Is widespread use of male contraception methods a solution for abortion reduction – a survey of abortion seekers.

Overview: The Woman's march was the largest inaugural protest in US history, and what inspired these women to gather was the looming threat to their reproductive rights under the current administration, namely the right to a safe abortion. More than one in five U.S. pregnancies ends in abortion.[1] 2008 data indicates that 30% of women will have an abortion by age 45, making it one of the most common surgical procedures experienced by women.[1] The answer to lowering these numbers does not lie in tighter abortion restrictions - supporting data has been available since the early 90s.

In Romania, after the ban on abortion, the crude birth rate fell, and maternal mortality rate became 10x that of any other European country.[2] In 23 years the anti-abortion law resulted in over 10000 maternal deaths from unsafe abortion, elevated rate of infant deaths, and institutionalization of thousands of children.[2] As it turned out, the policy had a complete opposite effect than intended. Adding reduced fertility from widespread gynecological infection and higher rates of birth defects, Romania ultimately had fewer healthy people. [2] Conversely, with lowest abortion rates in Europe,[3] Netherlands tells a different story. Since the 1970s the pill, IUD, diaphragm, and sterilization became available free of charge.[3] Most notably, even though both male and female sterilization was widespread (second most widely used method[3]), the males bore the majority of responsibility. Historically, the only way to decrease abortion rates is to decrease unwanted pregnancies.[2]

Even though US abortion rates are steadily declining over the years,[1,4] poor women are the exception. Accounting for 42.4% of total abortions in 2008, abortion rate

for poor women increased 17.5% between 2000 and 2008.[1] The same trend continued through 2014, but with higher proportion of abortion seekers in poverty being college graduates compared to 2000.[4] Any proposed legislature limiting abortion access will disproportionately affect the poor and contribute to the cycle of poverty. 2000-2014 slightly more than 50% of abortion seekers reported using contraception.[4] Condoms showed the highest failure rates 28%-24% followed by the pill 14%-13% for years 2000 to 2014 respectively.[4] More effective methods like sterilization or IUD are unaffordable to the poor and those without insurance, indicating a need of more accessible methods. Those methods should also be enticing to the slightly less than 50% of people who did not use any contraception.

Currently men have limited options to control their fertility. Vasectomy is the most effective, but it takes 3-4 months to take full effect.[5] In addition to post-operative pain, 10%-15% experience chronic testicular discomfort, and the procedure is not truly reversible.[5] It gets increasingly harder to repair the vas deferens with time, and even with structural repair, 20%-30% of men develop antisperm antibodies[5] losing their fertility permanently. Condom use comes with no side effects, but results in 15%-20% pregnancies per year due to improper, inconsistent use or breakage.[5] In the last 50 years of research, several alternatives have been proposed. Experimental methods include: Testosterone-induced suppression to spermatogenesis via injections, testosterone and progestin combination injections, testosterone and progestin transdermal gels, and most recently Dimethandrolone undecanoate in pill form.[5] Even though these methods are fairly successful in inducing azoospermia,[5] they come with similar side effects to female hormonal birth control and require the male to abide by a

strict schedule that sometimes involves shots. The most advanced development up to date was a Phase II study of intramuscular injections of 200mg norethisterone enanthate combined with 1000mg testosterone undecanoate.[6] Results showed great contraception efficacy with 95.9% suppression of spermatogenesis and 94.8% reversibility.[6] But the trial was terminated prematurely following a decision of a safety review committee that considered adverse events (acne, injection site pain, increased libido, and mood disorders) to be too great of a risk to subjects.[6] The side effects were mild compared to those women are expected to tolerate to control their fertility that often include blood clots, stroke and death. The reasoning there is that the risk of a full-term pregnancy is greater than the risk of hormonal birth control, but that reasoning is flawed. In the absence of birth control women would choose to terminate their unwanted pregnancies, the risk of which is much less than a full-term birth given safe early options. Luckily, we don't have to tackle the hypocrisy of the patriarchy to solve this issue because a long acting, reversible, non-hormonal method is close to being available to men.[7]

Currently undergoing Phase III clinical trials in India, RISUG (Reversible Inhibition of Sperm Under Guidance), is an injectable compound used to occlude the vas deferens and disrupt the membranes of spermatozoa.[7] It is a gel made of two non-hormonal polymers: Styrene Maleic Anhydride (SMA) and Dimethyl Sulfoxide (DMSO).[7] The gel's electrical charge disrupts sperm membrane resulting in swelling and rupture of the sperm head and release of enzymes necessary for fertilization.[7] Once the sperm pass the partial gel occlusion, they become functionally unable to fertilize the ova. Via a single bilateral injection into the lumen of the vas deferens, RISUG provides

contraception for up to 10 years.[7] The reversal is equally simple – an injection of sodium bicarbonate solution.[7] Being a non-hormonal method, it causes no side-effects and unlike a vasectomy, there is no chance of an autoimmune response or granulomas.[7] The benefits don't stop there. The electrical charge of RISUG has anti-microbial and anti-viral properties.[7] RISUG can inhibit HIV entry into host cells by interfering with viral surface proteins.[7] A double edged sword of this method is the price. It is remarkably cheap to implement (the reversal is just baking soda), which is why big pharma is reluctant to finance its FDA approval. It is simply more profitable to charge women for daily pills and expensive IUDs than providing single injections that can last up to 10 years to men.

Luckily, the Parsemus Foundation and Revolution Contraceptives LLC are pursuing the FDA approval of RISUG (rebranded as Vasalgel) with collaboration of NEXT Life Sciences, Inc., which has been selected to continue the clinical development of the Vasalgel male contraceptive in the US.

Despite setbacks in getting male birth control on the market, there have already been studies anticipating the potential impact of novel male contraceptive methods on averting unintended pregnancies.[8] Men are interested in exploring options to control their fertility; they just want a method that is convenient, and affordable with no side effects. Even when assuming only 10% interested implement a male method, a model estimated that introduction of the male pill or reversible vas occlusion would decrease unintended pregnancies in the United States by up to 5.2%.[8] Not surprisingly, the same model[8] predicted that reversible vas occlusion will be more effective in averting unintended pregnancies than a male pill.

Methods: This survey study will take place after the eventual approval of Vasalgel male contraception method in the US, preferably after a few years of it being on the market. The study population would be women seeking abortions in a time period before Vasalgel market availability and a comparable time period after. Similarly to previous studies conducted on abortion seekers,[1,4] Guttmacher Institute's Abortion Patient Survey (APS) and National Survey of Family Growth (NSFG) will be used to gather nationally representative data. The independent variables to consider will be the ages, ethnicities, financial standings, and contraception methods used by abortion seekers. The dependent variable will be the abortion rate. The contraception methods in both time periods will include all available contraception methods on the market at the time. A bivariable logistic regression method will be used to determine whether there is a significant difference in population characteristics, contraceptive use and abortion rates between the two time periods. Even though overall abortion rates have been steadily declining before Vasalgel availability,[1,4] this study can determine how much of the expected decline could be attributed to a decrease of abortion seekers using condoms or nothing as their contraceptive methods. Knowing the relatively inexpensive cost of Vasalgel, it would be interesting to see if its market availability will play a larger role in curbing abortion use in the financially underprivileged. If so, an argument could be made that not only can wide-spaced use of Vasalgel decrease abortion rates but break the cycle of poverty all together.

References:

1. Jones R K, Kavanaugh M L. Changes in Abortion Rates Between 2000 and 2008 and Lifetime Incidence of Abortion. *Obstet Gynecol*. 2011;117(6):1358-1366. doi: 10.1097/AOG.0b013e31821c405e
2. Stephenson P, Wagner M, Badea M, and Serbanescu F. Commentary: the public health consequences of restricted induced abortion--lessons from Romania. *Am J Public Health.* 1992;82(10):1328-1331. doi: 10.2105/AJPH.82.10.1328
3. Ketting E, Visser AP. Contraception in the Netherlands: the low abortion rate explained. *Patient Educ Couns.*1994;23(3):161-171. doi: 10.1016/0738-3991(94)90032-9
4. Jones RK. Reported contraceptive use in the month of becoming pregnant among U.S. abortion patients in 2000 and 2014. *Contraception.* 2018;97(4):309-312. doi: 10.1016/j.contraception.2017.12.018
5. Amory JK. Male Contraception. *Fertil Steril.* 2016;106(6):1303-1309. doi: 10.1016/j.fertnstert.2016.08.036
6. Behre HM, Zitzmann M, Anderson RA, et al. Efficacy and Safety of an Injectable Combination Hormonal Contraceptive for Men. *J Clin Endocrinol Metab.* 2016;101(12):4779–4788. doi: 10.1210/jc.2016-2141
7. Thakur V, Choudhary M, Mehta V, Kumar D, Nitesh. RISUG: A new perspective in non–hormonal male contraception. *Asian Pac J Reprod.* 2013;2(2):159-162. doi: 10.1016/S2305-0500(13)60138-4
8. Dorman E, Perry B, Polisd CB, et al. Modeling the impact of novel male contraceptive methods on reductions in unintended pregnancies in Nigeria,

South Africa, and the United States. *Contraception.* 2018;27(1):62-69.

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