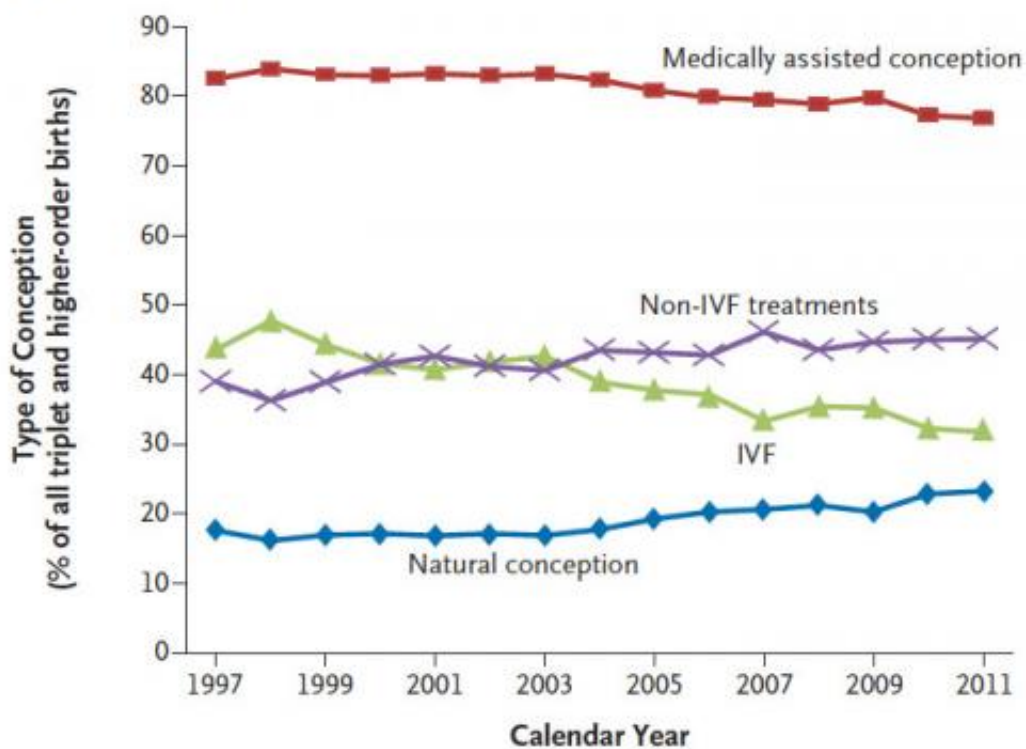


IVF improving but fertility treatments keep multiple births high

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B Triplet and Higher-Order Births



New estimates of multiple births suggest that while guidelines have reduced IVF's contribution to the percentage of medically-assisted triplet (or higher order) births, non-IVF means are increasing their share. Credit: CDC/Brown University

Fertility technology in the United States has a huge influence on the frequency of twins, triplets, and other multiple births, according to new

estimates published Dec. 5 in the *New England Journal of Medicine*. Dr. Eli Y. Adashi, professor of obstetrics and gynecology at Brown University, and his colleagues calculated that more than a third of twin births and more than three-quarters of triplets or higher-order births in the United States in 2011 were the result of fertility treatments.

The proportion of triplets or more related to medical assistance has actually dropped from a peak of 84 percent in 1998 after in vitro fertilization (IVF) guidelines discouraging implantation of three or more embryos took effect that year, the study reports. IVF has also improved enough that single embryo transfers now often succeed in producing healthy pregnancies. But in the meantime, non-IVF fertility treatments such as ovarian stimulation and ovulation induction—for instance, with the drug clomiphene citrate—have increased to become the predominant source of medically assisted multiple births in the country while IVF is increasingly producing twins.

Some mothers and couples may hope for twins through fertility treatments, Adashi said, but more often multiple births are not desired. In those cases, he said, the new parents and children incur unwarranted medical risk and long-term financial costs that doctors should strive to prevent.

"We do have a real problem with way too many multiple births in the United States with consequences to both mothers and babies," said Adashi, the study's senior author and former dean of the Warren Alpert Medical School of Brown University. "It's an unintended consequence of otherwise well intentioned and remarkable technology."

To arrive at their estimates, the team, including lead author Aniket Kulkarni of the U.S. Centers for Disease Control and Prevention, gathered data on multiple births from 1962 to 1966 (before any medical fertility treatments were available) and from 1971 through 2011. Data on

IVF procedures has been available since 1997, but no data is available that directly reflects the contribution of non-IVF procedures to rates of multiple births.

The team therefore estimated the role of non-IVF technologies by subtracting the multiple births arising from IVF from the overall number of multiple births, while also accounting for the impact of maternal age on birth plurality. The data from the 1960s, meanwhile, provided a statistical baseline for natural multiple birth rates without medical intervention that the team also used in their estimates.

Multiples multiply

The contribution of fertility treatments over the last 40 years is unmistakable: Between 1971 and 2011, the percent of U.S. births that were multiples doubled to 3.5 percent from 1.8 percent. Even after adjusting for maternal age, the rate of twin births rose 1.6 times between 1971 and 2009, the authors reported.

And while triplets or more due to IVF have dropped to 32 percent of cases from 48 percent between 1998 and 2011, the percent of triplets or more due to non-IVF procedures rose to 45 percent of cases from 36 percent during that same time.

"IVF is moving, in a sense, in the right direction and cleaning up its act, whereas the non-IVF technologies are at a minimum holding their own and possibly getting worse," Adashi said. "From a policy point of view what that means is that [we] need to focus on the non-IVF technologies, which really hasn't been done in a concerted way because they weren't considered all that relevant to this mix."

Ultimately, Adashi said, it may be harder to curb multiple births from non-IVF treatments than from IVF. While multiple births from IVF are

a direct result of the number of embryos that are fertilized and intentionally implanted, non-IVF therapies involve medications that stimulate ovulation and follicle growth in ways that cannot be precisely predicted or controlled.

The new estimates will at least focus more attention on the major contribution non-IVF treatments make on multiple births, the authors wrote. That may spur improved data gathering, such as creation of a registry of non-IVF treatments and outcomes, and ultimately more careful practice regimens.

"Increased awareness of multiple births resulting from non-IVF fertility treatments may lead to improved medical practice patterns and a decrease in the rate of [multiple births](#)," the paper concludes.

Provided by Brown University

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