Commonly used drug may extend women's fertility, claim scientists—what you need to know about rapamycin

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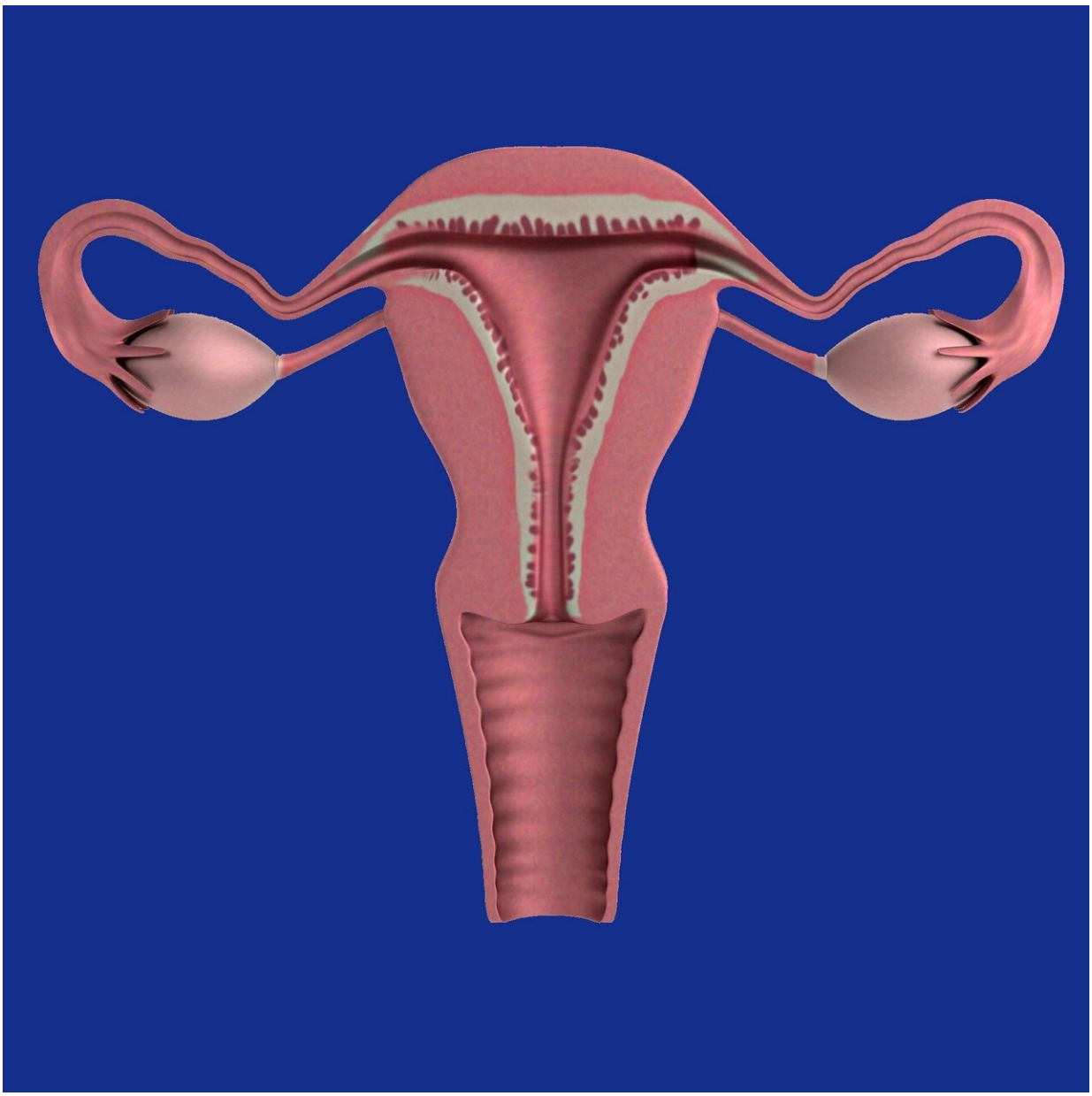

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A growing number of people are waiting longer to have kids. While there are many reasons people may want to hold back on that decision, about one-third of couples will have difficulties getting pregnant if the female partner is over 35. This is because women's fertility begins declining around that age.

But the researchers of an ongoing clinical trial claim rapamycin, a drug commonly used to prevent organ transplants from failing, may be able to extend a woman's fertile years by up to five years. This is based on the early communication of results from the small pilot study they conducted, which has not yet been peer reviewed.

While it's still too early to say whether rapamycin could be the future of fertility treatments—we'll need to wait two years now for the clinical trial to finish—there is some reason to be optimistic about the findings they've reported. Numerous studies in mice have shown rapamycin is beneficial for many aspects of aging—including fertility.

Future fertility can originate before birth. While in the mother's womb, female gametes (eggs) surrounded by specialized cells in the ovaries form "primordial follicles." Each follicle contains a single egg which enters into a dormant state until it's recruited for use at puberty.

Numerous follicles die even before birth. This means that every women is born with all the follicles she will ever have. This is known as the "ovarian reserve." This early-established ovarian reserve can affect a person's ability to become pregnant throughout their reproductive years.

During each menstrual cycle, several dozens of follicles will be recruited (selected)—but only a single dominant follicle will release its egg to be fertilized. The other recruited follicles will be degraded by the ovary. As a woman ages, her ovarian reserve diminishes until she has only a limited number of good-quality follicles remaining. At this point, some ovarian hormones circulating in her body decrease, initiating menopause.

The average age of menopause is 51 years—though this can vary broadly between women depending on their ovarian reserve. Some women experience early menopause (which happens before the age of 45). Around 1% of women may even experience premature menopause, which happens before 40. Since menopause directly affects fertility, early menopause could seriously affect a woman's parenting plans.

But if it were possible to delay ovarian aging, this could extend a woman's fertility. This is something rapamycin may be able to do.

Re-purposing rapamycin

Rapamycin is a bacterial compound that allows cells to survive longer in lab settings.

It's commonly used in organ transplant patients to dampen their immune system so that the body doesn't reject the new organ. It's also used to treat certain vascular conditions by slowing down cell growth (such as tumor).

A growing body of evidence shows rapamycin may also have benefits when it comes to aging.

Research in mice shows it can counteract age-related muscle loss. A daily dose of rapamycin has also been shown to improve the lifespan of older mice by 10%.

When it comes to fertility, studies have demonstrated that a daily dose of rapamycin delays ovarian aging and menopause in mice. Older female mice who were given a diet containing rapamycin had an increase in their pool of primordial follicles—the ovarian reserve. Moreover, these mice also had successful litters later in life. This suggested that rapamycin could have the potential to delay premature menopause in women.

But can the drug do the same in humans? This is what a research team has set out to investigate. The team recruited 50 women aged 35–45 years, who were perimenopausal, to their pilot study.

For three months, women either received a weekly dose of rapamycin or a placebo. The ovarian reserve was monitored by transvaginal ultrasound and several blood tests to detect various ovarian hormones.

The researchers claim the initial results were very encouraging—suggesting that the drug might decrease ovarian aging by 20% in women without any side-effects from the drug. The researchers hope that this could mean an additional five years of fertility.

Rapamycin might trigger this positive effect by restricting the number of primordial follicles being recruited and activated per menstrual cycle. In women who received rapamycin, only 15 follicles were recruited per menstrual cycle—compared to 50 in women at a similar age. With less follicle recruitment, the ovarian reserve seems to be prolonged.

Previous research in mice has shown that rapamycin recruits fewer follicles, which may preserve ovarian reserve.

Maintaining fertility

The cohort size of the initial study was rather small. But given the

promising results the researchers claim to have had, this means they will now be able to move into the next phase of their experiment—recruiting 1,000 women.

Hopefully, the initial results will be confirmed again and show that rapamycin is a useful treatment for ovarian aging in a peer-reviewed study. Additional studies will then be needed to investigate whether this fertility is prolonged.

But if the clinical trial shows rapamycin is beneficial, this could help women with low ovarian reserve and those hoping to prolong their fertility.

Moreover, this study highlights the potential of re-purposing existing drugs to treat other conditions for women's health and well-being. This is something my team members and I are doing at the University of Central Lancashire, as well. We're currently investigating in cells whether re-purposing commonly used diabetes drugs can improve the uterus and make it easier for an embryo to implant itself. We're also investigating these targets to treat ovarian cancer.

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