psychiatry Rep. 2013; 15(12): 420.

- Klein AA, Slaymaker VJ, Dugosh KL, McKay JR. Computerized continuing care support for alcohol and drug dependence: A preliminary analysis of usage and outcomes. J Subst Abuse Treat 2012; 42: 25–34.

- Knight JR, Wechsler H, Kuo M, Seibring M, Weitzman ER, Schuckit MA. Alcohol abuse and dependence among U.S. college students. Journal of Studies on Alcohol 2002; 63: 263–70.

- Kuntsche E, Rehm J, Gmel G. Characteristics of binge drinkers in Europe. Social Science and Medicine 2004; 59(1): 113–27.

- Kypri K, Hallett J, Howat P, McManus A, Maycock B, Bowe S, Horton NJ. Randomized controlled trial of proactive Web-based alcohol screening and brief intervention for university students. Arch Intern Med. 2009a; 169: 1508–1514.

- Kypri K, Paschall MJ, Langley J, Baxter J, Cashell-Smith M, Bourdeau B. Drinking and Alcohol-Related Harm Among New Zealand University Students: Findings From a National Web-Based Survey. Alcohol Clin Exp Res. 2009b; 33: 307–14.

- Kypri K, Vater T, Bowe SJ, Saunders JB, Cunningham JA, Horton NJ, McCambridge J. Web-based alcohol screening and brief intervention for University students a randomized trial. JAMA 2014; 311: 1218–24.

- Laghi F, Baiocco R, Lonigro A, Capacchione G, Baumgartner E. Family functioning and binge drinking among Italian adolescents. J Health Psychol. 2012; 17(8): 1132-41.

- Liu C, Zhua Q, Holroydb KA, Seng EK. Status and trends of mobile-health applications for iOS devices: A developer's perspective. J Syst Softw 2011; 84: 2022–2033.

- Mäkelä P, Gmel G, Grittner U, Kuendig H, Kuntsche S, Bloomfield K, Room R. Drinking patterns and their gender differences in Europe. Alcohol Alcohol Suppl. 2006; 41(1): i8-18.

- Marsch LA, Carroll KM, Kiluk BD. Technology-based interventions for the treatment and recovery management of substance use disorders: a JSAT special issue. J Subst Abuse Treat. 2014; 46: 1–4.

- Martinotti G, di Iorio G, Tedeschi D, De Berardis D, Niolu C, Janiri L, Di Giannantonio M. Prevalence and intensity of basic symptoms among cannabis users: an observational study. The American Journal of Drug and Alcohol Abuse 2011; 37(2): 111–6.

- Martinotti, Carli V, Tedeschi D, Di Giannantonio M, Roy A, Janiri L, Sarchiapone M. Mono- and polysubstance dependent subjects differ on social factors, childhood trauma, personality, suicidal behaviour, and comorbid Axis I diagnoses. Addictive Behaviors 2009; 34(9): 790–3.

- McCallum S. Gamification and serious games for personalized health. Stud Health Technol Inform 2012; 177: 85–96.

- McCambridge J, Bendtsen M, Karlsson N, White IR, Nilsen P, Bendtsen P. Alcohol assessment and feedback by email for university students: Main findings from a randomised controlled trial. Br J Psychiatry 2013; 203: 334–40.

- McClure EA, Acquavita SP, Harding E, Stitzer ML. Utilization of communication technology by patients enrolled in substance abuse treatment. Drug Alcohol Depend. 2013; 129: 145–50.

- Mellor JM, Freeborn BA. Religious participation and risky health behaviors among adolescents. Health Econ. 2011; 20(10): 1226-40.

- Miller JW, Naimi TS, Brewer RD, Jones SE. Binge drinking and associated health risk behaviors among high school students. Pediatrics 2007; 119(1): 76–85.

- Mitchell AJ, Coyne JC. Do ultra-short screening instruments accurately detect depression in primary care? A pooled analysis and meta-analysis of 22 studies. Br J Gen Pract. 2007; 57(535): 144-51.

- Mouilso ER, Fischer S, Calhoun KS. A prospective study of sexual assault and alcohol use among first-year college women. Violence Vict. 2012; 27:78-94.

- Naimi TS, Brewer RD, Mokdad A, Denny C, Serdula MK, Marks JS. Binge drinking among US adults. Journal of the American Medical Association 2003; 289(1): 70–5.

- Newbury-Birch D, White M, Kamali F. Factors influencing alcohol and illicit drug use amongst medical students. Drug Alcohol Depend. 2000; 59(2): 125-30.

- Norman CD, Yip AL. eHealth promotion and social innovation with youth: using social and visual media to engage diverse communities. Stud Health Technol Inform. 2012; 172: 54-70.

- Oei TP, Morawska A. A cognitive model of binge drinking: the influence of alcohol expectancies and drinking refusal self-efficacy. Addict Behav. 2004; 29: 159-79.

- Olmstead TA, Ostrow CD, Carroll KM. Cost-effectiveness of computer assisted training in cognitive-behavioral therapy as an adjunct to standard care for addiction. Drug Alcohol Depend 2010; 110: 200–7.

- Paljärvi T, Koskenvuo M, Poikolainen K, Kauhanen J, Sillanmäki L, Mäkelä P. Binge drinking and depressive symptoms: a 5-year population-based cohort study. Addiction. 2009; 104(7): 1168-78.

- Patrick ME, Schulenberg JE, O'Malley PM, et al. Age-Related Changes in Reasons for Using Alcohol and Marijuana From Ages 18 to 30 in a National Sample. Psychology of addictive behaviors: journal of the Society of Psychologists in Addictive Behaviors. 2011; 25(2): 330-9.

- Plant MA, Plant ML, Miller P, Gmel G, Kuntsche S. The social consequences of binge drinking: a comparison of young adults in six european countries. Journal of Addictive Diseases 2009; 28(4); 294–308.

- Reed MB, Wang R, Shillington AM, Clapp JD, Lange JE. The relationship between alcohol use and cigarette smoking in a sample of undergraduate college students. Addict Behav. 2007; 32(3): 449-64.

- Reifman A, Watson K. Binge drinking during the first semester of college. J Am Coll Health 2003; 52: 73–81.

- SAMHSA - Substance Abuse and Mental Health Service Administration. Results From the 2011 National Survey on Drug Use and Health: Summary of National Findings. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2012. NSDUH Series H-45, HHS Publication No. (SMA) 12–4725.

- SAMHSA - Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. The NSDUH Report: Trends in Adolescent Substance Use and Perception of Risk From Substance Use. Rockville,

MD: Substance Abuse and Mental Health Service Administration; 2013. http://www.samhsa.gov/data/2k13/NSDUH099a/sr099a-risk-perception-trends.pdf

- Sanchez ZM, Martins SS, Opaleye ES, Moura YG, Locatelli DP, Noto AR. Social factors associated to binge drinking: a cross-sectional survey among Brazilian students in private high schools. BMC Public Health. 2011; 11:201.

- Siliquini R, Colombo A, Berchialla P, Bert F, TEN-D Group. Binge drinking and psychoactive drug use in a cohort of European youths. J Public Health Res. 2012; 1: e15.

- Slutske WS. Alcohol use disorders among US college students and their non-college-attending peers. Archives of General Psychiatry 2005; 62(3): 321–7.

- Soler-Vila H, Galàn I, Valencia-Martin JL, Leon-Muñoz LM, Guallara-Castillon P, Rodriguez-Artalejo F. Binge Drinking in Spain, 2008-2010. Alcohol Clin Exp Res 2013; 2: 1-10.

- Sønderlund AL, O'Brien K, Kremer P, Rowland B, De Groot F, Staiger P, Zinkiewicz L, Miller PG. The association between sports participation, alcohol use and aggression and violence: a systematic review. J Sci Med Sport. 2014; 17: 2-7.

- Stein LA, Katz B, Colby SM, Barnett NP, Golembeske C, Lebeau-Craven R, Monti PM. Validity and Reliability of the Alcohol Expectancy Questionnaire-Adolescent, Brief. J Child Adolesc Subst Abuse. 2007; 16(2): 115-27.

- Suffoletto B, Callaway CW, Kristan J, Monti P, ClarkDB. Mobile phone text message intervention to reduce binge drinking among young adults: study protocol for a randomized controlled trial. Trials. 2013; 14: 93.

- Sutfin EL, McCoy TP, Morrell HE, Hoeppner BB, Wolfson M. Electronic cigarette use by college students. Drug Alcohol Depend. 2013; 131(3): 214-21.

- Swahn MH, Simon TR, Hammig BJ, Guerrero JL. Alcohol-consumption behaviors and risk for physical fighting and injuries among adolescent drinkers. Addict Behav. 2004; 29: 959-63.

- Tanner-Smith EE, Lipsey MW. Brief alcohol interventions for adolescents and young adults: a systematic review and meta-analysis. J Subst Abuse Treat 2015; 51:1-18.

- Tao FB, Xu ML, Kim SD, Sun Y, Su PY, Huang K. Physical activity might not be the protective factor for health risk behaviours and psychopathological symptoms in adolescents. J Paediatr Child Health. 2007; 43: 762-7.

- Teunissen SC, de Graeff A, Voest EE, de Haes JC. Are anxiety and depressed mood related to physical symptom burden? A study in hospitalized advanced cancer patients. Palliat Med. 2007; 21(4): 341-6.

- Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic-explanatory continuum indicator summary (PRECIS): A tool to help trial designers. J Clin Epidemiol 2009; 62: 464e75.

- Tin ST, Ameratunga S, Robinson E, Crengle S, Schaaf D, Watson P. Drink driving and the patterns and context of drinking among New Zealand adolescents. Acta Pædiatr. 2008; 97: 1433–7.

- Toner CC, Broomhead CJ, Littlejohn IH, et al. Prediction of postoperative nausea and vomiting using a logistic regression model. Br J Anaesth. 1996; 76: 347–51.

- Townshend JM, Kambouropoulos N, Griffin A, Hunt FJ, Milani RM. Binge Drinking, Reflection Impulsivity, and Unplanned Sexual Behavior: Impaired Decision-Making in Young Social Drinkers. Alcohol Clin Exp Res. 2014; 38(4): 1143-50.

- Treno AJ, Gruenewald PJ, Lee JP, Remer LG. The Sacramento Neighbourhood Alcohol Prevention Project: Outcomes from a community prevention trial. J Stud Alcohol Drugs 2007; 68: 208–19.

- Viner RM and Taylor B. Adult outcomes of binge drinking in adolescence: findings from a UK national birth cohort. Journal of Epidemiology and Community Health 2007; 61(10): 902– 7.

- Warwick I, Chase E, Spencer G, Ingold A, Aggleton P. Young people and alcohol: meanings, practices and contexts. University of London. Institute of Education. Thomas Coram Research Unit 2009.
  http://www.alcohollearningcentre.org.uk/_library/Young_People_and_Alcohol_-_Meanings_Practices_and_Contexts.pdf

- Wechsler H, Davenport A, Dowdall GW, et al. Health and behavioral consequences of binge drinking in college: A national survey of students at 140 campuses. JAMA 1994; 272: 1672-7.

- Wechsler H, Dowdall GW, Davenport A, Castillo S. Correlates of college student binge drinking. Am J Public Health. 1995; 85(7): 921-6.

- Weisner C, Matzger H. A prospective study of the factors influencing entry to alcohol and drug treatment. Journal of Behavioral Health Services and Research 2002; 29: 126–137.

- Weitzman ER, Chen YY. Risk modifying effect of social capital on measures of heavy alcohol consumption, alcohol abuse, harms, and secondhand effects: national survey findings. J Epidemiol Community Health. 2005; 59(4): 303–9.

- Weitzman ER, Nelson TF, Wechsler H. Taking up binge drinking in college: the influences of person, social group, and environment. J Adolesc Health. 2003; 32(1): 26-35.

- World Health Organization. Global Status Report on Alcohol and Health.Geneva: WHO Press, World Health Organization; 2011. http://www.who.int/substance_abuse/publications/global_alcohol_report/msbgsruprofile.pdf

- Woicik PA, Stewart SH, Pihl RO, Conrod PJ. The Substance Use Risk Profile Scale: a scale measuring traits linked to reinforcement-specific substance use profiles. Addict Behav. 2009; 34: 1042-55.

- Wood MD, Read JP, Palfai TP, Stevenson JF. Social influence processes and college student drinking: the mediational role of alcohol outcome expectancies. J Stud Alcohol 2001; 62: 32–43.

- Wood SK, Eckley L, Hughes K, et al. Computer-based programmes for the prevention and management of illicit recreational drug use: a systematic review. Addict Behav. 2014; 39: 30–8.

- Wu LT, Kouzis AC, Leaf PJ. Influence of comorbid alcohol and psychiatric disorders on utilization of mental health services in the National Comorbidity Survey. American Journal of Psychiatry 1999; 156: 1230–6.

- Wu LT, Pilowsky DJ, Schlenger WE, Hasin D. Alcohol Use Disorders and the Use of Treatment Services Among College-Age Young Adults. Psychiatric Services 2007; 58(2): 192–200.

- Zeger SL, Liang KY, Albert PS. Models for longitudinal data: a generalized estimating equation approach. Biometrics 1988; 44: 1049–60.

Appendix 1

D-ARIANNA (Digital - Alcohol RIsk Alertness Notifying Network for Adolescents and young adults)

Questionnaire

Q1. You are

    a. Male   b. Female

Q2. How old are you?

    a. 16   b. 17   c. 18   d. 19   e. 20   f. 21   g. 22   h. 23   i. 24

Q3. What's your favorite thing to do on night out?

    a. Cinema   b. Clubs, parties   c. Pub   d. Other

Q4. Do you spend time volunteering?

    a. No   b. Yes

Q5. Do you study?

    a. No   b. Yes, in high school   c. Yes, in college/university

Q6. What's your grade point average?

    a. I don't study anymore   b. E-F   c. D   d. C

    e. B   f. A

Q7. Do you smoke?

    a. No   b. Yes

Q8. Have you used cannabis in the past 30 days?

    a. No   b. Yes

Q9. How many of your friends drink too much?

    a. Only a few   b. Most of them

Q10. In the last two weeks, have you ever had *4 (or 5)** drinks in a row?

                *5 if male; 4 if female

    a. No   b. Yes

Q11. Had you ever drunk more than a few sips of alcohol before you were 17?

    a. No   b. Yes

Q12. Does anyone in your family drink too much?

    a. No   b. Yes

Answer according to how much you agree or disagree

Q13. Would you say about yourself: "I often don't think things through before I speak."

a. Disagree strongly   b. Disagree somewhat   c. Agree somewhat   d. Agree strongly

Q14. Would you say about yourself: "I often involve myself in situations that I later regret being involved in."

a. Disagree strongly   b. Disagree somewhat   c. Agree somewhat   d. Agree strongly

Q15. Would you say about yourself: "I usually act without stopping to think."
a. Disagree strongly   b. Disagree somewhat   c. Agree somewhat   d. Agree strongly

Q16. Would you say about yourself: "Generally, I am an impulsive person."
a. Disagree strongly   b. Disagree somewhat   c. Agree somewhat   d. Agree strongly

Appendix 2

eReferences. Studies with data used for the model

- Beets MW, Flay BR, Vuchinich S, Li KK, Acock A, Snyder FJ, the Tobacco Etiology Research Network (TERN). Longitudinal patterns of binge drinking among first year college students with a history of tobacco use. *Drug Alcohol Depend.* 2009; 103(1-2): 1-8.

- Castellanos-Ryan N, Rubia K, Conrod PJ. Response Inhibition and Reward Response Bias Mediate the Predictive Relationships Between Impulsivity and Sensation Seeking and Common and Unique Variance in Conduct Disorder and Substance Misuse. *Alcohol Clin Exp Res*. 2011; 35(1): 140–55.

- Centers for Disease Control and Prevention. *National High School YRBSS 2003/2011 Data Files*. http://www.cdc.gov/healthyyouth/yrbs/data/index.htm

- Cranford JA, McCabe SE, Boyd CJ. A New Measure of Binge Drinking: Prevalence and Correlates in a Probability Sample of Undergraduates. *Alcohol Clin Exp Res*. 2006; 30(11): 1896–905.

- Digrande L, Perrier MP, Lauro MG, Contu P. Alcohol use and correlates of binge drinking among university students on the Island of Sardinia, Italy. *Subst Use Misuse.* 2000; 35(10): 1471-83.

- Donath C, Grässel E, Baier D, Pfeiffer C, Bleich S, Hillemacher T. Predictors of binge drinking in adolescents: ultimate and distal factors - a representative study. *BMC Public Health*. 2012; 12: 263.

- Eaton DK, Forthofer MS, Zapata LB, et al. Factors related to alcohol use among 6th through 10th graders: the Sarasota County Demonstration Project. *J Sch Health*. 2004; 74(3): 95-104.

- Engs RC, Hanson DJ, Diebold BA. The drinking patterns and problems of a national sample of college students, 1994. *Journal of Alcohol and Drug Education*. 1997; 41(3): 13-33.

- Friedel LK. *How are Personality, Implicit Behavioral Factors and Binge Drinking among Adolescents Related?* Essay (Bachelor), University of Twente, 2011. http://purl.utwente.nl/essays/60967

- Gallimberti L, Chindamo S, Buja A, et al, Underage drinking on saturday nights, sociodemographic and environmental risk factors: a cross-sectional study. *Subst Abuse Treat Prev Policy*. 2011; 6:15.

- Griffiths S, Lau JT, Chow JK, Lee SS, Kan PY, Lee S. Alcohol use among entrants to a Hong Kong University. *Alcohol Alcohol.* 2006; 41(5): 560-5.

- Hanewinkel R, Sargent JD, Poelen EA, et al. Alcohol Consumption in Movies and Adolescent Binge Drinking in 6 European Countries. *Pediatrics*. 2012; 129(4): 709-20.

- Hanewinkel R, Sargent JD. Longitudinal study of exposure to entertainment media and alcohol use among german adolescents. *Pediatrics.* 2009; 123(3): 989-95.

- Harakeh Z, de Looze ME, Schrijvers CT, van Dorsselaer SA, Vollebergh WA. Individual and environmental predictors of health risk behaviours among Dutch adolescents: the HBSC study. *Public Health*. 2012; 126(7): 566-73.

- Harrison EL, Desai RA, McKee SA. Non-daily Smoking and Alcohol Use, Hazardous Drinking, and Alcohol Diagnoses among Young Adults: Findings from the NESARC. *Alcohol Clin Exp Res*. 2008; 32(12): 2081–7.

- ISTAT - Istituto Nazionale di Statistica. *Uso e abuso di alcol in Italia - Periodo di riferimento: anno 2012.* http://www.istat.it/it/archivio/59033

- Jonas HA, Dobson AJ, Brown WJ. 2000. Patterns of alcohol consumption in young Australian women: socio demographic factors, health-related behaviours and physical health. *Aust N Z J Public Health*. 2000; 24(2): 185-91.

- Kim JH, Chan KW, Chow JK, et al. University binge drinking patterns and changes in patterns of alcohol consumption among chinese undergraduates in a Hong Kong university. *J Am Coll Health*. 2009; 58(3): 255-65.

- Maggs JL, Williams LR, Lee CM. Ups and downs of alcohol use among first-year college students: Number of drinks, heavy drinking, and stumble and pass out drinking days. *Addict Behav*. 2011; 36(3): 197-202.

- McGee R, Williams S, Kypri K. College students' readiness to reduce binge drinking: Criterion validity of a brief measure. *Drug Alcohol Depend*. 2010; 109(1-3): 236–8.

- Miller JW, Naimi TS, Brewer RD, Jones SE. Binge drinking and associated health risk behaviors among high school students. *Pediatrics*. 2007; 119(1): 76-85.

- Porter SR, Pryor J. The Effects of Heavy Episodic Alcohol Use on Student Engagement, Academic Performance, and Time Use. *Journal of College Student Development*. 2007; 48(4): 455-67.

- Rasic D, Kisely S, Langille DB. Protective associations of importance of religion and frequency of service attendance with depression risk, suicidal behaviours and substance use in adolescents in Nova Scotia, Canada. *J Affect Disord*. 2011; 132(3): 389-95.

- Sanchez ZM, Martins SS, Opaleye ES, Moura YG, Locatelli DP, Noto AR. Social factors associated to binge drinking: a cross-sectional survey among Brazilian students in private high schools. *BMC Public Health.* 2011; 11: 201.

- Schorling JB, Gutgesell M, Klas P, Smith D, Keller A. Tobacco, Alcohol and Other Drug Use among College Students. *J Subst Abuse*. 1994; 6(1): 105-15.

- Vickers KS, Patten CA, Bronars C, et al. Binge drinking in female college students: the association of physical activity, weight concern, and depressive symptoms. *J Am Coll Health*. 2004; 53(3): 133-40.

- Wechsler H, Davenport AE, Dowdall GW, Grossman SJ, Zanakos SI. Binge drinking, tobacco, and illicit drug use and involvement in college athletics. A survey of students at 140 American colleges. *J Am Coll Health*. 1997a; 45(5): 195-200.

- Wechsler H, Dowdall GW, Davenport A, Castillo S. Correlates of College Student Binge Drinking. *Am J Public Health*. 1995; 85(7): 921-6.

- Wechsler H, Fulop M, Padilla A, Lee H, Patrick K. Binge drinking among college students: a comparison of California with other states. *J Am Coll Health*. 1997b; 45(6): 273-7.

- Weitzman ER, Chen YY. Risk modifying effect of social capital on measures of heavy alcohol consumption, alcohol abuse, harms, and secondhand effects: national survey findings. *J Epidemiol Community Health*. 2005; 59(4): 303–9.

- Weitzman ER, Kawachi I. Giving means receiving: the protective effect of social capital on binge drinking on college campuses. *Am J Public Health*. 2000; 90(12): 1936-9

- Wickholm S, Galanti MR, Söder B, Gilljam H. Cigarette smoking, snuff use and alcohol drinking: coexisting risk behaviours for oral health in young males. *Community Dent Oral Epidemiol.* 2003; 31(4): 269–74.

Ringraziamenti