2014

ERAB
THE EUROPEAN FOUNDATION FOR ALCOHOL RESEARCH

REPORT 2014

EDITORIAL

This year has been marked by a number of important milestones for ERAB. Some of these are listed below. In 2014 ERAB has:

- funded seven new research projects which started in January and granted 10 more to start next year (see page 8);
- particularly encouraged applications on the subject of "lifestyle and drinking patterns" in the call for applications to ensure a more balanced representation across the spectrum of research, which has led to an increase in high quality applications in these important areas;
- received a record 59 applications;
- helped four young investigators to present their research at conferences;
- awarded one new publication award for publishing 5 or more papers as a result of ERAB funding;
- attracted some 75 delegates, both scientists and brewing sector representatives, to the 38th IMAG conference - restyled the International Meeting on Alcohol and Global Health, being the third of these conferences which ERAB has organised (see page 9);
- awarded ERAB's first "Lifetime Achievement Award" to mark its 10th Anniversary (see page 3); and
- been cited as a source of funding in 17 new publications in peer reviewed journals, bringing the total to date to 143, several of which are in top scientific journals with a high impact factor, demonstrating the quality of the science which ERAB is funding.

We would like to take this opportunity to thank:

- all members of both the Advisory Board and the Board of Directors for their help and support for ERAB;
- all grantees for their hard work on their research;
- all our reviewers for their dedicated efforts to help us decide which applications to fund;
- all our sponsors without whose commitment and contributions ERAB could not continue to make the substantial progress it has over the last eleven years.

Emeritus Professor Oliver James
Chairman of the ERAB Board of Directors

Emeritus Professor Philippe De Witte
Chairman of the ERAB Advisory Board

ERAB'S 10TH ANNIVERSARY LIFETIME ACHIEVEMENT AWARD

To mark its first 10 years ERAB asked for nominations for a lifetime achievement award. 7 excellent nominations were received, from Europe, Japan and the USA and the final decision as to who should receive the award was very difficult.

The Advisory Board's decision was that the recipient should be Professor Gianluigi Gessa, Emeritus Professor at the University of Cagliari. His award was €20,000 and this was announced at the International Meeting on Alcohol and Global Health (IMAG) Conference in Amsterdam in October.

His scientific career spanned more than 50 years and has made him an internationally recognized innovator and leader of modern "alcohology".
A brief summary of his outstanding career in the field of alcohol research follows:

- He discovered the stimulating effect of alcohol on the firing of dopamine "reward" neurons (*Brain Research 1985*);

- He discovered the electrophysiological and neurochemical changes of the dopamine system associated with withdrawal from alcohol (*Alcoholism: Clinical and Experimental Research (ACER) 1992; Proceedings of the National Academy of Sciences (PNAS) 1993*);
- He developed and validated animal models of alcoholism, including the Sardinian alcohol-preferring (sP) and -nonpreferring (sNP) rats (*Addiction Biology 2006*);
- At the beginning of the 1980s, using the line of sP rats, he discovered the efficacy of Sodium Oxybate (GHB) in the treatment of alcoholism. Subsequent clinical studies confirmed the efficacy of this drug in the treatment of Alcohol withdrawal syndrome (AWS), and in relapse prevention in alcohol use disorder (AUD) patients. GHB has been available in Italy for the treatment of alcoholism since 1992 and more recently in several European and South American Countries as the gold standard in the pharmacotherapy of alcoholism (*Lancet 1989; ACER 1992*);
- He described preclinical evidence of the anti-alcohol properties of the GABAB receptor agonist, baclofen (*ACER 2000; European Addiction Research 2013*); and clinical studies showing the efficacy of baclofen to increase abstinence and to prevent relapse in alcohol use disorder AUD patients (*ACER 2000; Alcohol and Alcoholism 2002*) as well as in the treatment of AWS (*American Medical Journal 2002; 2006*);
- He discovered the anti-alcohol properties of positive allosteric modulators of the GABAB receptor and the "second generation" of GABAB receptor ligands with therapeutic potential (*ACER 2012*);
- He described preclinical characterization of the anti-alcohol profile of multiple synthetic compounds [e.g., calcium channel antagonists (*ACER 1992*), cannabinoid receptor antagonists (*ACER 1998*) and extracts or active ingredients of medicinal herbs [e.g., Salvia miltiorriza, miltirone (*ACER 2006*)];
- Additionally he was Chief Editor for *Alcoholism: Clinical and Experimental Research (ACER)* between 1998 and 2000 and *Alcohol and Alcoholism* between 2001 and 2004.

Professor Giovanni Addolorato
Catholic University of Rome, Italy, Member of the ERAB Advisory Board

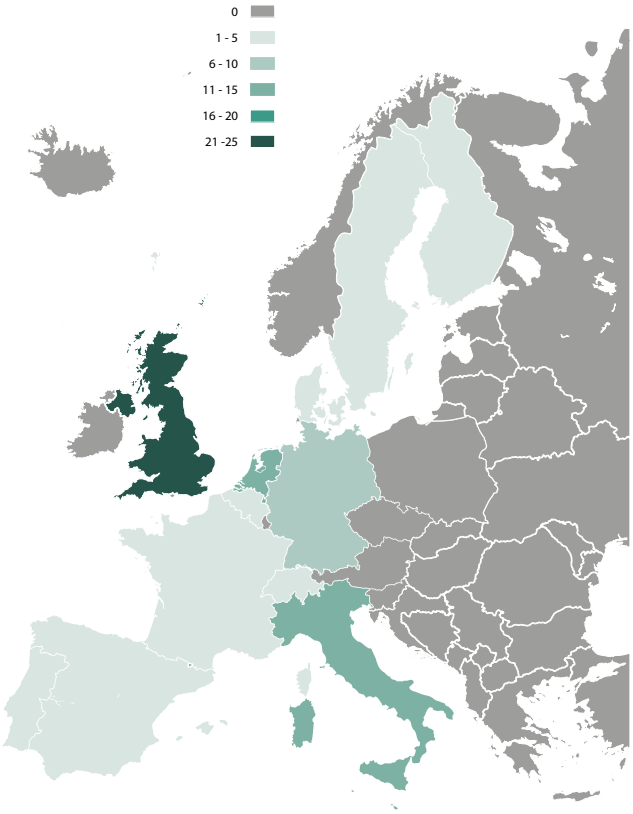
INTRODUCTORY INFORMATION

In 2003, the European Foundation for Alcohol Research (ERAB) was established in Brussels as an independent Charity to fund European biomedical and psychosocial research into the effects of beer and other alcohol beverages.

KEY PERFORMANCE INDICATORS 2003 - 2014

Total subscriptions 2003 to 2014	€ 5,426,887	
Total grant spend 2003 to 2014	€ 5,134,345	
Total Applications (funded)	440	(78)
Of the grants funded		
Number of two year grants	59	
Number of biomedical grants	45	
Number of psychosocial grants	33	
Number of publications citing ERAB	143	
Total Travel Award Applications (funded)	81	(57)
Total Exchange Award Applications (funded)	12	(9)
Number of Thesis Awards funded	4	
Number of Special Publication Awards funded	5	

To date, ERAB funded projects have been undertaken in 12 different EU countries: Belgium; Denmark; Finland; France; Germany; Italy; the Netherlands; Portugal; Spain; Sweden; Switzerland and the UK.



Map showing funding distribution 2003/4 - 2014/5

CONTRIBUTORS

Without the continued support of the European brewing sector, ERAB would not be able to continue to fund independent research into the biomedical and socio-behavioural aspects of alcohol consumption.

Subscriptions to ERAB have again been received from all 29 member associations of The Brewers of Europe and additionally from the four major brewers in Europe.

ERAB would like to thank all of its supporters for their sustained commitment and their recognition of the value of developing a better understanding of how alcohol affects health and behaviour:

- **APCV - Associação Portuguesa dos Produtores de Cerveja, Portugal**;
- **Asociatia Berarii Romaniei, Romania**;
- **Association of Hungarian Brewers, Hungary**;
- **Association of Slovene Brewers, Slovenia**;
- **Associazione degli Industriali della Birra e del Malto, Italy**;
- **Beer and Malt Producers´ Association of Turkey, Turkey**;
- **Belgian Brewers, Belgium**;
- **Brasseurs de France, France**;
- **Bryggeriforeningen, Denmark**;
- **Cerveceros de España, Spain**;
- **Croatian Chamber of Commerce Association of beer, malt and hop producers, Croatia**;
- **Cyprus Brewers Association, Cyprus**;
- **Czech Beer and Malt Association, Czech Republic**;
- **Deutscher Brauer-Bund e.V., Germany**;
- **Grants Committee of the British Beer & Pub Association and the Institute of Brewing & Distilling, UK**;
- **Fédération des Brasseurs Luxembourgeois, Luxembourg**;
- **Greek Brewers' Association, Greece**;
- **Lithuanian Brewers' Guild, Lithuania**;
- **Nederlandse Brouwers, The Netherlands**;
- **Norwegian Brewers, Norway**;
- **Panimoliitto, Finland**;
- **Slovak Beer and Malt Association, Slovakia**;
- **Sveriges Bryggerier AB, Sweden**;
- **Swiss Breweries´ Federation, Switzerland**;
- **The Irish Brewers' Association, Ireland**;
- **The Malta Chamber of Commerce, Enterprise and Industry, Malta**;
- **The Union of Brewing Industry Employers in Poland - Polish Brewers, Poland**;
- **Union of Brewers in Bulgaria (UBB), Bulgaria**;
- **Verband der Brauereien Österreichs, Austria**.

- **The Brewers of Europe**.

- **Carlsberg Breweries A/S**;
- **Heineken International B.V.**;
- **Anheuser Busch InBev N.V.**;
- **SABMiller Europe A.g.**

THE ERAB WEBSITE

The ERAB website includes; biographies of the members of both Boards; information about how to apply for grants and awards, including the deadlines; details of grants already funded; the publications resulting from these grants; and proforma report forms and a sample contract for grantees to download. It also provides links to the newsletters and other ERAB publications.
www.erab.org

NEWSLETTER

As well as the Annual Report, ERAB has an electronic newsletter which is sent to around 700 European scientists who have applied to ERAB for funding, or have helped with the peer reviews. Issues are kept short and are used to notify the research community about application deadlines and research applications which have been granted. This helps to maintain the visibility of ERAB and strengthen its profile. Copies of the newsletters are also available on the ERAB website
www.erab.org/newsletter

FINANCE

An average of five grants of up to €100,000 are funded each year, together with four or five travel awards, and one or two exchange awards. The research grant expenditure accounts for the majority of the annual budget.

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014*
	€	€	€	€	€	€	€	€	€	€
Industry contributions	445,000	425,000	535,000	535,000	474,000	473,073	522,997	520,772	530,772	530,772
Investment income	6,620	1,926	6,098	2,450	110	374	962	862	40	10
Donations								50,000	0	0
Expenditure										
Grants and Awards										
Grants	496,600	421,846	426,398	727,315	422,482	391,900	395,056	390,000	345,000	509,834
Awards	2,500	11,656	12,219	9,504	8,590	5,351	4,287	7,478	4,400	25,396
Projects							51,200	72,069	1,010	1,864
Sub Total	499,100	433,502	438,617	736,819	431,072	397,251	450,543	469,547	350,410	537,094
Other Expenditures										
Communications	9,334	5,310	17,017	5,490	9,638	12,944	12,000	12,015	12,648	5,987
Meetings and Conferences	33,838	19,222	32,371	13,696	17,078	22,538	24,000	9,260	7,318	33,285
Other	7,077	5,370	5,562	5,631	20,208	29,682	16,737	30,946	79,123	48,817
Total Expenditure	549,349	463,404	493,567	761,636	477,996	462,416	503,298	521,768	449,498	625,183
Assets carried over	329,470	231,742	195,264	242,795	0	0	0	49,866	81,314	103,664
Reserve					18,608	14,722	25,754	41,885	25,753	91,751
Endowment	25,000	25,000	25,000	25,000	25,000	25,000	25,000	25000	25,000	25,000

*provisional

BOARDS

ERAB has two boards: a Board of Directors, and an Advisory Board. The members of both Boards generously give their time and expertise without reward and ERAB is very grateful for this support.

BOARD OF DIRECTORS

ERAB's independence is guaranteed by a Board of Directors made up of a majority of public members. Their role is to administer the funds.

Public Members

Emeritus Professor Oliver F. W. James
Former Pro Vice Chancellor, Faculty of Medical Sciences, University of Newcastle-upon-Tyne, UK. **(Founder Member, Chairman)**.

Professor Daniel Bessa
COTEC, Portugal.

Count Rodolphe de Looz Corswarem
President of European Historic Houses Association.

Raymond Georis
Former Managing Director of the Madariaga European Foundation. **(Founder Member and Past Chairman of ERAB Board of Directors)**.

Dipl.-Ing. Markus Ferber
Member of the European Parliament.

Jean Martin
Former President of the European Confederation of the Food & Drink Industry.

Professor Mack Mitchell
ABMRF / The Foundation for Alcohol Research, USA.

Dr. Erik Skovenborg
Medical Doctor, Denmark.

Emeritus Professor Philippe De Witte
Université Catholique de Louvain-la-Neuve, Belgium. **Chairman of the ERAB Advisory Board.**

Janet Witheridge
ERAB: The European Foundation for Alcohol Research. **Secretary-General**.

Representatives of the Brewing Sector

Demetrio Carceller
President of The Brewers of Europe, Spain.

Morten Jensen
Carlsberg Group, Denmark.

Kieran Simpson
Heineken, The Netherlands.

Simon Jackson
Institute of Brewing and Distilling, UK.

Jacobo Olalla Marañón
Cerveceros de España, Spain.

Honorary Members (According to Article 6 of the By-Laws)

Dr. David Long MBE
Consultant, Former Director, Brewing, British Beer & Pub Association, UK.

Piero Perron
Former President of The Brewers of Europe. **(Founder Member)**.

Emeritus Professor Richard Smallwood
Former Commonwealth Chief Medical Officer (1999-2003), Australia.

ADVISORY BOARD

The members of the Advisory Board have a proven international independent scientific reputation. Their role is to examine the applications, suggest peer reviewers and, based on the reviews received, recommend to the Board of Directors which applications should be funded.

Emeritus Professor Philippe De Witte
Department of Biology, Université Catholique de Louvain-la-Neuve, Belgium. **Chairman**.

Professor Giovanni Addolorato
Department of Internal Medicine, Università Cattolica del Sacro Cuore, Rome, Italy.

Professor Christopher P. Day
Faculty of Medical Sciences, University of Newcastle-upon-Tyne, UK.

Associate Professor Ramon Estruch
Department of Internal Medicine, University of Barcelona, Spain.

Professor Wolfgang Koenig
Department of Medicine, University of Ulm, Germany.

Professor Pekka Sulkunen
Department of Sociology, University of Helsinki, Finland.

Professor Matty P. Weijenberg
Department of Epidemiology, Maastricht University, The Netherlands.

ERAB GRANTS

ERAB invites applications for funding European biomedical and psychosocial research into the effects of beer and other alcohol beverages. The applications are sent for peer review to experts (in the relevant subject) from all over the world. The recommendations as to which grants are funded are based on these reviews which give great emphasis to the scientific merit of the application. Grants are funded up to the maximum of €50,000 for one year or €100,000 over two years. After several years of particularly encouraging applications for research in the **psychosocial field**, in 2014, ERAB for the first time, particularly encouraged applications for research on **lifestyle and drinking patterns**.

Applications received by the April deadline are reviewed during the Summer. Applicants are notified in the Autumn with a view to the research starting in January the following year.

To date ERAB has funded 78 full grants - an average of 7 per year. Of these, seven were completed at the end of 2006, four at the end of 2007, three at the end of 2008, seven at the end of 2009, seven at the end of 2010, six at the end of 2011, five in 2012, eight in 2013 and six in 2014. Nine will complete in 2015, five in 2016 and seven in 2017. Four projects had to be discontinued due to poor health or other difficulties.

2014 GRANTS

At its fifteenth meeting on 13th October 2014, the ERAB Board of Directors agreed that the following ten research projects should receive funding during 2015 / 2016.

Name of Principal Researcher	Department	Institution	Town	Discipline / Grant length
Dr. Rita NEGRÃO	Faculty of Medicine	University of Porto	Porto, Portugal	Psychosocial / 2 year
	Changing lifestyle may prevent or revert pulmonary arterial hypertension			
Dr. Ina KONING	Faculty of Social & Behavioural Sciences	Utrecht University	Utrecht, The Netherlands	Psychosocial / 2 year
	More is caught than thought: A ground-breaking study on the role implicit parenting processes on adolescents' alcohol use			
Dr. Giovanni ARESI	Faculty of Psychology	Catholic University of the Sacred Heart	Milan, Italy	Psychosocial / 2 year
	Study abroad students' drinking behaviour: a mixed methods longitudinal study on social norms and sojourner adjustment			
Professor Isabelle SZMIGIN	Birmingham Business School	University of Birmingham	Birmingham, UK	Psychosocial / 1 year
	Lifestyle, social media and alcohol consumption			
Dr Richard Oliver DE VISSER	School of Psychology	University of Sussex	Falmer, UK	Psychosocial / 1 year
	Intervention to measure impact of using unit-marked glasses for alcohol consumption in adults			
Dr. Ascensión MARCOS	Institute of food Science Technology and Nutrition (ICTAN)	Spanish National Research Council	Madrid, Spain	Biomedical / 2 year
	Effects of alcohol consumption on gut microbiota composition in adults (ALMICROBHOL)			
Professor Matthew C. WRIGHT	Institute Cellular Medicine	Newcastle University	Newcastle Upon Tyne, UK	Biomedical / 2 year
	The effect of alcohol on the absorption and toxicity of food chemicals via the gut			
Dr. Janne Schurmann TOLSTRUP	National Institute of Public Health	University of Southern Denmark	Copenhagen, Denmark	Biomedical / 2 year
	Alcohol and bleeding in the general population			

PUBLICATIONS RELATING TO ERAB FUNDED RESEARCH

Grantees are encouraged to publish the results of their research in peer reviewed journals independent of ERAB, but are asked to acknowledge ERAB as the source of funding. ERAB monitors these publications and publishes a list on the website.

Up to the end of 2014, ERAB grantees have published the results of the research funded by ERAB in 142 papers in peer reviewed journals and more are in press. For a list of publications, visit http://www.erab.org/

The website also lists the number of publications in different journals together with the most recent calculation of the impact factor for each journal. This measures the average number of citations to recent articles in that journal. Many publications from ERAB-funded research have been published in high impact factor journals – an indication of the high quality of the science.

ERAB AWARDS

AWARDS FOR YOUNG RESEARCHERS

As well as providing major research grants, ERAB is keen to encourage young researchers to work in the field of alcohol research and offers a number of much smaller travel and exchange awards for researchers under the age of 35. The travel awards enable scientists to travel to conferences to present their data. The exchange awards allow periods of study / collaboration in centres of excellence anywhere in the world.

In addition to the above awards for young researchers, small awards are available to help publish relevant PhD theses.

PUBLICATIONS AWARD

In 2012, a new award was launched to acknowledge the outstanding scientific contribution made by some of its grantees. This "Publications Award" is for any former ERAB grantees who have had five or more papers, of three or more pages, published in peer reviewed journals with an acknowledgement of the funding received from ERAB. To date the average is just under 3 peer reviewed publications per grant.

38th IMAG MEETING

INTERNATIONAL MEETING ON ALCOHOL AND GLOBAL HEALTH AMSTERDAM – 13-14th OCTOBER 2014

INTRODUCTION

This 38th IMAG conference was organised by ERAB: the European Foundation for Alcohol Research. An open invitation attracted some 75 delegates; both scientists and brewing sector representatives. The speakers had been selected to provide expert overviews of key biomedical and psychosocial topics of relevance to both the medical community and, importantly, the brewing sector. This was the first IMAG designed to be readily accessible to a lay audience. Panel sessions had been introduced to encourage constructive and wide-ranging debate involving both the medical scientists and the brewing sector delegates.

The meeting was opened by Demetrio Carceller, President of The Brewers of Europe. He stressed the need for good science to inform the attitudes of consumers and policy makers. He considered that European brewers should be as proud of funding independent medical research as they were of the beers they brewed.

SESSION I
DRIVERS OF BEHAVIOUR

Professor Helene White (Rutgers University Centre of Alcohol Studies, USA) presented the social learning model which had been designed to explain how people learn to drink. This model proffers that drinking behaviour is based on a reciprocal interaction of alcohol effects, personal characteristics, and social environmental factors. A comprehensive analysis of this subject is provided in "Underage Drinking, a Report on Drinking in the Second Decade of Life in Europe and North America", edited by Philippe De Witte and Mack Mitchell Jr. (supported by ERAB and ABMRF/The Foundation of Alcohol Research).

Professor Marianne van den Bree (Cardiff University, UK) reported that her group, with ERAB funding, had found that experimentation with alcohol in the young is predominantly influenced by environmental factors, while progression to heavy/ problem use is mostly under the influence of genetic factors. Specific gene systems that have been implicated in the development of alcohol use disorder include those involved in: the breakdown of alcohol in the liver (metabolising genes); the rewarding effects of alcohol (reward pathway); and, stress regulation. However, there is also evidence that the environment interacts with alcohol-related genes, with evidence that low levels of parental monitoring, affiliation with a deviant peer group, or negative life events may be more likely to lead to alcohol problem-use in young people at higher genetic risk.

Professor Anneke Goudriaan (University of Amsterdam, The Netherlands) referred to the fact that impulsivity is an important construct in addiction that has been linked both to the development and continuation of addictive disorders such as alcohol dependence, gambling disorder, and drug dependence. The relation between executive functions, the abilities related to self-regulation of behaviour and addictive disorders and the directionality between cognitive functions and the influence of alcohol and other substances on the brain were highlighted.

The influence of pharmacological interventions on impulsivity, the potential value of non-invasive neuro-stimulation for addictive disorders and the effects of neuromodulation on emotion-regulation were presented.

Professor Jon Nelson (Pennsylvania State University, USA) indicated that numerous statistical studies and reviews had examined the role of alcohol advertising and alcohol prices as drivers of behaviour. Some policy models emphasized a possible role for population-level alcohol consumption. He summarized empirical studies and literature reviews that he had conducted. Issues examined included: effects of advertising bans; effects of alcohol marketing and advertising on youth initiation and consumption; effects of prices and taxes on binge drinking and other heavy drinking for adults, men vs. women, youth adults and youth; and, meta-analysis of alcohol price elasticities, with corrections for publication bias.

Conclusions drawn from these studies included the following:

- Advertising bans were shown to be not statistically significant in a sample of 17 OECD countries for 1975-2000, after controlling for prices, incomes, etc. An index of stringency for other alcohol policies was significant.
- Two reviews of youth studies found that:
  - longitudinal studies of alcohol marketing and advertising fail to adequately model advertising relationships and only 21 of 63 estimates were significant; and,
  - meta-analyses of youth drinking onset and behaviours were contaminated by publication bias. Corrected mean effect sizes for advertisements were insignificant or very small in magnitude.
- Three systematic reviews of binge/heavy drinking studies found these behaviours are not very responsive to changes in alcohol prices or taxes. Null results hold across gender and various age groups; e.g., only 3 of 18 studies for youth binge drinking found a significant effect of prices. This result also is supported by natural experiments (tax changes) and field studies.
- Three meta-analyses examined the price elasticity of demand by beverage with corrections for publication bias. Mean price elasticities were smaller by about 50% after corrections: beer (-0.20), wine (-0.40), spirits (-0.60), and total alcohol (-0.50).

He concluded that increases in prices will not reduce average population-level alcohol consumption by as much as claimed in some policy studies.

Session I Panel Discussion

It was noted that parents had an important role to play in influencing the attitude of their children towards drinking behaviour. However, a distinction should be drawn between authoritative and authoritarian parenting. It was advocated that parents should be strict but not administer punishment. It had been demonstrated that teaching rule-setting to parents (and to colleges) was particularly effective in influencing children not to start drinking as early as they otherwise may.

With regard to the impact of advertising on drinking behaviour, it was felt that a distinction should be drawn between responsible and irresponsible advertising (there are industry codes to ensure responsibility). It was suggested that some advertising could be positive in encouraging responsible consumption. It was acknowledged that internet advertising would become a growing area for future attention.

The robustness of social norming had been questioned by some commentators. However, it should be recognized that there were a number of different forms of social norming interventions. Whereas the use of posters and leaflets to raise awareness were of questionable value, interventions amongst college students had been shown to be very effective. In such studies, participants were asked how much alcohol they drank and how much they thought their peers consumed. The students tended to overestimate the amount that they thought others drank. When they were given feedback on the actual amount that their peers consumed (norm discrepancy information) this was effective in re-setting the norm and consequently reducing their consumption, particularly on a short-term basis.

This panel session highlighted the imperative for public health policies to be based on balanced science. It was felt that some public health scientists adhered to a perverse interpretation of the data they presented. Such scientists seemed to be particularly influenced by certain economic studies and were selective in the medical studies they cited. In the UK, there had been a proposal to introduce minimum pricing for alcoholic beverages. Studies of this proposal should be considered in the context that they were looking at the economics rather than health outcomes. There were a number of flaws in studies on population-level consumption control (dealt with in more detail in Session III below).

Concern was expressed that WHO Europe had referred to alcohol as the "new tobacco" and that the same controls as applied to tobacco (reduced availability and increased price) were proposed for alcohol. Balanced science did not seem to have the visibility it should have. In considering what more the brewing sector could do to be "part of the solution", it was strongly advocated that ERAB should continue to support independent research.

SESSION II
ALL CAUSE MORTALITY

Professor Wolfgang Koenig (University of Ulm Medical Centre, Germany) referred to the fact that large meta-analyses show a J-shaped association between alcohol intake and all-cause mortality in both genders and in various countries. Results from epidemiological research indicated that alcohol use increases the risk for many chronic diseases (liver disease, various cancers) and acute health consequences (e.g. traffic accidents), but a certain pattern of regular light-moderate drinking may have beneficial effects on coronary heart disease. Prior moderate alcohol consumption before an acute myocardial infarction (AMI) is associated with reduced mortality thereafter as well as long-term moderate alcohol intake after survival of an acute AMI. Currently, with regard to coronary heart disease, there seems to be no strong data to support a beverage specific preference regarding the beneficial effects of alcohol.

Professor Filipo Grea (Catholic University of Rome, Italy) reiterated that there was an inverse relationship between moderate alcohol consumption and vascular risk that has been shown in many epidemiological studies. The beneficial effects of moderate drinking on atherosclerosis have been attributed to changes in the lipoprotein profile and in the coagulation system as well as to induction of preconditioning (a potent form of endogenous myocardial protection).

After wine intake was suggested as a possible explanation for the lower than expected CHD mortality rates in France, many studies had addressed the question of whether different alcoholic beverages are equivalent in their protective effect.

Atherosclerosis is a disease in which the adhesion of monocytes to endothelial cells plays a pivotal early event in pathogenesis. It is worth noting that some compounds, such as flavonoids found in alcoholic beverages, can reduce this adhesion. In one study, TNF–induced adhesion of monocytes to endothelial cells was virtually abolished after red wine consumption but was only partially reduced after gin consumption. These findings raise the intriguing possibility that protective anti-inflammatory effects might be limited to specific alcoholic beverages. However, few data are available on the effects of various alcoholic beverages with different polyphenolic content on the early phases of atherosclerosis in humans.

Professor Chris Day (Newcastle University, UK) pointed out that whilst the vast majority of heavy drinkers will have steatosis (alcoholic fatty liver), only a minority will ever develop alcoholic steatohepatitis (ASH), fibrosis and cirrhosis. He asked the intriguing question as to why this should be.

Alcoholic liver disease (ALD) is best considered a complex disease trait. Genetic and environmental risk factors

for advanced ALD seem likely to include factors that influence the severity of steatosis and oxidative stress, the cytokine milieu, the magnitude of the immune response and/or the severity of fibrosis.

The dose and pattern of alcohol intake are important in ALD risk. There is an increased risk when drinking without food and/or when binge drinking (i.e. where the resultant BAC is higher). There seems to be an increased risk when drinking beer or spirits rather than wine (although this may be explained by other lifestyle factors). The largest risk factor is when the individual is overweight; the risk of cirrhosis being 10 times higher when drinking and being overweight. There is also increasing evidence of the importance of the role that gut bacteria (the 'microbiome") plays in increasing gut permeability with bacterial toxins reaching the liver.

Women develop ALD at lower levels of intake. This is partly due to the higher amount of body fat (since alcohol partitions into the water fraction thus resulting in a higher BAC). Oestrogen may also be involved by increasing gut permeability to endotoxins.

An interesting observation is that there is an inverse risk of ALD with those who consume alcohol and drink 4 or more cups of coffee a day (an 80% risk reduction).

Family studies and inter-ethnic variations in susceptibility suggest that genetic factors are also important in determining disease risk. A decade after first sequencing of the human genome, the development of technologies to support the comprehensive study of genomic variation has now begun to identify these factors; with the PNPLA3 gene (encoding adiponutrin) by far the most significant association reported thus far.

Professor Matty Weijenberg (Maastricht University, The Netherlands) referred to the fact that the International Agency for Research on Cancer had classified ethanol in alcoholic beverages as "carcinogenic to humans" (Group 1). In addition to upper digestive tract cancers (oral cavity, pharynx, larynx, and esophagus) and liver cancer, two of the most common cancers, breast and colorectal cancer, had now been added to the list of cancers causally related to alcohol.

She said that the strongest evidence for the carcinogenic effect of acetaldehyde, the first metabolite of alcohol metabolism, in humans is derived from observations in Asian populations. Acetaldehyde is metabolized by acetaldehyde dehydrogenase (ALDH) which is encoded by the ALDH2 gene. The ALDH2*2 allele, which is relatively common in Asian populations, results in an almost inactive ALDH enzyme, in turn resulting in accumulation of acetaldehyde and dramatically increased risk of cancer.

She advised that a considerable proportion of cancer cases can be attributed to alcohol consumption, especially consumption higher than the recommended upper limits. However, she pointed out that there were still numerous issues in the research field on alcohol and cancer that need to be addressed. These include studies of the effect of different drinking patterns, the role of different beverages, life-time consumption, and the definition of abstainers. Additionally, epidemiologic studies need to address residual confounding and effect modification by other lifestyle factors in more detail. Teasing out the role of genetic variation in genes involved in alcohol metabolism and in one-carbon metabolism in modifying cancer risk is also an insufficiently explored area. Accounting for tumour heterogeneity in future studies, may increase insights into alcohol-related carcinogenic pathways involved.

Professor Weijenberg advocated establishment of consortia and pooling of data in order to enlarge the sample sizes required to address these factors through further stratification of data.

Session II Panel Discussion

It was confirmed that there was a direct correlation between per capita consumption and incidence of ALD. The higher the per capita consumption in any country, the higher the incidence of ALD. Over time, ALD incidence increased and decreased in line with per capita consumption. In looking at the mechanisms of ALD, it was becoming evident that not only should the genetics of the individual be taken into account, but also those of the microbiome. This could be a fruitful area for future research. There was the consideration of 'good' v 'bad' microbiome. Alcohol from fermentation in the gut would increase permeability of endotoxins leading to inflammation and consequent damage in the liver. It was acknowledged that gene treatment would become an increasing target for research over the next decade.

Epidemiological studies supported the observation that moderate consumption of alcohol was associated with a reduction in cardiovascular risk. However, there were confounders to take into account. For example, those who consumed moderately were less likely to smoke and more likely to eat a healthier diet and take more exercise.

It was confirmed that binge drinking abolished the protective effect of moderate alcohol consumption both in terms of myocardial infarction and cardiovascular disease. In short, binge drinking abolishes ischemic pre-conditioning.

An increase in HDL cholesterol associated with alcohol consumption provided a functional mechanism for the CHD beneficial effect. However, this still remained an issue open to question; one that ERAB might consider funding.

There was a discussion on the trade off between alcohol consumption, cancer and cardiovascular disease. Whilst there was a "J shaped" relationship between alcohol and cardiovascular disease, there was an inverse relationship between alcohol consumption and cancer. Combining these two relationships resulted in a "U-shaped" curve.

Against this background, there was an interesting debate on the advice to be given by the medical community. With 1-2 drinks/day there was around 5% of attributable risk for certain cancers, but a 10-14% reduction in cardiovascular risk and all cause mortality. Advice from the WHO and WCRF was for countries to reduce per capita consumption. This might be considered to be disingenuous and, in fact, dishonest. Would it not be more appropriate to advise that, if an individual had a family history of cancer, they should be careful with regard to alcohol consumption but that if there was no such family history, consumption of 1-2 drinks/day could significantly reduce all cause mortality risk. Whereas, this view was not shared by everyone in the room, the discussion drew attention to the dilemma facing medical practitioners in offering balanced advice. It was added that advice to patients should include the caveat that 1-2 glasses / day could be beneficial to health if one did not smoke, since smoking abolished the positive effect of alcohol.

SESSION III INDIVIDUAL V POPULATION PREVENTION

Dr. Anu Katainen (University of Helsinki, Finland) highlighted the fact that alcohol-related problems are a major burden to population health especially in high and medium-income countries. A variety of methods for preventing such problems exist including population, local level and individual approaches to prevention, but these give rise to moral concerns.

Population prevention is based on price controls, rule enforcement of sales practices and restrictions on availability, sales and marketing. All advanced consumer societies face difficulties in implementing such policies as they restrict individual freedom of choice. On the other hand, the difficulty with individual prevention is that it relies on the "moral management of the self".

Mr. John C. Duffy (Edinburgh) reviewed the research on population-based approaches to alcohol-related harm; from the Ledermann theory developed in the 1950s to current proposals (in the UK) for a minimum unit price of alcohol, and associated statistical analyses.

The paradigm applied to population prevention is that: individuals consuming large amounts of alcohol experience high levels of alcohol-related harm; the proportion of these individuals in a population is positively correlated with average consumption; hence, reduction of average consumption will reduce alcohol-related harm.

However, this is tautological. Clearly, average consumption must be correlated with problems, since it is individuals with problems that increase the average. It does not follow, however, that average consumption is a 'problem' that needs to be addressed, but rather an indicator that might signal a need for further investigation.

Duffy pointed out significant statistical flaws in the Ledermann theory. This started from the idea that the amounts people consumed must always follow a particular mathematical distribution applying throughout the population. He said that this was untenable. He showed that various subsequent attempts to 'rescue' the theory by a number of economists were equally flawed.

Detailed critiques of examples from the literature in this area illustrated widespread misunderstandings of statistical concepts, spurious correlation and inappropriate applications of statistical methods.

With regard to minimum unit pricing, Duffy presented a detailed analysis of the 'Sheffield Model'. He referred to an exhaustive analysis of the faults of the 'Sheffield model' (Duffy, 2013, The price of a drink – too exactly? Flawed evidence for minimum unit pricing, 'Significance', 10, 2, 23-27).

Dr. Kari Poikolainen (Hjelt Institute, University of Helsinki, Finland) presented a further critique of population-based approaches to reducing the harms associated with excessive alcohol consumption. He considered that the scientific basis for the total consumption model is poor, because there are:

- periods where the national cure is worse than the disease;
- objections to the idea that countries drink;
- findings on the high risk of death among alcoholics but not among other drinkers;

- hypoelastic drinkers; and,
- no significant associations between the hardness of alcohol policy and an indicator of disease and premature death - the number of disability-adjusted life years due to alcohol-related diseases.

Normal consumers were price elastic. They decreased intake when price increased and supply was restricted. However, heavy drinkers were more inelastic. Alcoholics were the most hypoelastic drinkers.

From his detailed analysis, he concluded that:

- high prices and supply restrictions do not solve the problems of disease and premature death due to alcohol-related diseases;
- the total consumption model is just an excuse for high taxes and state alcohol monopolies; and,
- the main problem remains as how to deal with alcoholism.

He indicated that further evidence was presented in his book Perfect drinking and its enemies (Minneapolis; Mill City Press, 2014).

Session III Panel Discussion

This session had brought into question the value of population-based research. However, it was clarified that the scepticism was about research that did not 'know its own limitations'. The concern was about the misuse of statistics for political ends, rather than a criticism of the statistical tools themselves.

With regard to population-based research demonstrating a positive effect for alcohol, the panel accepted that moderate alcohol consumption had a positive effect, but there were questions around the 'quasi-accuracy' of this occurring at a specific number of drinks since the data were so variable. It was the pretence of numerical accuracy that was of concern. A more general approach was advocated to recognising alcohol problems (e.g. What is the status of the individual's health? Do they sleep well? What is their blood pressure? How do they feel? What is their family history? etc.)

SESSION IV HEALTH EFFECTS OF BEER, WINE AND SPIRITS

Professor Ramon Estruch (Barcelona University, Spain) reiterated that high alcohol consumption shows an increased risk of certain cancers, cirrhosis and death from accidents. Three or more drinks per day may increase the risk of heart disease, hypertension, stroke, obesity, hypertriglyceridemia, breast cancer, neurodegeneration, depressive disorders, weakening of bones, suicide and injuries. Binge drinking, defined by the NIAAA as drinking so much within ~2 h that blood alcohol concentration levels reach 0.08 g/dL (approximately four drinks for women and five for men), and heavy irregular drinking seem to counteract the protective cardiovascular effects of moderate alcohol consumption by increasing the risk of stroke and overall mortality.

However, although excessive alcohol consumption is unquestionably harmful at several levels, consistent epidemiological evidence has pointed out that moderate alcohol consumption (up to two drinks per day for men and up to one drink per day for women) is inversely associated with cardiovascular risk factors and cardiovascular events. In fact, several epidemiological studies have found an association between alcohol (ethanol) intake and a reduced risk of coronary heart disease and ischemic stroke, but in these epidemiological studies it is difficult to differentiate between the effects of ethanol from other non-alcoholic compounds of alcoholic beverages, mainly polyphenols, on the cardiovascular system.

There is evidence for a J-shaped association between wine or beer (but not spirits) consumption and vascular risk. However, dose-response curves from comparable studies have appeared to be substantially similar for wine and beer. One out of three people drinking an average daily amount of 25 grams of alcohol, as either wine or beer, appear to be maximally protected from the risk of suffering a fatal or non-fatal cardiovascular event.

Several randomized, crossover trials have shown that part of the protective effects of alcoholic beverages is due to the ethanol (increase in HDL cholesterol and an improvement in haemostatic factors) but also due to their content in polyphenols (decrease in blood pressure, improvement in glucose metabolism and reduction in oxidative stress and inflammatory parameters related to atherosclerosis).

However, although there is increasing evidence on the beneficial effects of moderate alcohol consumption on health, without data from large randomized clinical trials which evaluate hard end-points (cardiovascular death, myocardial infarction and stroke), he considered that it was unclear how a physician could be in a position to advise his or her patients.

Dr. Diewertje Sluik (Wageningen University, The Netherlands) had conducted a systematic literature

review of 14 cross-sectional and 2 ecological studies from the United States and Europe. Her team had found that individuals with a beer or spirit preference displayed less healthy dietary habits. A wine preference was strongly associated with a healthier diet in Western populations, but to a lesser extent in Mediterranean countries.

Within the Dutch National Food Consumption Survey, they had observed among 2,100 adults, individuals who preferred beer (18%) had a higher intake of meat, soft drinks, margarine and snacks; whilst those who preferred wine (20%) had a higher intake of healthy foods. However, after correcting for several lifestyle and socio-demographic factors, overall diet quality did not differ between categories of alcoholic beverage preference.

It was concluded that the preference for a specific alcoholic beverage was mainly associated with cultural, social, demographic, and personal factors including diet. It may not be the alcoholic beverage, but the underlying lifestyle patterns and socio-demographic factors that are related to health outcomes.

Professor Rosa M. Lamuela-Raventós (University of Barcelona, Spain) reported that her team had observed that polyphenols seemed to play an important role in the prevention of cardiovascular events and in reduced mortality within the PREDIMED population.

One drink of red wine (150 mL) or beer (330 mL) contains 300 mg and 92 mg of total polyphenols, respectively. These polyphenols may contribute to the total polyphenol effect observed in the prevention of cardiovascular events and reduction of mortality. Moreover, in some European populations, beer and wine represented the major food contributors of some polyphenols such as stilbenes and hydoxybenzoic acids, respectively and these compounds significantly decreased mortality and cardiovascular events. She concluded that moderate consumption of wine and beer, in combination with a healthy life style, may contribute to the decrease of the ongoing effects of chronic diseases and mortality.

Session IV Panel Discussion

Discussion centered on the potential importance of polyphenols. Whereas the observed positive effect had been largely focused on resveratrol in red wine, it was noted that there were some 47 polyphenols in beer. In fact, recent research, funded by ERAB, had characterised 7 new polyphenols in beer. It had been suggested that there were some 92 mg of polyphenols present in beer compared to 48 mg in white wine. It was agreed that bioavailability remained a key issue to be adressed.

Reference was made to the health effects of relative strengths of alcoholic beverages. Recent research by Professor Mack Mitchell and colleagues had quantified the BAC levels associated with consumption of different alcoholic beverages. It was considered that the area under the BAC peak was a more important parameter than the peak level per se. It was agreed that more work needed to be carried out in this area.

Alcohol consumption was only part of a healthy lifestyle. There was a need to focus on the lifestyle as a whole in future research.

Conclusions

The new format proved to be very successful in attracting and engaging delegates from both the medical and brewing communities. The latter were given clear and concise overviews of the health harms associated with excessive consumption of alcohol. They were also provided with the evidence for health benefits associated with moderate consumption. There was a balanced debate on individual and population-based interventions to address health harms. The success of this new format was aided by the balanced and open approach taken by the presenters. Whilst adhering to the key principle of scientific independence, they did not necessarily reflect the views of the "public health community" as expressed through what the WHO or the OECD commonly refers to as "best buys" in respect of health policy. During the course of the meeting, a number of new avenues for research were identified.

The presentations have been posted on the ERAB website.

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