

The Effect of Per- and Polyfluoroalkyl Substances on Female

Fertility: A Systematic Review

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Introduction

Infertility is a very prevalent issue among individuals. Infertility is defined as a couple not being able to become pregnant despite having unprotected intercourse for at least a year. In 2023, infertility reached the highest prevalence recorded in multiple regions of the world, China had a 25% prevalence, with infertility among females increasing by 7.06 million over the past three decades.¹

Women in their childbearing years are more likely to suffer from infertility than men.² 53-64% of women experiencing infertility feel alienated from society and have a negative self perception.¹ Physiological burdens can also arise from the extensive treatment that infertile women go through when trying to become pregnant.¹ The most common cause of female infertility is ovulatory dysfunction, which accounts for 25% of infertility cases, with 70% of dysfunction being polycystic ovarian syndrome (PCOS).³ It is suggested that infertility and other female reproductive disorders such as PCOS could arise from or be worsened by exposure to PFAS.⁴ PFAS are able to disrupt the endocrine system of females, which could lead to these adverse effects on fertility.^{2,5}

The role that PFAS play on female fertility is still not well understood, so research to understand these effects is necessary.² To address this issue, we must relate PFAS exposure to reproductive outcomes. By looking at the concentrations of PFAS throughout the body and how the concentration levels affect fertility, we can better understand this correlation.

The purpose of this study is to review relevant research to determine the long-term effects that PFAS have on the fertility of women. The findings of this study should bring knowledge and awareness to women and healthcare providers so that they can make informed decisions and implement practices regarding fertility. This may include minimizing PFAS exposure and considering PFAS as a factor for infertility

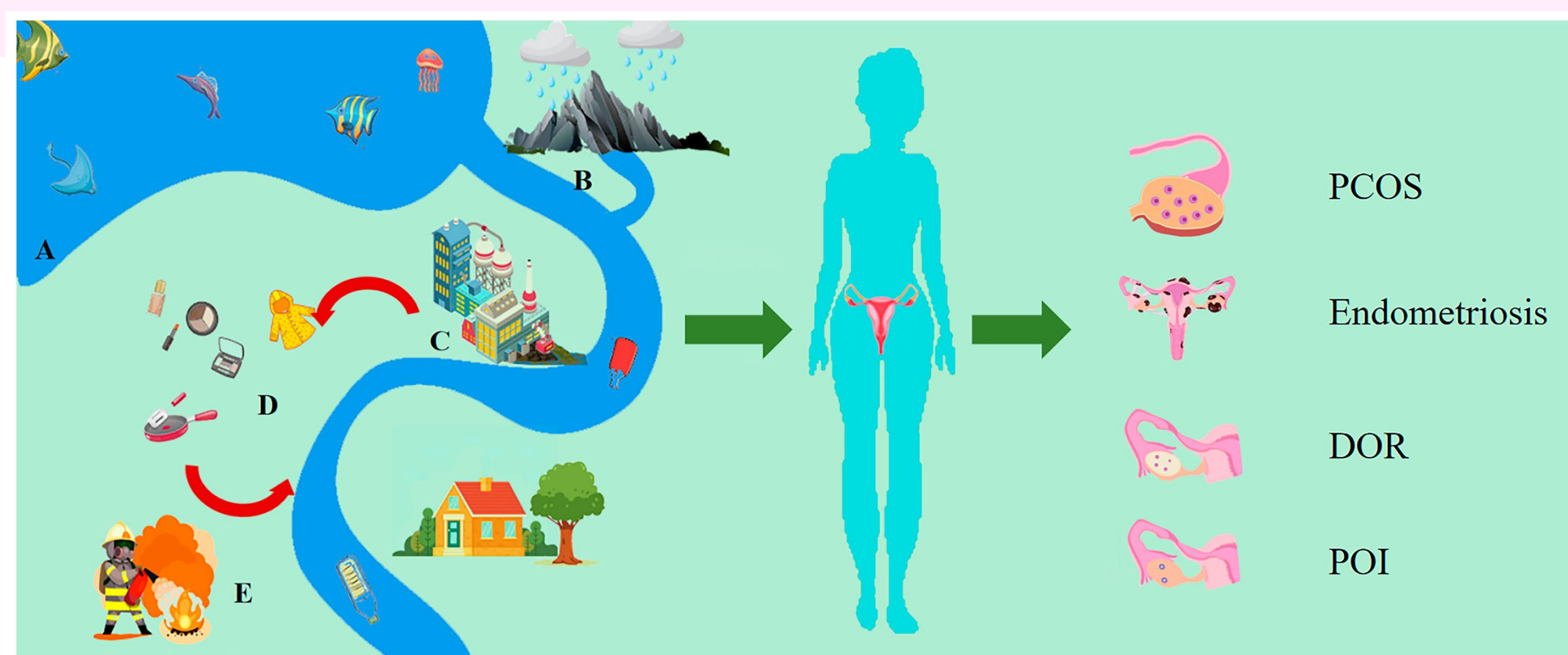


Figure 1. Various routes of PFAS exposure that can harm the female reproductive system in various ways.⁴

Discussion

Studies analyzed in this review provided evidence that greater exposure to PFAS, specifically PFOA, can have adverse effects on fertility outcomes in females. However, not all results were consistent. Multiple studies showed a positive association between particular PFAS exposure and reproductive outcomes.^{2,5,6,10} This means that while the majority of PFAS exposure is harmful to female fertility, not all have adverse effects.

This systematic review benefits from the various methodologies performed in the analyzed studies. Inconsistencies within the study designs, such as multiple exposure concentrations and durations, could affect the comparability of the studies.

The findings of this systematic review can help females and healthcare providers understand the potential risks associated with PFAS exposure. Given this information, females, especially those of reproductive age, should be advised to minimize their exposure to PFAS. Healthcare providers should include PFAS exposure when assessing women for reproductive issues. Further research should look at interventions to counteract the adverse effects of PFAS on hormone signaling. Overall, this review found that PFAS can have harmful effects on female fertility but that not all exposure is damaging.

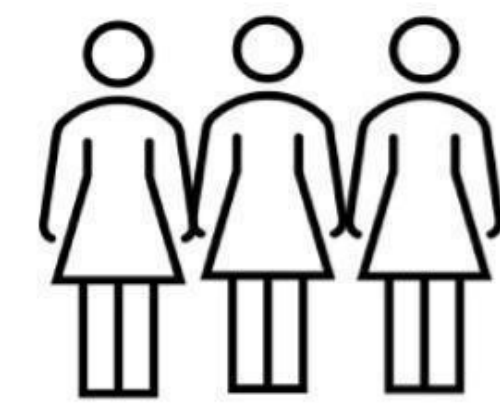
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Population

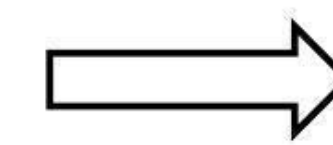


502 Subfertile Women with PFAS Levels
Similar to the General U.S. Population

Findings



Serum
Concentrations of
PFOS, PFHxS



Higher Risk of Polycystic
Ovary Syndrome

Figure 2. Findings from a cohort study showing higher PFOS and PFHxS serum concentration result in higher risk of polycystic ovarian syndrome (PCOS).⁷

Methods

Primary sources were searched for and gathered for this systematic review in the Fall of 2024 using PubMed and CINAHL. Keywords used to search on both platforms were [female infertility and PFAS] and [PCOS and PFAS]. The search was narrowed down to eight articles after screening.

Results

Of the eight articles reviewed, there were four cohort studies,^{5,7-9} three case-control studies,^{6,10,11} and one survey.² All studies focused on the associations between PFAS exposure and adverse reproductive outcomes, such as PCOS or infertility. The majority of studies showed a significant relationship between higher levels of PFAS (specifically PFOA and PFOS) and increased odds of having PCOS or reduced fertility. One study showed women with higher PFOS exposure had almost twice the risk of developing PCOS,⁸ while another study showed PFOA concentrations were significantly associated with an increased risk of PCOS ($p=0.032$).⁶

However, some studies showed complicated associations between PFAS and reproductive outcomes, such as a U-shaped association between Sm-PFOS.² One study showed a positive relationship between PFUnDA concentration and successful live births from fresh embryo transfer.⁵ These findings suggest that not all PFAS may impact female reproduction the same, and while some may have positive effects, the majority of PFAS exposure has adverse outcomes on female fertility.