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Modern non-hormonal contraceptive methods: development prospects and current state of knowledge

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ABSTRACT

More and more people today are looking for reliable birth control that doesn't involve taking hormones or dealing with the side effects that come with them. This article reviews the options available right now and also takes a look at the new technologies currently being developed. We went through the research on standard methods like condoms and cycle tracking to see how well they actually work. The data shows that the copper IUD is currently the most effective hormone-free choice, and it is safe for almost everyone, even women who haven't had a baby yet. We also found that modern phone apps have made tracking fertility much more accurate and easier to use than in the past. Increasing attention is being paid to new possibilities for male contraception, such as targeting proteins to inhibit sperm motility. We also cover breakthroughs involving special antibodies that trap sperm and new materials like nanofibers that can do multiple jobs at once. Developing these new alternatives is really important because it gives people safe, personalized ways to manage their health without relying on hormones.

Keywords: non-hormonal contraception, intrauterine devices, barrier methods, fertility awareness, male contraception, immunocontraception, effectiveness, future development

1. INTRODUCTION

Contraceptive methods are classified as hormonal and non-hormonal. When picking a method of birth control, the most important thing for most people is simply how well it works. The table below breaks down the different non-hormonal options that are currently available and explains what makes each one unique. In user-dependent hormonal methods such as the pill (e.g., 9% typical use vs. 0.3% perfect use), the vast difference reflects the consequences of imperfect use. In LARC methods (IUD/IUS), this contrast is minimal (Trussell, 2011).

The rise in failure rates seen in recent hormonal birth control studies—frequently called the "creeping Pearl"—is mostly because researchers are testing for pregnancy more often and using much better tests. It is also because the people in these studies are often less strict about following the directions than they used to be (Trussell & Portman, 2013). Given adherence difficulties as well as the need for safe, highly effective options where hormones are contraindicated (Nguyen et al., 2024), non-hormonal methods- especially LARC- are essential alternatives.

The purpose of this paper is to examine how safe and effective modern non-hormonal birth control is, as well as to look at new methods currently being developed. We want to show that these options are a key alternative, especially for people who cannot use hormones for medical reasons or who find it hard to stick to a routine.

2. REVIEW METHODS

Search Strategy: This review paper was prepared based on a search of the PubMed database to identify relevant publications in English and Polish. The search process utilized combinations of keywords such as non-hormonal contraception, intrauterine devices, barrier methods, fertility awareness, male contraception, immunocontraception, effectiveness, and future development.

The review included clinical trials, review papers, studies evaluating the safety and effectiveness of modern hormone-free methods, including IUDs, barrier methods, and fertility awareness approaches, as well as research on new options such as male contraception. Studies that focused only on hormonal methods, as well as case reports and articles that were not peer-reviewed, were excluded from the analysis.

Study Selection and Data Extraction: The study selection was performed by independent authors, with data extraction and conflict resolution achieved by consensus. A total of 72 records were screened, resulting in 10 articles included in the final synthesis. The entire selection process is illustrated in the PRISMA chart (Figure 1).

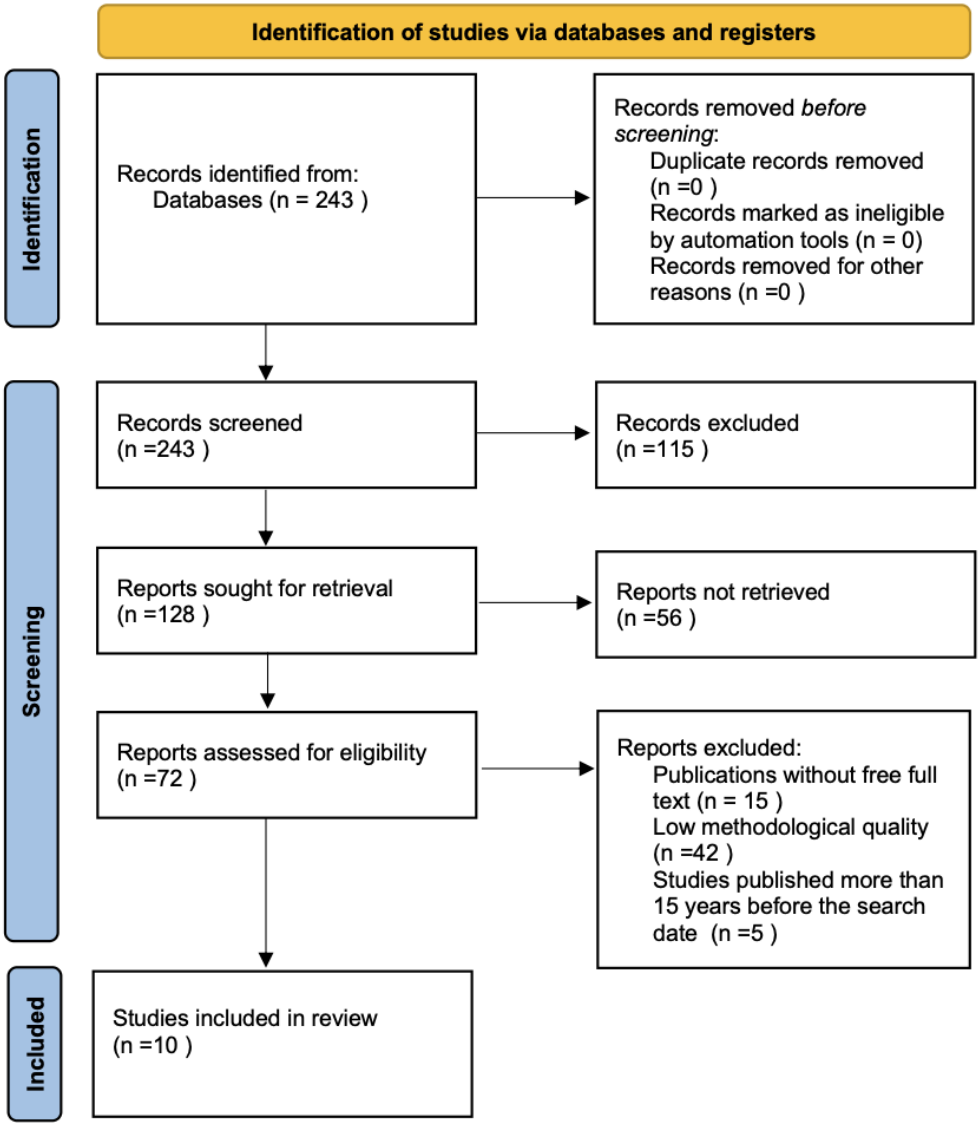

Figure 1: PRISMA chart

3. RESULTS & DISCUSSION

Modern non-hormonal contraception methods – development prospects and current state of knowledge

Contemporary medicine places increasing emphasis on patient-centred care, which in the context of family planning includes consideration of wide-ranging preferences, including the desire to avoid exogenous hormones. There is a call for potent non-hormonal methods, which include both a modern approach to fertility awareness methods (FAM) and the development of new medicinal compounds for men.

Fertility awareness-based methods (FABM) and digital technologies

Determining the fertile phase in FABM and NFP methods is based on ongoing monitoring of the body's bodily reactions. In practice, this means analyzing key biomarkers such as changes in cervical mucus, basal body temperature (BBT) charts, and the concentration of hormones—LH and estrogen—in urine. Thanks to the use of algorithms that are confirmed by scientific research, it is possible to precisely determine the fertility window during the cycle. The literature emphasizes that the effectiveness of FABM is frequently underestimated by the medical community, which is due, among other things, to the confusion of modern methods with the outdated rhythm method. According to data from the Centres for Disease Control and Prevention, the typical-use efficacy of FABM methods ranges from 77% to 98%, rendering them an important option in the family planning "toolbox" (Davidson & Butler, 2023).

Technology has made these methods more modern and easier to use. FDA-approved apps such as Natural Cycles and Clue now help people track their menstrual cycles. Studies also show that the Dot app can reliably identify the days when someone is most fertile. Even so, many doctors—about 60% in some specialties—are not fully aware of how effective these innovative technological aids can be, so they are often left out of family planning discussions (Davidson & Butler, 2023).

Non-hormonal barrier and intrauterine methods

Among the available non-hormonal methods, condoms and copper intrauterine devices (IUDs) play an important role. Although condoms are one of the oldest methods of contraception (used since ancient times), their typical-use failure rate is sometimes lower than that of long-acting methods, which poses a challenge in terms of population effectiveness (O'Rand et al., 2016).

On the other hand, non-hormonal copper intrauterine devices (e.g., Paragard) are mentioned as one of the highly effective options. In surveys of physicians, these IUDs are perceived as highly effective, and their typical-use effectiveness is higher than that of barrier methods or FABM. However, it should be noted that, unlike hormonal methods, these methods do not interfere with the patient's endocrine system, which is key for people with medical contraindications to hormone use (Davidson & Butler, 2023).

Prospects for the development of male contraception – the EPPIN molecular target

Currently, men have a limited choice of contraceptive methods, which in practice boils down to condoms or vasectomy. The development of new, reversible medicinal compounds for men faces difficulties related to the need to secure safety and the absence of side effects (O'Rand et al., 2016).

A hopeful avenue of research is targeting sperm surface proteins, which avoids interference with spermatogenesis and hormone balance. A key candidate is the EPPIN (Epididymal Protease Inhibitor) protein, found on the surface of human sperm. EPPIN has protective functions (antibacterial activity) and modulates PSA activity against semenogelin I (SEMG1). Under natural conditions, EPPIN binds to SEMG1, which inhibits sperm motility by lowering intracellular pH and calcium levels, avoiding early capacitation (O'Rand et al., 2016).

The mechanism of action of a potential contraceptive agent involves the use of small organic molecules (e.g., a compound designated B4) that mimic the action of anti-EPPIN antibodies or bind to SEMG1. These compounds reversibly block sperm motility. In vitro and primate studies indicate that targeting the EPPIN-SEMG1 complex may be an effective method of contraception, which, unlike spermatogenesis inhibitors, would not require a waiting period of several weeks for the therapeutic effect or for fertility to return (O'Rand et al., 2016).

Copper Intrauterine Devices

Copper IUDs are one of the most effective non-hormonal ways to prevent pregnancy. They trigger a small, harmless reaction in the uterus and release copper, which makes it harder for sperm to reach the egg. Most women can use them without problems. This

includes teenagers and women who have never had children. People used to worry that these groups might have more issues, but studies show that this is not true (Howard & Benhabbour, 2023).

Systemic Health Factors and Comparison with Hormonal Methods

Non-hormonal methods do not change hormone levels like hormonal contraceptives do. They are easier on the body in that way. Women using non-hormonal methods for a long time do not usually have significant changes in metabolism or hormones (Moreira et al., 2020). This can be helpful for women who cannot take estrogen or progestin, or who want to avoid changes in mood, sex drive, or weight. For women at risk of HIV, hormonal contraceptives can affect the immune system. Non-hormonal methods do not, so they can be safer in these situations (Hofmeyr et al., 2014).

Emerging Technologies and Future Directions

New non-hormonal methods are being developed using things like eco-friendly substances, nanofibers, and products that also protect against sexually transmitted infections. They are made to last a long time, be easy to use, and cause few side effects (Howard & Benhabbour, 2023). Many of these methods are still being tested, but early results show they could give women effective options without hormones.

Prospects for development and innovation in non-hormonal contraception

Current research on non-hormonal birth control looks at specific biological targets involved in sperm and egg development, sperm movement, and fertilization, as well as new biomaterials and protein-based technologies. This work responds to the growing demand for reversible methods that do not cause the whole-body side effects commonly associated with hormonal contraception.

Targeting sperm liquefaction and motility

A cutting-edge method is to interfere with the process of sperm liquefaction, which is essential for releasing sperm from the seminal coagulum and enabling them to reach the egg. This process is regulated by prostatic serine proteases, mainly prostate-specific antigen (KLK3/PSA), which hydrolyse semenogelin (SEMG). Blocking the activity of KLK3 stops semen from liquefying, which leaves sperm trapped in a gel and unable to move forward. Animal studies have shown that applying a serine protease inhibitor (AEBSF) in the vagina can prevent semen from breaking down, significantly reducing the number of sperm that can travel toward the fallopian tubes. However, a significant hurdle to the use of this compound resides in its low selectivity, which poses a risk of cytotoxic effects on epithelial cells (Anamthathmakula & Winuthayanon, 2020).

Another molecular target is the EPPIN protein present on the surface of sperm, which modulates semenogelin hydrolysis. An alternative approach is to use the EPPIN protein ligand—a compound called EP055—which inhibits ejaculate liquefaction and thus eliminates the ability of sperm to move forward. Verification of this mechanism in a macaque model showed that intravenous infusion of EP055 achieves a contraceptive effect that is both safe and fully reversible.

Advances in immunological contraception and antibody engineering

Classic strategies to immunological contraception have relied on vaccines that induce a response against sperm antigens or the zona pellucida. Despite promising results in animal models (e.g., kangaroos and guinea pigs), many of these methods have not achieved a sufficient success rate in humans or have been associated with the risk of irreversible infertility (Howard & Benhabbour, 2023).

A breakthrough in this field may be the use of passive immunisation with monoclonal antibodies (mAb). Recent research by Schaefer et al., (2025) presents the "LamH" platform, based on the fusion of laminin 511 trimmer domains with Fab fragments of anti-sperm antibodies (directed against CD52g). The best version, known as LamH10, has ten different gripping points, making it excellent at clumping sperm together and getting them stuck in mucus. In tests done on sheep, using just a tiny amount of it stopped more than 99% of the sperm from moving in under two minutes, whereas naturally occurring IgG and IgM antibodies were far less effective.

New barrier approaches and nanotechnology

Barrier birth control is evolving into a technology that does more than one job at a time. A great example is Ovaprene, a vaginal ring that uses a mesh to physically block sperm while also releasing ingredients that stop them from swimming. A breakthrough within materials science is the use of nanofibers. Studies on polymer meshes made of nanofibers saturated with glycerol monolaurate (GML)

have shown in vitro spermicidal and antiviral (against HIV-1) activity, suggesting that nanotechnology may enable the creation of dual-action physicochemical barriers (Howard & Benhabbour, 2023). Table 1 summarizes how effective methods are used ideally versus how they tend to perform in real-life situations. Contraceptive performance is assessed by distinguishing between: Method Efficacy: Measured during perfect use (correct and steady compliance) (Trussell, 2011) and Method Effectiveness: Measured during typical use (accounting for error and inconsistencies) (Trussell, 2011).

Table 1. Assessing Contraceptive performance

Category	Methods included	Key Characteristics & Efficacy
Long-Acting Reversible Contraception (LARC)	Copper intrauterine devices (Cu-IUD, e.g., ParaGard) and levonorgestrel-releasing intrauterine systems (LNG-IUD, e.g., Mirena) (Trussell, 2011; Nguyen et al., 2024)	These methods provide the highest effectiveness in typical use, closely mirroring perfect use (Trussell, 2011). **Failure rates (1st year):** • Cu-IUD: 0.8% (typical) vs. 0.6% (perfect) (Trussell, 2011). • LNG-IUD: 0.2% for both (Trussell, 2011).
Barrier Methods	Male and female condoms, the diaphragm, the sponge, and spermicides (Trussell, 2011).	The efficacy of these methods relies heavily on consistent and correct use (Trussell, 2011).
Fertility Awareness-Based Methods (FABMs)	Standard Days, Two-Day, Ovulation, and Symptothermal methods (Trussell, 2011).	Constitute a further category of non-hormonal contraception (Trussell, 2011).
Surgical (Permanent) Methods	Female sterilisation and vasectomy (male sterilisation) (Trussell, 2011).	Represent another primary category of non-hormonal contraception (Trussell, 2011).

4. CONCLUSION

There is a real need for birth control that works well without using hormones, so people can avoid side effects. Right now, the copper IUD is the best non-hormonal option available. It is safe for most people to use, including women who have not yet had children. Technology has also improved natural tracking methods, making them more accurate through validated algorithms and mobile apps. Future research is heavily focused on male contraception, targeting specific proteins like EPPIN to stop sperm from moving without affecting hormones. There are also notable breakthroughs in using antibodies to trap sperm, specifically the "LamH" system, and in new multipurpose technologies based on nanofibers. Pushing these methods forward is essential to provide safe, personalized care for anyone who cannot use hormonal therapy.

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Authors' Contributions

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All authors have read and agreed with the published version of the manuscript.

Informed consent

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Ethical approval

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Conflict of interest

The authors declare that they have no conflicts of interest, competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data and materials availability

All data associated with this study will be available based on reasonable request to the corresponding author.

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