



Association of preconception paternal alcohol with offspring development and pregnancy outcomes: A systematic review and meta-analysis

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Introduction



- There is growing evidence that paternal alcohol use during the preconception period may be linked to offspring and pregnancy related outcomes.

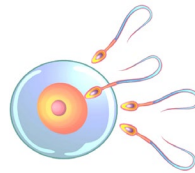
Paternal preconception drinking



Maternal drinking



Germ cell quality



Pregnancy outcomes

Fertility



Pregnancy loss
Gestational age



Physical health

- Physical defects
- Cancer
- Growth



Offspring outcomes

Socio-emotional

- Behavioural
- Cognitive

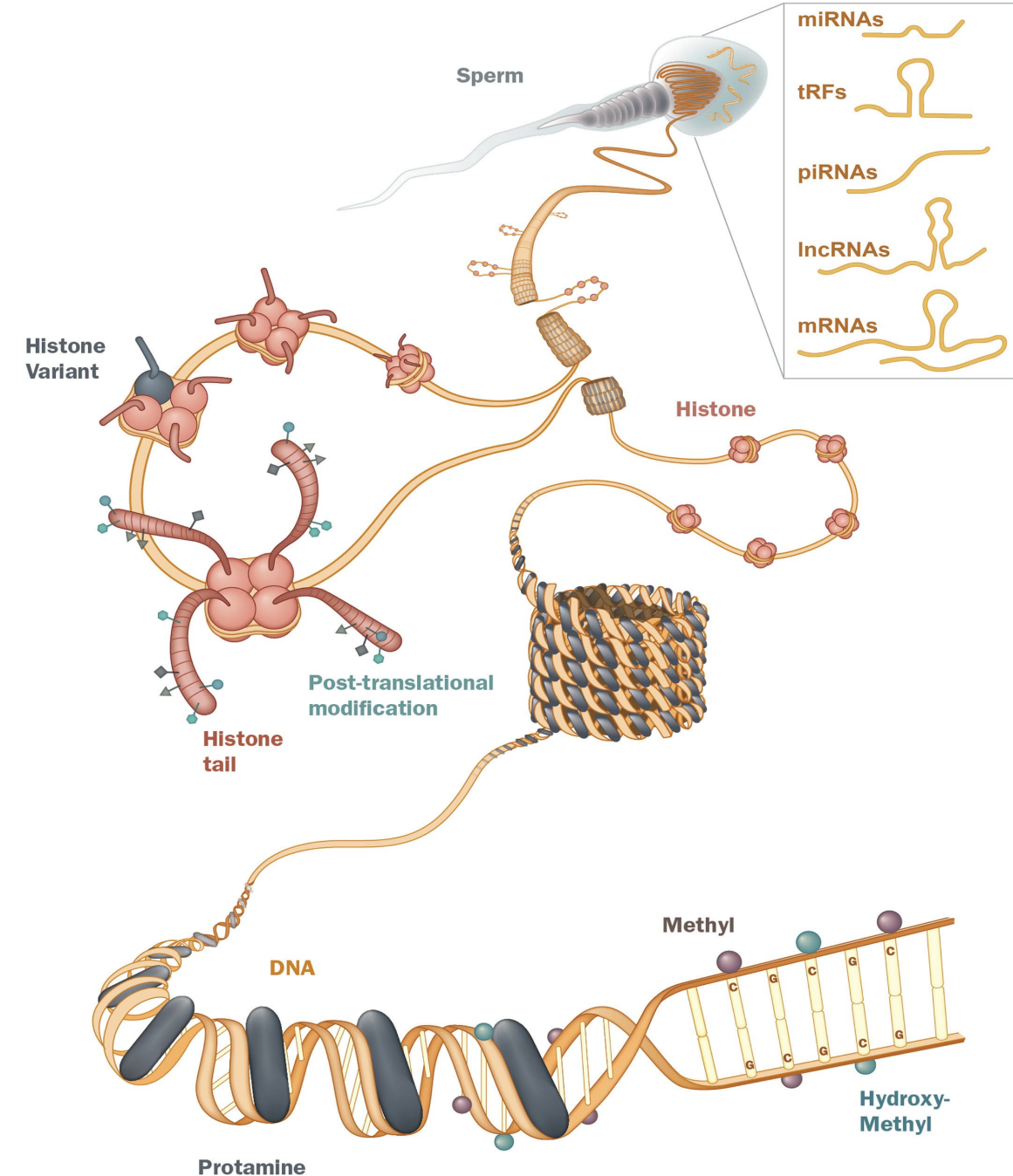
Alcohol-related outcomes

- Early alcohol experience
- Problematic alcohol use



Introduction

- Alcohol and its metabolite have mutagenic properties with a growing body of evidence implicating genotoxicity and cellular damage.
- Epigenetic mechanisms in the male germline have been suggested to occur when exposed to alcohol in rodent models.
- Despite this evidence, there is currently no comprehensive synthesis of the literature on paternal alcohol use during this period and the association with offspring developmental outcomes.



Aims



- This systematic review aims to examine the research evidence on the relationship of preconception paternal alcohol use with a range of outcomes, spanning fertility, pregnancy and offspring development.

Definitions	Description
Preconception	Human fathers' alcohol use any timepoint prior to conception, with most literature focused on adulthood and the months proximal to conception.
Exposure	Variables included any alcohol use vs. none, quantity (e.g. drinks per occasion, drinks per week), risky use/dependence (e.g. binge drinking frequency; >14 drinks per week).
Outcomes	<u>Offspring outcomes:</u> • Physical health – Physical defects, cancers, weight/growth • Psychosocial – Behaviour, cognitive, socio-emotional • Alcohol-related – Early alcohol experience, problematic alcohol use <u>Pregnancy outcomes:</u> • Fertility – Gamete quality, delays to conception • Pregnancy – Spontaneous abortion, recurrent miscarriage, maternal alcohol use

Methods



- A literature search was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines
 - MEDLINE, Embase, PsycINFO and CINAHL databases were searched (up to Nov 2022)
- Analyses:
 - Multilevel mixed-effects meta-regression in Stata 18 for studies that reported an effect size
 - Combined p -value analysis weighted for sample size to account for studies that only report p -values

Characteristics of studies (N=62)

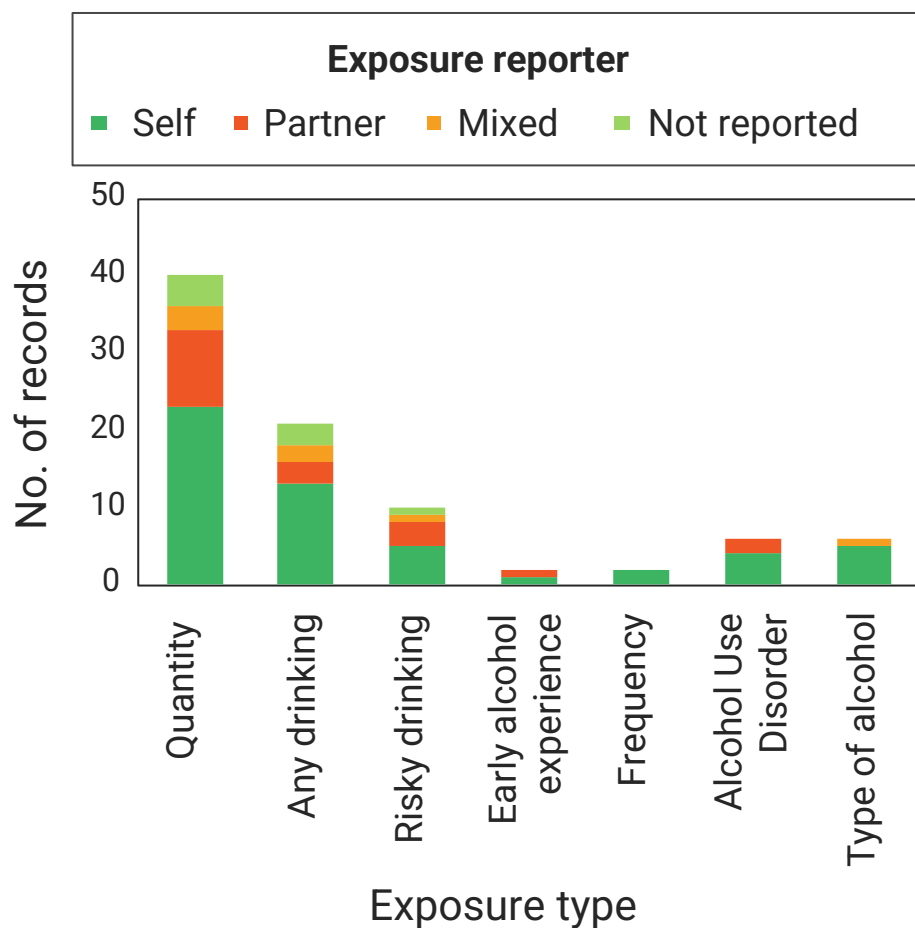


- Quality of the evidence was rated as moderate overall, but variability was evident (e.g., better quality for sample selection, poorer quality for prospective designs).
- Publications dated back to 1990, with an increasing number of publications from 2015.
- Proportions of longitudinal studies has been increasing since 2010.
- Studies largely from Europe (34%), North America (31%) and Asia (19%)

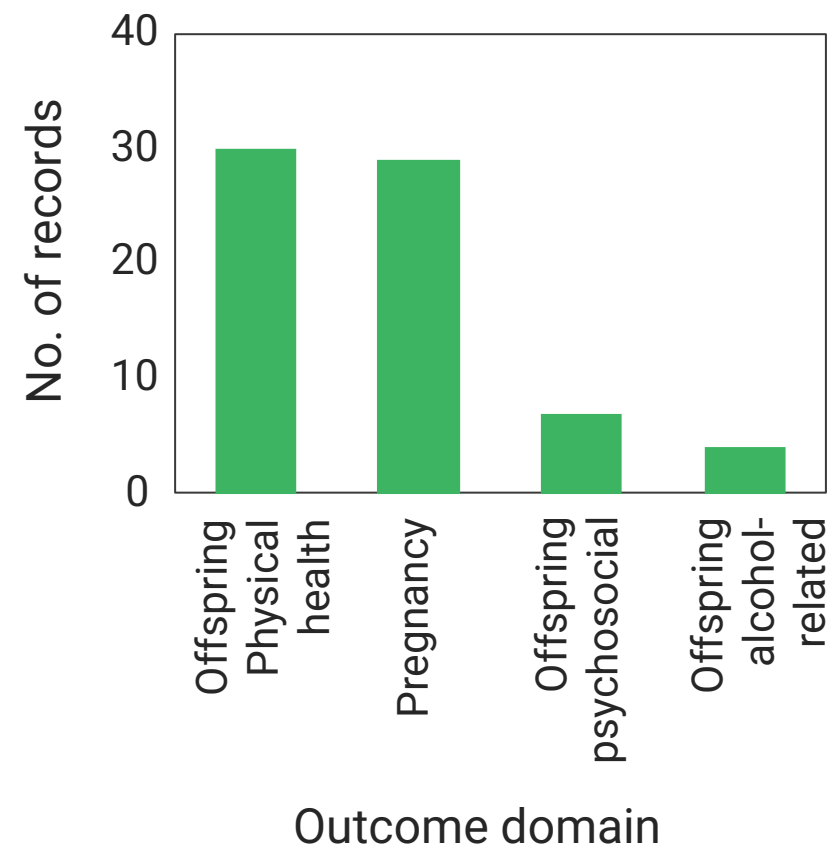
Exposure and outcome characteristics



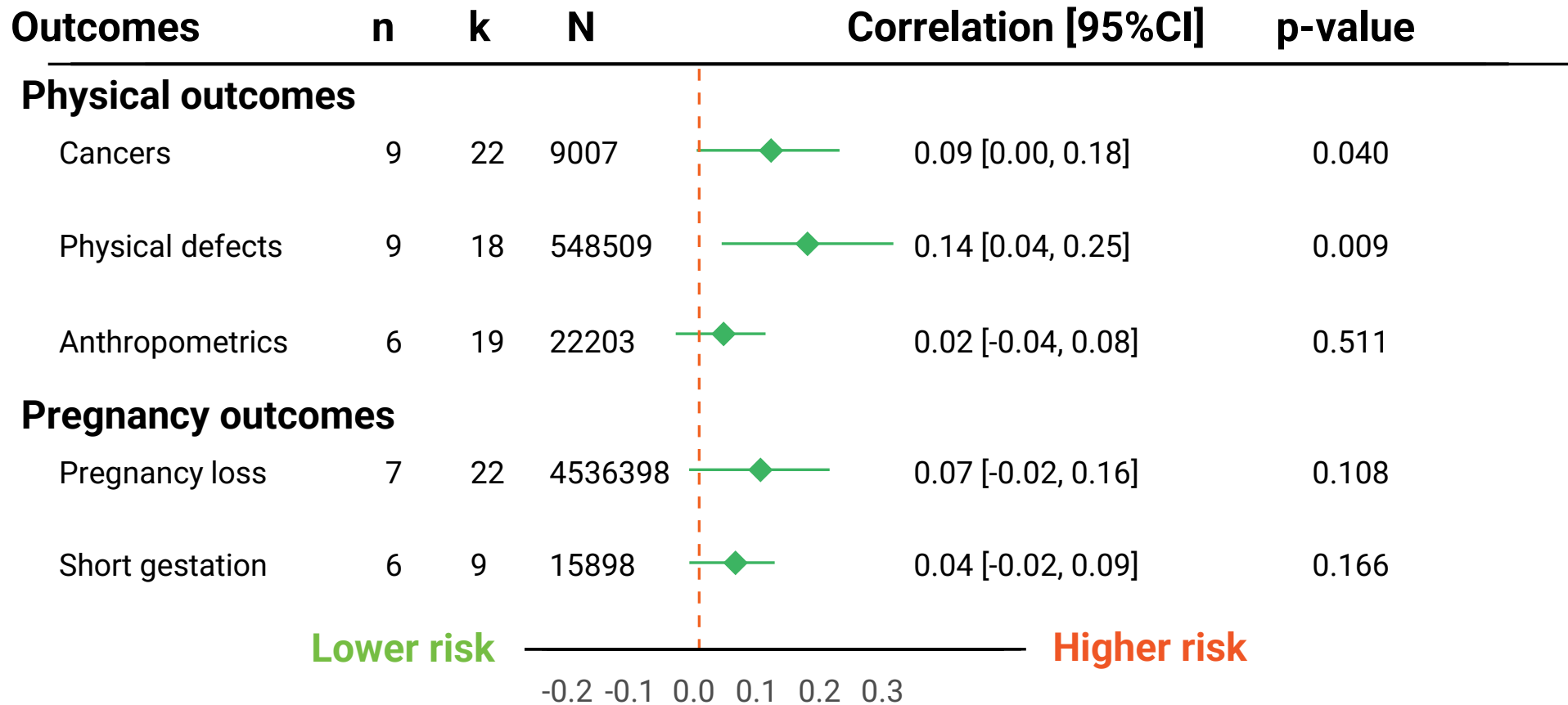
Number of records by exposure type and measure reporter



Number of records reported by outcome domain



Associations of preconception paternal alcohol use with physical and pregnancy outcomes



- Small effects for preconception drinking by men and offspring physical defects and cancers.
- Whilst the association for infant growth and pregnancy loss was not statistically significant, there was a limited number of studies, and results were in the expected direction suggesting likely adverse effects.

Gamete quality



Gamete outcome	n for weighted Z	Sample size	Combined p-val (Weighted-Z)	n for meta-analysis	k associations for meta-analysis	r (95% CI)
Sperm concentration	2	368	.999	-	-	-
Sperm count	4	2707	.040	-	-	-
Sperm DNA fragmentation	3	1235	< .001	-	-	-
Sperm motility	5	1779	.002	2	3	0.02 (-0.09, 0.14)
Sperm morphology	4	2572	< .001	-	-	-
Sperm volume	2	1424	.506	-	-	-

- Although paternal alcohol use is adversely associated with some sperm outcomes, these findings require validation.
- Studies on gamete condition were analysed using a combined p-value approach as effect sizes were unavailable.

Limitations



- Variability of studies precluded analysis moderating for exposure timeframes before conception.
 - 40% of studies reported alcohol use in the 3 months leading up to pregnancy/conception.
- Unadjusted associations used for meta-analyses did not control for maternal drinking/smoking.
 - However, maternal drinking in pregnancy was generally low in pregnancy.
- Generalisability of findings is limited by:
 - Literature concentrated in Western Europe and North America.
 - Predominant retrospective reports for studies on physical defects and cancer outcomes.
 - Self- or partner-reported exposure measures commonly lacked validation studies.



Implications

- Due to the potentially adverse impacts of men's drinking in preconception on offspring physical health outcomes, limiting alcohol consumption three months prior to conception is recommended.
- We recommend that national health guidelines incorporate advice on preconception drinking in men which are currently lacking.



Next steps

- Search update currently underway
- Finalise analyses and manuscript
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