

## B4: IVF outcomes

### B4.1 Male partner age influence on the pregnancy outcome after in vitro fertilisation

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**Aims and objectives:** The aim of this study was to assess the possible impact of paternal age on IVF outcome. The contribution of advancing female age to pregnancy outcomes is well recognised. By convention, maternal age is highly correlated with paternal age, and the contributions of maternal age and paternal age on pregnancy outcomes are important to separate.

**Content:** This study analysed 30,841 fresh IVF/ICSI cycles from women of 18-42 years of age excluding donated gametes between January 2000 and January 2017. Data were combined from six UK centres. A logistic regression model was used to estimate the adjusted probability and 95% confidence interval (CI) of clinical pregnancy with advancing paternal partner age while adjusting for maternal age, body mass index, endometrial thickness and oocyte number retrieved as continuous variables.

**Relevance/impact:** There has been conflicting evidence regarding the role of paternal age on pregnancy outcomes. Our data show that the success of an IVF/ICSI cycle is independent of the paternal age.

**Outcomes:** We found a strong association of maternal (OR 0.924; 95% CI 0.918-0.929) and paternal (OR 0.966; 95% CI 0.962-0.97) age with clinical pregnancy outcome. However, the maternal and paternal ages were highly correlated ( $p < 0.001$ ). We found no statistically significant association between male partner age and likelihood of clinical pregnancy after controlling for female partner age, body mass index, endometrial thickness and number of oocytes retrieved (OR 0.995; 95% CI 0.987-0.929-1.003). Even when we examined the impact of male partner age for women of 20-30 years, where no significant decline is expected because of maternal age, paternal age had no influence on the clinical pregnancy outcome ( $p = 0.408$ )

**Discussion:** Previous claims of an association of male partner age and pregnancy outcomes are likely to be a result of residual confounding. There is no evidence that the male partner age influences the IVF/ICSI outcome.

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### B4.2 Novel measures of sperm DNA damage increase its usefulness to diagnose male infertility and predict live births following both IVF and ICSI

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**Aims and Objectives:** Sperm DNA fragmentation is a biomarker of male infertility resulting in poorer IVF outcomes. In addition to using conventional average Comet Score (ACS), we aim to quantify the proportion of sperm with low (LCS) or high (HCS) DNA damage to assess their effectiveness.

**Content:** Conventional ACS (mean of all comets scored) and two novel parameters LCS and HCS (% sperm with a statistically designated low or high score respectively) were assessed in 76 fertile sperm donors and 166 men with couples with idiopathic subfertility with Receiver Operator curve (ROC) analysis to determine their potential to diagnose male infertility. ROC analysis was further performed on samples from 381 male partners of subfertile couples undergoing IVF (101) or ICSI (280) to determine thresholds for each parameter and assess the livebirth rates (LBR) following ART using these ACS, LCS and HCS thresholds.

**Relevance/Impact:** The proportion of sperm with low or high levels of DNA damage provides discriminatory information for male infertility diagnosis and choice of ART pathway.

**Outcomes:** ACS >26%, HCS >4% and LCS <74% were all highly predictive of male infertility (ROC >0.9,  $p < 0.0001$ ). IVF LBR declined sharply once sperm DNA damage exceeded all ROC threshold levels identified with HCS >6% the most predictive of IVF failure (38% vs 13%;  $p < 0.05$ ). A trend for worsening ICSI LBR was also demonstrated using all parameter ROC thresholds but not achieving statistical significance. Trends in IVF and ICSI differed in that IVF LBRs decreased as damage increased whereas in ICSI, LBRs decreased but then remained stable.

**Discussion:** Unlike other assays, the Comet assay measures DNA damage in individual sperm enabling the degree of heterogeneity of the whole sperm population to be assessed.

This increases its accuracy to both diagnose male infertility and predict ART outcome.

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### B4.3 The effect of alcohol, smoking and male age on semen parameters and IVF/ICSI outcome: is there a correlation?

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