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Commentary

"Shared risk": Reframing risk analysis in the ethics of novel male contraceptives, ☆,☆☆,★

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1. The need for a new ethical framework for assessing risks and benefits in novel male contraception

Novel male contraception has the potential to enhance reproductive autonomy for men [1,2–4] and offer greater equity in contraceptive responsibility for monogamous or non-monogamous heterosexual relationships [1]. However, novel male contraceptives have been in development for decades, with no method able to reach the market to-date. Technical challenges inherent in the development of novel reversible male contraceptives have been detailed in other publications [5,6]. The negative impact of gender bias in this setting has also been explored [1]. Moreover, medicolegal issues have presented enormous challenges in female contraception development, leading to the discontinuation of some approved products. Similar concerns are likely to affect the development of novel male contraception, which is thus far unexplored and will require further analysis. For our purposes here, we will focus on one of the key ethical challenges in this domain. How ought medical professionals and researchers assess the balance of nonmaleficence (do no harm or avoid risks) and beneficence (seek the greatest good or benefit) [7], when male contraception has impacts that extend beyond the user of the contraceptive?

The FDA currently offers no ethical guidance about how to assess risks and benefits in the context of male contraceptives [8]. This should not be surprising, given that standard ethical frameworks for weighing these obligations are historically focused on individual patients. Female contraceptives are easily justified according to the standard individual framework: the contraceptive poses small risks to the user in comparison with the substantial benefits of avoiding unplanned pregnancy.

While male contraceptives, have not been justified in similar terms, a novel male contraceptive would mitigate a myriad of biopsychosocial risks to the male user and their partner(s), with the substantial and direct benefits of pregnancy prevention *in a partner*, and avoidance of parenthood and its obligations on the male user and partner. In the United States, every state is required to enact laws that ensure child support payments from a non-custodial parent until the child achieves majority [9]. Willful failure to pay court ordered child support by a non-custodial, out-of-state parent, can result in federal misdemeanor or felony charges [10]. With female *and* male contraception options, each partner would have an actual opportunity to control being a parent, and a reason to assume some risk to avoid an unplanned pregnancy.

How risks and benefits should be assessed for individual contraceptive users in the context of interdependent relationships is ethically complex, but also a known process in other areas of healthcare. Public health ethics considers interdependent societal relationships and justifies small harms to one individual for the purpose of securing substantial benefits to the individual and broader public, such as vaccinations [11]. However, this framework does not justify the risk of a male contraceptive, which may pose uncertain and possibly substantial risks to men [12], while offering significant benefit to women and men alike. Similarly, living organ donation utilizes a risk-benefit model that justifies substantial health risks to an individual in order to benefit the health of another, but key differences prevent application in this context. Living organ donation is considered and extreme form of altruism because donors typically do not hold responsibility for the underlying medical condition of the recipient [13], which cannot account for dyadic responsibility in contraception. Additionally, the possibility of living organ donation arises in a setting in which few if any medical alternatives exist [13]. In contrast, there are effective medical alternatives to novel male contraception: female contraceptives and traditional male contraceptives. Nevertheless, relying on those alternatives fails to acknowledge men's desire for greater reproductive autonomy [1,2–4], the adverse effects experienced by

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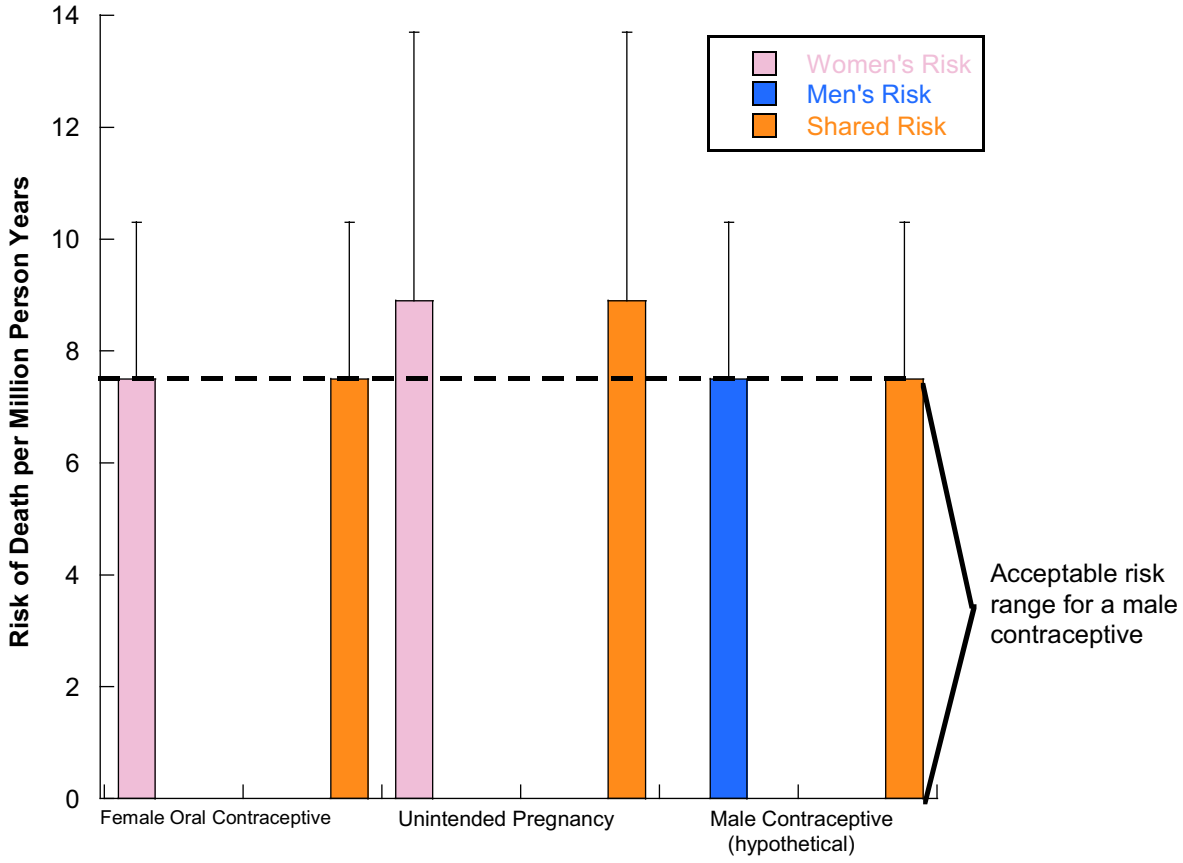

Fig. 1. The risk of death from female oral combination contraceptives (left), unintended pregnancy (middle) and of a potential male contraception (right) to women (pink), men (blue) and couples (orange). Potentially acceptable risk for a male contraceptive is depicted on the far right as less than 7.5 deaths/million user years. Note that a male contraception with a rate of 1 death per million user years would result in an approximately 86% reduction in shared risk of death for the couple.

women using novel female contraceptives [1], and the need for a more equitable distribution of risks and benefits in contraception.

2. "Shared risk: A novel ethical framework for male contraception

The ethical obligations in the context of male contraceptives are fundamentally relational. Though women take on some of the greatest risks of unintended pregnancy, men face a corresponding set of risks [14] and need for support in family planning [15]. Given these complexities, we suggest a new framework for understanding the risks of male contraception that accounts for the interdependent nature of family planning.

Ethically, this shift can be grounded in care ethics, which conceptualizes humans as unassailably interdependent and interconnected [16]. Conceptualizing risk to one sexual partner is inextricably linked to the risks of another. We call this "shared risk." Shared risk is defined as the sum of the risks to both members of a sexual dyad associated with contraceptive use by either or both members, and is compared to the risk of unintended pregnancy to the dyad as a whole. This is justifiable because although modes of family planning differ within any type of sexual pairing, in the context of contraception, the shared responsibility remains the same for each partner, and risk calculations should take this into account. This lowering of the overall risk to a couple is especially important when the risk of health complications from unintended pregnancy are considered, most of which accrue to the female member of the couple.

For example, consider a sexual partnership that primarily relies on a combined hormonal contraceptive. If the risk of death from thromboembolism associated with the use of a combined hormonal contraceptive is 7.5 deaths in one million users-years [17,18], then the risk of death from thromboembolism to either individual would be 7.5 deaths in one million sexual dyads (effectively two million person years). Using this paradigm of "shared risk," if the risk of death from use of a novel male contraceptive were less than 7.5 deaths per one million user-years, the "shared risk" would actually be lower than the shared risk where the female partner used a combined hormonal contraceptive. If the risk of death from a long-acting male contraceptive were as low as one in ten million, the risk of death from contraception or pregnancy that accrued to the dyad from contraception would be reduced by 99%. Such a male contraceptive, even one associated with a low but non-zero risk of death, would seem to be strongly favored from a "shared risk" perspective over the use of a combined hormonal contraceptive in a couple desiring to prevent an unintended pregnancy (see Fig. 1).

Though these examples are simplistic, they offer a basic framework for drawing together different risks accrued to monogamous and non-monogamous relationships in the context of contraception. Applying this framework will require more knowledge about particular relationships to better assess the diversity of risks that should be considered. For instance, do both partners plan to continue using individual contraceptives? Some risks may be difficult to quantify (e.g. social costs) and others may be easy to quantify (e.g. risk of death from unintended pregnancy or failure rates of different contraceptive methods), but all should be incorporated in the risk-benefit analysis. Another limitation of this model is that

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it is based largely on the risks of current contraceptive use, consisting mostly of risk of death from unintended pregnancy and thromboembolism in women, and doesn't include detailed consideration of potential long-term risks and benefits of a male contraceptive, which may take years to fully appreciate. In addition, as the use of long-acting reversible contraceptives with much lower risk of serious adverse effects becomes more common [19, 20], the acceptable risk level for male contraceptive may decrease as well. Nevertheless, a case can be made that use of a male contraceptive, even one associated with a very small risk of serious side effects and even death, is justifiable in a risk-benefit analysis as long as the overall risk to a given couple, the "shared risk," is at or below the risk of currently available combined hormonal contraceptives or unintended pregnancy.

Much work remains in order to develop a more robust understanding of this ethical framework for risk, how it should apply in particular cases, and how it should be balanced against other ethical considerations, such as respect for autonomy. For instance, could this framework affect the authority of women in reproductive decision making? Or, how would it apply differently to monogamous and non-monogamous relationships? And, how ought other risks and benefits be integrated that may be more difficult to quantify, such as mental health risks? Ultimately, we hope this skeletal framework of "shared risk" provides a starting point for more robustly addressing the inequities in risk and shared responsibility and autonomy in contraception.

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