

# Association of alcohol per capita (APC) with national, regional, and global prevalence of alcohol use during pregnancy: a systematic review and meta-analysis

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## Abstract

Alcohol is a teratogen that crosses the placenta. While studies have estimated the global burden of alcohol use in pregnancy, reliable and valid data on alcohol consumption during pregnancy in many countries is lacking. Alcohol consumption per capita (APC) data is available worldwide. This systematic review investigates the association between APC and alcohol consumption in pregnancy by country, to evaluate the validity of using APC data to predict the prevalence and examine the outcome of alcohol exposed pregnancies. This study updates a review by Popova et al. 2017 on the prevalence of alcohol consumption in pregnancy and the prevalence of Fetal Alcohol Syndrome (FAS). A systematic search of MEDLINE identified 112 unique articles meeting inclusion criteria, 17 included FAS prevalence, published since 2015 to update the original systematic review. APC data by year available from the World Health Organisation by country was assigned to all review articles. A meta-analysis, assuming a random effects model was performed. Sensitivity analyses were conducted. Studies represent data from 1989-2020 from 6 WHO regions. Preliminary analysis shows a statistically significant correlation between prevalence of alcohol consumption during pregnancy and population APC. Publicly available data on APC can inform research into the epidemiology of congenital anomalies.

## Introduction

**Estimate of persons born each year in Ireland with FASD.** The best estimate available, based on 58,443 births in ROI in 2021, suggests that 526 babies were born in Ireland with FAS (Fetal Alcohol Syndrome) in 2021 and that a further 2715 babies were born that year with (non-FAS) Fetal Alcohol Spectrum Disorder. These numbers are reflected in the number of children in receipt of Special Needs Assistance in Irish primary and secondary schools.<sup>1</sup> The numbers are reflected in the referral rate to the HSE Child and Adolescent Mental Health Service.<sup>2</sup>

**Prenatal alcohol is harmful to the foetus.** The US Institute of medicine (IOM) in its report to Congress in 1996 concluded "that FAS (*Fetal Alcohol Syndrome*), ARBD (*Alcohol Related Birth Defect*), and ARND (*Alcohol Related Neurodevelopmental Disorder*) are a completely preventable set of birth defects and neurodevelopmental abnormalities, that FAS is arguably the most common known non-genetic cause of mental retardation, and that FAS, ARBD, and ARND constitute a major public health concern."<sup>3</sup> Alcohol fulfils causal criteria as the cause of Foetal Alcohol Syndrome.<sup>4</sup>

**The Null Hypothesis is not biologically plausible.** There is no evidence based safe amount of alcohol in pregnancy. The risk to the fetus from prenatal alcohol exposure is very high. It only takes 67 women to consume alcohol in pregnancy for one child to be born with FAS.<sup>5</sup> It only takes 13 women to drink alcohol while pregnant for a child to be born with a (non-FAS) Fetal Alcohol Spectrum Disorder (FASD).<sup>6</sup> These are the population average risks. When more alcohol is consumed during pregnancy the individual risk is higher. When less alcohol is consumed during pregnancy the individual risk is lower. "All things are poison, and nothing is without poison; the dosage alone makes it so a thing is not a poison." Paracelsus, 1538

**Cycle and recycle of alcohol in utero.** Alcohol crosses the placenta providing a complete pathway of exposure from maternal blood alcohol to the fetus. The infant's metabolic capacity to process alcohol (via liver alcohol dehydrogenase) is approximately 20% that of the mother

## Introduction contd.

at birth, rising to about 40% at 6 months, whereas that of the fetus is about 3-4%.<sup>7</sup> From about 12 week's gestation, the fetus swallows and excretes amniotic fluid, with recycle of tainted amniotic fluid. In Ireland, it's the social norm to drink including when pregnant.<sup>8</sup> This is a societal factor exposing the foetus to risk.

**Biological variability factors in the mother.** The rate at which individuals breakdown alcohol varies by a factor of eight.<sup>9</sup> This is a genetic component to risk. The rate of metabolism of alcohol varies by other factors including the speed of intake, whether taken with or without food, one's body composition, the frequency of intake, the amount consumed, one's state of health.<sup>10</sup>

**Biological variability factors in utero and the foetus.** A National Geographic article of February 1992 on Fetal Alcohol Syndrome (FAS) featured a photo of fraternal twins from France aged 5 months. One twin reportedly had severe FAS, while the other was mildly affected. The in utero fate of multiple births vary by foetus. Even identical twins are not born with an identical birthweight.

**Fetal risk from alcohol exposure throughout the whole of pregnancy.** The brain continues to develop throughout pregnancy. Persons with acquired brain injury (ABI) experience some recovery with abstinence.<sup>11</sup> Maternal abstinence from alcohol is of benefit at all stages of pregnancy.

**Diagnosis of FASD.** There is no register of FAS or FASD in Ireland. International Guidelines require confirmation of alcohol use in pregnancy for diagnosis. This limits ascertainment as there is generally no screening for alcohol in pregnancy.

## Method

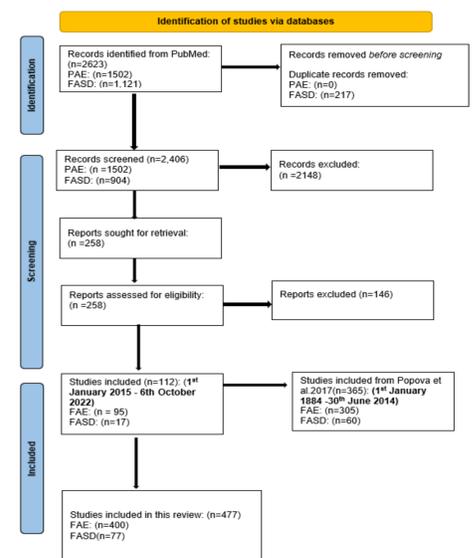
To update the 2017 review by Popova et al, we conducted a systematic search of MEDLINE from 2015 through 6th October 2022 to identify additional articles published since 2015 which report on prevalence of alcohol consumption in pregnancy and the prevalence of FAS. Two authors independently screened titles, abstracts, full-text articles and performed data extraction and quality assessment. APC data by year was downloaded from the World Health Organization website for each country and assigned to corresponding articles. A meta-analysis, assuming a random effects model was performed. Sensitivity analyses, including restricting by population, timing of exposure, time and method of ascertainment of alcohol consumption were done.

## Results

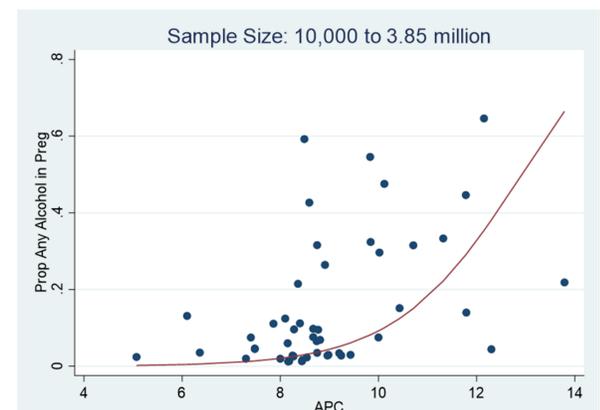
Of 1,502 PAE and 1,121 FAS prevalence articles identified, 95 PAE studies and 17 FAS studies met the inclusion criteria. Studies represent data from 1989-2020 from all 6 WHO regions, with APC between 3.07-10.87. The majority of studies used self-reported measures, with some using validated tools. Whilst the minority used direct measurement, through breathalyser tests, foetal meconium analysis or blood tests. Studies ranged in design and size, from local cross-sectional analyses, to national birth cohort studies. Preliminary analysis suggested a statistically significant correlation between prevalence of alcohol consumption during pregnancy and APC.

The updated systematic review represents data from 400 PAE and 77 FAS unique studies from 1959-2020 from all 6 WHO regions, with APC between 0.012-14.78. These studies alone met inclusion criteria from the 25,935 PAE and 12,321 FAS prevalence articles identified and screened.

## PRISMA flow Diagram



## Correlation between country prevalence (proportion) of alcohol consumption in pregnancy by APC \_ sample size



## Discussion

Cases of FASD are a hidden harm of alcohol, a major determinant of a population's physical, social and mental health. Fetal alcohol syndrome is widely under-reported worldwide. This preliminary analysis shows that population measurements of APC are associated with levels of alcohol consumption in pregnancy and therefore also associated with the prevalence of fetal alcohol syndrome. The World Health Organisation publishes the APC level for each country annually. Therefore these readily available measures could be used to approximately predict the prevalence of fetal alcohol syndrome in different countries and enables the comparison of the effectiveness of any policies aimed at reducing alcohol consumption.

A population's alcohol use is measured by the World Health Organisation measure APC. The European WHO region reports a male APC of 16 litres pure alcohol per annum, a female APC of 4.4 litres p.a. The country's APC level indicates what percentage of the population drink alcohol above low risk guidance.

## Conclusions

If the APC can be used to indicate the level of alcohol use in pregnancy this opens up the opportunity to estimate the prevalence of alcohol related birth defects and neurodevelopmental outcomes of children in all countries of the world.

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