# Embracing post-fertilisation methods of family planning: a call to action

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## ABSTRACT

Family planning methods that act when administered after fertilisation would have substantial benefits: they could be used longer after sex than current emergency contraceptives, and potentially a woman could use them only on relatively rare occasions when her menstrual period is delayed. Although such methods would displease abortion opponents, they would likely be welcomed by many women. Research to develop post-fertilisation fertility control agents should be pursued.

## BACKGROUND

Family planning methods that act after fertilisation have considerable appeal. Compared to currently available contraceptives, which are all designed primarily to keep sperm and egg apart, drugs that would act during or after union of these gametes might offer notable advantages. If used postcoitally, such drugs would be effective later after sex than emergency contraceptives that work only if taken before ovulation,[1] and therefore they could serve more women and provide more benefit at a population level. A woman could potentially use a post-fertilisation method on a planned schedule only once in each menstrual cycle, no matter how many prior coital acts she had had in that cycle. If the drug were effective when administered after implantation of an embryo, timing would be flexible, and she might even be able to limit its use on average to a few times a year when her menstrual period was late. Importantly, post-fertilisation methods would eliminate the conceptual and logistical challenge of needing to obtain and initiate contraception before having sex, which can be daunting for both women and men.

Technically, development of a pharmaceutical regimen that reliably disrupts the pregnancy process after fertilisation, either before or after implantation or both, might be challenging. Progesterone receptor modulators such as mifepristone, given in adequate doses at certain times in the menstrual cycle, can inhibit endometrial implantation of a blastocyst.[2 3] Mifepristone, particularly in combination with a prostaglandin, does have the well-established ability to terminate pregnancy when administered after implantation. However, its efficacy very early in gestation is unclear.[4] Other compounds, in this class of drugs or in others,[5] may offer more promise. Multidisciplinary research may be needed to define the best option, but given our rapidly increasing understanding of reproductive physiology, ultimate success seems likely.

## POLITICAL ASPECTS

The real hurdle is politics. Both the UK and USA governments define pregnancy as beginning at implantation[6] (US Code of Federal Regulations 45 CFR 46.202), implying that a method that acted after fertilisation but before implantation should not be considered abortifacient. However, not everyone is comfortable with this definition. Interrupting the course of pregnancy *after* implantation is abortion by any definition. In face of the vehement opposition to abortion among some individuals and institutions, development of a method that does not act exclusively before fertilisation would take fortitude.

But support for a post-fertilisation fertility control drug may be substantial. Abortion is legally available in the UK, the USA, Canada, most of Europe, India, China and many other countries with established pharmaceutical industries that are capable of developing and marketing a new drug product. Most of the British and North American public supports access to abortion, particularly in early pregnancy;[7 8] indeed, in both England and Wales and in the USA, nearly

one-third of women will actually have abortions at some point in their lifetimes.[9 10] A large body of international data now clearly indicates that abortion is safer the earlier it is performed and that increasing access to legal early medical abortion methods is associated with reduced morbidity and mortality.[11] Research from diverse settings has found that many women view medical abortion methods, particularly when used at home, as more natural and more compatible with their religious or ethical views than clinic- or hospital-based surgical procedures.[12] Menstrual regulation – evacuation of uterine contents after missed menses without confirmation of pregnancy – is considered acceptable in some communities where explicit abortion is prohibited.[13 14] Twenty years ago, a multicountry survey specifically designed to investigate women's feelings about a post-fertilisation contraceptive pill found remarkably high acceptance.[15] We have no evidence that women have changed since then; it is the current political environment that needs refocusing.

## FUTURE STRATEGIES

One strategy that we could implement immediately is to refrain from extolling pre-fertilisation mechanisms of action to justify the legitimacy of existing contraceptives. Such conduct implicitly stigmatises post-fertilisation mechanisms as illicit. This behaviour has been particularly pronounced recently in efforts to defend access to hormonal emergency contraception (EC), which has been relentlessly attacked as a supposed form of early abortion. In fact, considerable data now indicate that the most widely used EC regimen containing levonorgestrel acts primarily, and probably exclusively, by disrupting ovulation.[1 16] Certainly legislators and policymakers need to understand this evidence in order to avoid bad decisions based on misinformation. But women do not use EC to disrupt ovulation or another physiological event; they use it to avoid having babies. Indeed, the essential value of this method lies precisely in the attributes it shares with abortion: it is an efficacious, extremely safe, easily administered, postcoital means for reducing the serious medical and personal risks associated with unintended pregnancy.

Furthermore, we should openly acknowledge that some of the most effective standard contraceptive methods probably act, at least in part, after fertilisation. Both copper-bearing and hormone-releasing intrauterine devices are more likely to prevent intrauterine than ectopic pregnancies, which suggests that these devices sometimes disrupt embryo attachment to the endometrium.[17] The near-perfect efficacy of the copper-bearing device for EC also indicates a post-ovulation effect.[18] Chronic use of most hormonal contraceptives causes profound histological and biochemical changes to the endometrium;[19] these changes have been postulated to diminish receptivity to implantation in any cycles in which ovulation and subsequent fertilisation occur. Oral EC products containing mifepristone or the related compound ulipristal are more effective than the levonorgestrel regimen;[20 21] as noted above, mifepristone, at least, can affect pregnancy development after ovulation. Even breastfeeding, which is widely used for contraception in the first 6 months postpartum, has been postulated to impair implantation by altering hormone levels in ovulatory cycles.[22] Although the precise role of these post-fertilisation mechanisms is unknown, they should certainly be celebrated, because without them the methods would not provide as much benefit as they do.

## THE WAY FORWARD

Most importantly, we should get to work! Nothing is as compelling as success: given the importance of fertility control to women, an effective, safe method that fills gaps in the array of existing contraceptives will undoubtedly attract support regardless of its mechanism. Scientists and advocates are ready; they just need funding. Despite the political climate, surely intrepid donors exist who will step up to the mark. To meet the challenges of our increasingly complicated world, women deserve all possible options for controlling and preserving their reproductive health and lives.

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## Notes