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#### Review

# Semen quality and alcohol intake: a systematic review and meta-analysis

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#### **KEY MESSAGE**

The adage 'the dose makes the poison' is relevant when considering the relationship between alcohol intake and semen quality. High levels of alcohol intake do appear to be associated with changes in semen that may affect fertility, but this review finds no evidence for negative effects of occasional alcohol intake.

#### ABSTRACT

Alcohol consumption is widespread in the Western world. Some studies have suggested a negative association between alcohol intake and semen quality although others have not confirmed this. MEDLINE and Embase were searched using 'alcohol intake' OR 'alcohol consumption' OR 'alcohol drinking' OR 'lifestyle' combined with 'semen quality' OR 'sperm quality' OR 'sperm volume' OR 'sperm concentration' OR 'sperm motility' for full-length observational articles, published in English. Reference lists of retrieved articles were searched for other pertinent studies. Main outcome measures were sperm parameters, if provided as means (standard deviation or standard error) or as medians (interquartile range). Fifteen cross-sectional studies were included, with 16,395 men enrolled. Main results showed that alcohol intake has a detrimental effect on semen volume (pooled estimate for no/low alcohol consumption 0.25 ml, 95% CI, 0.07 to 0.42) and normal morphology (1.87%, 95% CI, 0.86 to 2.88%). The difference was more marked when comparing occasional versus daily consumers, rather than never versus occasional, suggesting a moderate consumption did not adversely affect semen parameters. Hence, studies evaluating the effect of changes on semen parameters on the reproductive outcomes are needed in advance of providing recommendations regarding alcohol intake other than the advice to avoid heavy alcohol drinking.

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#### Introduction

Alcohol consumption is widespread in the Western world. In Europe, according to the latest published data (Eurobarometer, 2010), an average 76% of citizens had consumed alcoholic beverages in the past 12 months, with proportions rising from the south (the lowest, 58%, in Portugal) to the north (the highest, 93%, in Denmark). In the USA (NIH, 2013), 70.7% of citizens were reported to have drunk alcohol in the past year and 56% to have drunk alcohol in the previous month.

Moderate alcohol consumption has been associated with reduced mortality and morbidity, albeit not consistently. Excessive alcohol intake, on the other hand, has a negative impact on health (e.g. coronary heart disease, stroke and liver disease) (Dawson et al., 2008; Farke and Anderson, 2007).

Some studies have also suggested a negative association between alcohol intake and semen quality (Gaur et al., 2010; Martini et al., 2004; Muthusami and Chinnaswamy, 2005; Stutz et al., 2004) although others did not confirm these findings (Hansen et al., 2012; López Teijón et al., 2007). In this context, it is difficult to make comparisons across studies, because populations as well as alcohol intake vary considerably among them. In addition, most studies only addressed average alcohol intake by use of a few questions, and within response categories consumption may vary considerably and is likely to be under-reported.

Mechanisms involved in association between alcohol consumption and reduction of semen quality have been suggested to be related to a direct adverse effect on both testosterone metabolism and spermatogenesis. The ratio between free oestradiol and free testosterone is modified by alcohol intake (Hansen et al., 2012) and spermatogenetic arrest and Sertoli-cell-only syndrome were found to be more frequently associated with high alcohol consumption (Pajarinen et al., 1996).

To summarize the currently available information, we conducted a systematic review and a meta-analysis of epidemiological data from observational studies on the relationship between alcohol consumption and semen quality.

#### Materials and methods

#### Identification of studies

We carried out a literature search of all observational studies published or in press as original articles in English, up to April 2016. We searched the electronic databases MEDLINE (1966 to 10 April 2016) and Embase (1985 to 10 April 2016) using 'alcohol intake' OR 'alcohol consumption' OR 'alcohol drinking' OR 'lifestyle' combined with 'semen quality' OR 'sperm quality' OR 'sperm volume' OR 'sperm concentration' OR 'sperm motility' (limit: 'human'). Furthermore, we reviewed reference lists of retrieved articles to search for other pertinent studies.

Two authors (ER and ABS) reviewed the papers and independently selected the articles eligible for the systematic review. Studies were selected for the review if they met all of the following criteria: observational studies reporting original data; parameters of semen quality provided as means and standard deviation (SD) or standard error (SE) or as medians and interquartile range (IQR); full-length articles, published in English. If multiple published reports from the same study were available, we included only the one with the most detailed information, or the more recently published.

#### **Quality of studies**

Study quality was independently evaluated by two reviewers using the STROBE checklist (von Elm et al. 2008).

#### Data collection for meta-analysis

Data were extracted independently by two investigators and discrepancies were resolved by discussion. For each study, the following information was collected in a standard form: first author's last name; year of publication; country of origin; number of subjects; mean age, if available; category of alcohol consumption, if available; mean and SD (or SE) or median and IQR; covariates adjusted for in the statistical analysis.

#### Statistical analysis

The inverse variance method was used to pool the mean difference. If data were provided as median and IQR these measures were transformed into mean and SD as indicated in the Cochrane Handbook (Higgins and Green, 2011). Estimates of the average effect of alcohol on semen parameters and 95% confidence intervals (CI) were calculated by using both fixed-effect and random-effect models. If the test for heterogeneity (apparent diversity in mean differences across studies) was significant, we presented the results of the random-effect model. Otherwise, estimated results based on a fixed-effect model were presented. If a study had two or more alcohol intake levels, an overall estimate was calculated to include the study in the ever vs never comparison (Higgins and Green, 2011).

Funnel plots and Egger's tests of all the measures were performed to detect publication bias.

## Subgroup analyses

We planned two subgroup analyses, by level of alcohol intake and by type of men included in the study (fertile men, infertile men, unknown fertility status).

All analyses were performed using Review Manager (RevMan; computer program, version 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark, 2014).

## Results

Running the search as in Materials and methods, we found 148 papers in MEDLINE and 200 in Embase, 169 of which were also recorded in MEDLINE, giving 31 more papers only present in Embase (Figure 1). Two authors read the abstracts of the 179 papers identified in the search. Out of these 104 were excluded for the following reasons: seven focused on fecundity, 10 on pregnancy outcome, 11 were laboratory studies, 30 considered exposure to chemicals, 16 were reviews or commentaries and 30 explored different issues such as time trend in semen quality, comparison between populations, methods to predict semen alterations, relationship between semen quality and mortality, effect of surgery or congenital defects or several diseases on sperm parameters, alternative medicine, or were intervention studies. The full text of the remaining 75 papers was retrieved for evaluation.

Among 75 papers read in full text, 60 articles were excluded for the following reasons: 30 reported that alcohol intake was adjusted

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